UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN
F A C U L T A D D E M E D I C I N A

EFECTO TERAPÉUTICO DE LA TOXINA BOTULÍNICA A PARA EL TRATAMIENTO DE LA FASCITIS PLANTAR

Por:
DR. JORGE ALBERTO ELIZONDO RODRÍGUEZ

Como requisito para obtener el grado de:

DOCTOR EN MEDICINA

Noviembre 2020

EFECTO TERAPÉUTICO DE LA TOXINA BOTULÍNICA A PARA EL TRATAMIENTO DE LA FASCITIS PLANTAR

Aprobación de la Tesis:

_____

Dr. Med Carlos Alberto Acosta Olivo
Director de Tesis

_____

Dr. Med. José Félix Vilchez Cavazos
Co-Director de Tesis

_____

Dr. Med. Víctor Manuel Peña Martínez
Miembro del Comité de Tesis

_____

Dr. Med. Jesús Dante Guerra Leal
Miembro del Comité de Tesis

_____

Dr. Med. David De La Fuente Villarreal
Miembro del Comité de Tesis

_____

Dr. Med. Felipe Arturo Morales Martínez
Subdirector de Estudios de Posgrado

AGRADECIMIENTO

Agradezco ser parte de la UANL y el Hospital Universitario. Agradezco al Dr. Med. José Félix Vilchez Cavazos y a todo el grupo de profesores del curso de doctorado por sus enseñanzas. Al Dr. Med. Víctor Manuel Peña Martínez y al Departamento de Traumatología y Ortopedia por su apoyo durante la realización de este trabajo. A los pasantes de medicina Carolina, Mauricio, Sofía y David por su ayuda y por su tiempo. A los pacientes que son los protagonistas de este estudio. Muchas gracias a todos.

Pero en especial al Dr. Med. Carlos Alberto Acosta Olivo y su equipo, Dr. C. Mario Alberto Simental Mendía y Dra. Med. Yadira Alejandra Tamez Mata del Área de Investigación del departamento de Traumatología y Ortopedia que sin su ayuda, conocimiento, apoyo e insistencia no hubiera podido terminar este trabajo; mi gratitud y admiración.

A Dios por todo.

DEDICATORIA

A mis papás Raúl César y María Cristina, mi papá Gene, mis suegros Fausto y Aurora. A mi esposa Ivonne y mi hija Keila, que son mi todo, y sin ellas nada; a mis hermanos Cristy, Lurdes, César, Alejandro, Martha, Ana y Chuy. Y a todos aquellos que de una u otra forma me han hecho lo que soy.

Porque siempre han confiado en mí… esto es para ustedes.

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ABREVIATURAS

- ANOVA Análisis Unidireccional de Varianza
- AOFAS Sociedad de Ortopedia Americana de Pie y Tobillo
- BoNT-A Toxina Botulínica A
- cm centímetro
- et al. y colaboradores
- EVA Escala Visual Análoga
- FADI Índice de Discapacidad de Pie y Tobillo
- IMC Índice de Masa Corporal
- kg/m^2 kilogramo por metro cuadrado
- mg miligramo
- mg/mL miligramos por mililitro
- mL mililitro
- mm milímetro

CAPÍTULO I

RESUMEN

1.1 ANTECEDENTES

La causa más común de dolor en el talón es la fascitis plantar y las terapias inyectadas son parte de las diferentes modalidades de tratamiento. Este trabajo tuvo como objetivo valorar el efecto terapéutico de la toxina botulínica A aplicada de forma intralesional en pacientes con diagnóstico de fascitis plantar.

1.2 MATERIALES Y MÉTODOS

Se utilizó un diseño de ensayo clínico controlado, experimental, longitudinal, comparativo, prospectivo, doble ciego, aleatorizado. Los pacientes fueron divididos en tres grupos: Grupo 1 (sólo anestésico), Grupo 2

(corticosteroide) y Grupo 3 (BoNT-A). Se realizó una evaluación ultrasonográfica para medir el grosor de la fascia plantar y se evaluaron los grados de dorsiflexión del tobillo con goniómetro. Los resultados fueron evaluados de acuerdo con la Puntuación de la Sociedad de Ortopedia Americana de Pie y Tobillo, Puntuación Maryland para Pie, el Índice de Discapacidad de Pie y Tobillo (FADI) y la Escala Visual Análoga de 10-cm (EVA). Todas las puntuaciones fueron obtenidas al inicio del estudio, a las 2, 4, 12 y 24 semanas.

1.3 RESULTADOS

Se evaluaron 78 pacientes para elegibilidad para el estudio. Los tres grupos de intervención fueron homogéneos. Todos los pacientes mostraron mejor evolución clínica comparado con su evaluación inicial. El grosor de la fascia plantar disminuyó en la evaluación final, además la dorsiflexión en tobillo mostró un incremento comparada con los valores iniciales de los pacientes, sin embargo, no se observó diferencia significativa entre los grupos de tratamiento.

1.4 CONCLUSIÓN

No se observó diferencia estadísticamente significativa en los valores de dolor y función entre las tres terapias inyectadas. El control del dolor y la mejoría

en la función obtenida con los diferentes tratamientos se mantuvo durante los seis meses de seguimiento.

1.5 Palabras Clave

Fascitis plantar; Corticosteroide; Toxina Botulínica-A; Anestésico

1.6 Nivel de Evidencia

Nivel I Estudio Terapéutico

CAPÍTULO II

INTRODUCCIÓN

La fascia plantar es una aponeurosis fibrosa de tejido conectivo denso que se origina en la tuberosidad anteromedial plantar del calcáneo y se inserta en la base de las falanges proximales. (Figura 1)

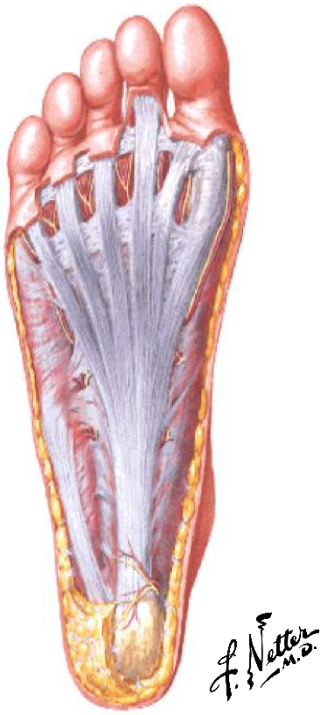

Figura 1. Fascia plantar

La función de la fascia plantar es prevenir el colapso del arco longitudinal del pie y ayudar a la propulsión en el ciclo de la marcha, esto se da tanto por la orientación anatómica de sus fibras como por su fuerza de tensión; ésta se origina de la base del calcáneo en la tuberosidad anteromedial y se extiende distalmente dividiéndose en cinco bandas hasta insertarse en la base de las falanges proximales. El estiramiento de la fascia plantar previene el desplazamiento del calcáneo y de los metatarsianos y mantiene el arco longitudinal medial. Simula un cable unido al calcáneo y a las articulaciones metatarsofalángicas. El mecanismo “windlass” (de polea) descrito por Hicks para la acción de la fascia plantar, suele explicarse cuando ocurre dorsiflexión de los dedos, esto lleva a un acortamiento efectivo de longitud de la fascia plantar causando una elevación del arco. La extensión de los dedos incrementa el arco de tensión con la articulación metatarsofalángica como eje o punto de anclaje. El acortamiento de la fascia plantar que resulta de la dorsiflexión de la articulación metatarsofalángica del primer ortejo es la esencia del mecanismo de polea, lo que incrementa la energía y estabilidad al momento del despegue del pie al final de la fase de estancia en el ciclo de la marcha. Cuando se realiza una fasciotomía, se pierde este mecanismo lo cual no permite una fase de estancia terminal estable.

Históricamente, el desarrollo de la fascitis plantar se atribuye a defectos biomecánicos como la hiperpronación lo que contribuye a una movilidad excesiva del pie, que incrementa el estrés aplicado a las estructuras músculo fasciales y tejidos blandos a través de una elongación de ésta.[7,9] Existen otros estudios que

han demostrado que uno de los principales factores para la aparición de esta enfermedad es la sobrecarga mecánica, y se ha reportado que la tensión necesaria para la ruptura del mecanismo de polea va desde 1.4 hasta 3.4 veces el peso corporal del sujeto.[19,20,23,27,39]

La fascitis plantar es diagnosticada en aproximadamente 80% de los pacientes con dolor de talón.[40] Este padecimiento es desencadenado por una degeneración de la colágena en el origen de la fascia plantar en el calcáneo atribuida a micro desgarros repetitivos que ocurren junto a una pérdida de continuidad de la colágena y un aumento del tejido conectivo y la vascularidad.[43] La obesidad es un factor de riesgo independiente para el desarrollo de fascitis plantar y se presume está presente hasta en un 70% de estos pacientes. La fascitis plantar también se asocia con actividades de soporte de peso relacionadas al trabajo.[38] El diagnóstico es generalmente clínico; la presencia de dolor que se presenta con los primeros pasos al levantarse después de dormir o al ponerse de pie después de un tiempo prolongado de estar sentado, es característico de fascitis plantar. Estos pacientes pueden experimentar disminución del dolor conforme realizan sus actividades habituales, pero el dolor se vuelve a presentar más tarde.[40] Se ha reportado la asociación entre la fascitis plantar y la contractura del complejo gastro-sóleo lo cual se manifiesta como limitación de la dorsiflexión del tobillo. Esta limitación se considera como el factor de riesgo más importante para el desarrollo de fascitis plantar. Con el uso de ultrasonido, que se ha vuelto una herramienta común para el diagnóstico, se puede identificar el engrosamiento

de la fascia y edema de tejidos blandos en la cara plantar del talón. El grosor de la fascia plantar también se considera como un indicador del grado de inflamación, en el cuál mayor grosor es consistente con más inflamación.[25] En el contexto de la fascitis plantar, la ecografía revela una fascia engrosada e hipoecoica.[26]

Se han propuesto distintas modalidades de tratamiento para el manejo de esta patología, incluyendo medicamentos antiinflamatorios no esteroideos, plantillas y taloneras, férulas nocturnas, terapia de choque extracorpórea, un programa de ejercicios de estiramiento (tratamiento de primera línea en muchos casos) y terapias inyectadas.[40]

Una de las terapias inyectadas más comunes para los pacientes con fascitis plantar es el uso de corticosteroides. Sin embargo, este tratamiento ha mostrado sólo reducir levemente el dolor de talón por hasta un mes, y esta mejoría no se logra mantener por seis meses.[10] Además, se ha relacionado el uso de corticosteroides con algunos efectos adversos, aunque con una tasa relativamente baja (tres pacientes con infección y dos pacientes con ruptura de fascia plantar) en un estudio de 2,492 pacientes.[10]

El uso clínico de toxina botulínica A se ha expandido más allá de las indicaciones originales por sus efectos en las neuronas colinérgicas. El aumento del interés en el potencial rol para tratar condiciones de dolor crónico

es parcialmente basado en los efectos de la toxina en la modulación de la liberación de la sustancia P, del péptido génico relacionado con calcitonina, y del glutamato. Por otra parte, la toxina ha mostrado su efecto en la inhibición del dolor inflamatorio y en la liberación de neurotransmisores de las neuronas sensitivas primarias en un modelo de rata. Además, inhibe la sensibilización periférica, lo cual lleva a una disminución indirecta de la sensibilización central.[2,8,16] No está claro si el tratamiento de la fascitis plantar crónica con toxina botulínica A, funciona causando parálisis muscular o por efectos analgésicos antiinflamatorios o por ambos mecanismos. Puede ocurrir un efecto combinado, esto es: (a) inducción de paresia de los músculos originados en el proceso medial del calcáneo, y por (b) analgesia directa debido a las propiedades analgésicas antiinflamatoria.[35]

Los reportes sobre el tratamiento inyectado en la fascitis plantar son contradictorios. Un meta-análisis reciente, reportó que las inyecciones con corticosteroides mostraban una efectividad similar al placebo para reducir el dolor tanto a corto plazo (0-6 semanas) como a mediano plazo (7-12 semanas). En contraste, también se concluyó que las inyecciones de corticosteroide eran más efectivas que algunas otras terapias utilizadas como la inyección autóloga de sangre, plasma rico en plaquetas o terapia de punción seca tanto para la reducción del dolor como para mejorar la función en pacientes con dolor en el talón.[47] Otra opción en terapias inyectables es la toxina botulínica A (BoNT-A), que ha sido cada vez más considerada como una terapia alternativa en condiciones musculoesqueléticas crónicas como esclerosis múltiple, marcha de

puntillas idiopática, epicondilitis lateral, parálisis cerebral o tortícolis.[42] El uso de BoNT-A intralesional para el tratamiento de fascitis plantar ha sido estudiado con anterioridad, mostrando reducción significativa de la intensidad del dolor. Una revisión sistemática y meta-análisis reportaron que el tratamiento con BoNT-A proporcionó una ventaja significativa a corto plazo para alivio del dolor, y el efecto seguía presente a los seis meses.[45]

Los estudios sobre el uso de terapias inyectadas (especialmente corticosteroides) en combinación con un anestésico son numerosos,[10] pero, reportes incluyendo un brazo de control usando anestésico únicamente son escasos.[25] La mayoría de los estudios comparan corticosteroides o BoNT-A con placebo.

El propósito de nuestro trabajo fue demostrar que la aplicación intralesional de toxina botulínica A presenta mejores resultados en el tratamiento de la fascitis plantar que la aplicación intralesional de corticosteroides realizando una comparación entre estos dos grupos y un tercer grupo como control usando un anestésico. Las inyecciones se aplicaron de forma intralesional y guiadas bajo control de ultrasonido. Evaluamos la evolución clínica (dolor y función) así como cambios en el grosor de la fascia plantar y la dorsiflexión del tobillo.

CAPÍTULO III

JUSTIFICACIÓN

Tratamos de establecer una terapia más segura y menos dolorosa para el paciente, ya que el uso de corticosteroides está asociado con complicaciones, ya descritas anteriormente. Consideramos que, las características y resultados clínicos publicados hacen considerar a la toxina botulínica A un medicamento seguro y eficaz para el tratamiento intralesional de la fascitis plantar, ya que además de su acción de relajación muscular tiene efecto analgésico y antiinflamatorio.

CAPÍTULO IV

HIPÓTESIS

La aplicación intralesional de toxina botulínica A presenta mejores resultados en el tratamiento de la fascitis plantar que la aplicación intralesional de corticosteroide.

CAPÍTULO V

OBJETIVOS

5.1 OBJETIVO GENERAL

Valorar el efecto terapéutico de la toxina botulínica A aplicada intralesional en pacientes con diagnóstico de fascitis plantar.

5.2 OBJETIVOS PARTICULARES

1. Evaluar mediante escalas clínicas la función y el dolor.

2. Evaluar la dorsiflexión del tobillo previo a la aplicación del medicamento y al final del estudio.

3. Evaluar el grosor de la fascia plantar antes de la aplicación del medicamento y al final del estudio.

4. Comparar resultados clínicos entre grupos.

CAPÍTULO VI

MATERIALES Y MÉTODOS

6.1 PACIENTES Y DISEÑO DE ESTUDIO

Se realizó un ensayo clínico controlado, experimental, longitudinal, comparativo, prospectivo, doble ciego y aleatorizado. El estudio fue autorizado por el Comité de Ética en investigación de la Facultad de Medicina y Hospital Universitario de la UANL. Todos los pacientes incluidos fueron informados sobre el estudio y firmaron consentimiento informado previo a su participación.

Los pacientes fueron reclutados en la consulta #15 de traumatología y ortopedia del Hospital Universitario. Los criterios de inclusión fueron dolor en talón en el origen de la fascia plantar (tuberosidad anteromedial del calcáneo), edad de entre 18 y 60 años, al menos dos meses con dolor persistente, sin respuesta a

otros tratamientos convencionales (ortesis, hielo, estiramientos y medicamentos antiinflamatorios no esteroideos), y no haber recibido algún tratamiento inyectado en el área afectada. Los pacientes fueron excluidos si tenían alguna alteración anatómica o patológica en la rodilla, pie o tobillo; artritis seronegativa; artritis reumatoide; espondilitis anquilosante; Síndrome de Reiter; *Diabetes Mellitus;* alguna anormalidad neurológica, patología psiquiátrica o discapacidad psicomotora, infecciones de la piel o historia de infección en el sitio de aplicación del tratamiento en los 3 meses previos, cirugía previa en el pie o tobillo afectado y embarazo o lactancia. Los pacientes que no el tratamiento, aquellos que no completaron el seguimiento (menos de 3 visitas), aquellos que voluntariamente declinaron participar en el estudio, y aquellos que presentaron una reacción adversa a alguno de los medicamentos fueron eliminados.

6.2 TAMAÑO DE MUESTRA

Utilizando una fórmula para prueba de hipótesis y diferencia de dos medias, con un valor zα de 1.96 con nivel de significancia del 95% para dos colas, y un valor zβ de 0.84 con una potencia del 80%, se obtuvo una muestra de 18 participantes para cada uno de los tres grupos.

Tabla 1. Cálculo del tamaño de muestra.

Valor k	7.9+1	79.21	46.31204		
Sigma 1	1.2	1.44	5.2036		n= 18
Sigma 2	1.94	3.7636			
Valor µ1	2	2.56			
Valor µ2	3.6				

Fórmula para comparación de medias de dos grupos con corrección de Lehr para tres grupos:

$$n = \frac{K(\sigma_1^2+\sigma_2^2)}{(\mu_1-\mu_2)}$$

6.3 Aleatorización y Grupos de Intervención

Usando tecnología de aleatorización generada por computadora (www.randomization.com), los pacientes fueron incluidos en uno de los tres grupos de tratamiento cegados al tratamiento aplicado. Los pacientes en el Grupo 1 (anestésico) recibieron una sola dosis de 5mL de ropivacaína (7.5 mg/mL; Naropin®, AstraZeneca LP, Wilmington, DE, USA), los pacientes en el Grupo 2 (corticosteroide) recibieron una dosis única de 1 mL de fosfato sódico de betametasona equivalente a 3mg de betametasona y acetato de betametasona equivalente a 2.71mg de suspensión inyectable de betametasona (3mg/mL; Celestone® Soluspan®, Shering-Plough Canadá Inc., Kirkland, Canadá), y los pacientes del Grupo 3 (BoNT-A) recibieron una dosis única de 200U de BoNT-A (Dysport®, IPSEN Ltd., Slough, UK) en un volumen total de 2mL. Se realizó asepsia de la región en talón usando un antiséptico (Avagard®, 3M Health Care, St. Paul, MN, USA) por dos minutos previo a la aplicación del medicamento.

6.4 Medición de la Dorsiflexión del Tobillo, Evaluación Ultrasonográfica y Aplicación del Medicamento

Durante la evaluación inicial, la movilidad de la articulación subastragalina fue evaluada mediante maniobras de inversión/eversión del retropié para detectar alteraciones funcionales. Se registró la máxima dorsiflexión del tobillo con la rodilla totalmente extendida utilizando un goniómetro. La dorsiflexión fue graduada en medidas positivas o negativas con respecto a la posición neutra del pie. (Figura 2)

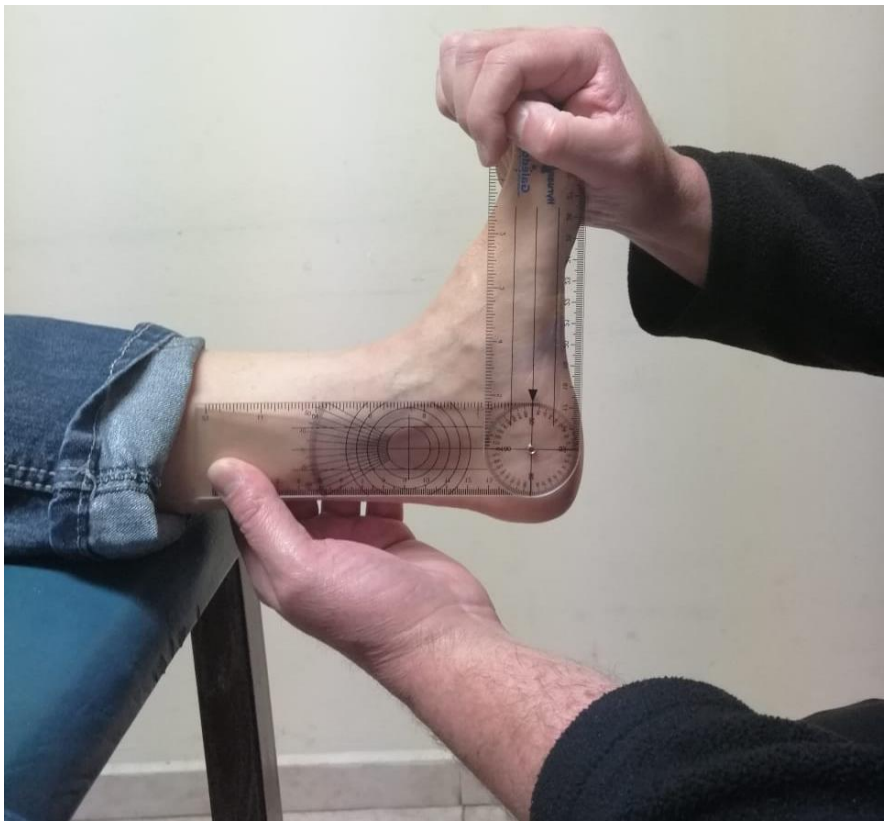

Figura 2. Medición de la dorsiflexión del tobillo usando goniómetro

Todos los pacientes fueron evaluados mediante ultrasonografía usando el sistema MyLab™One con un transductor SL3323 (Esaote Europe BV, Maastricht, The Netherlands). Con el objetivo de ser lo más consistente posible, el grosor de la fascia plantar se midió justamente al final de la línea brillante del calcáneo (línea hiperecoica) en el borde anterior del tubérculo medial. (Figure 3)

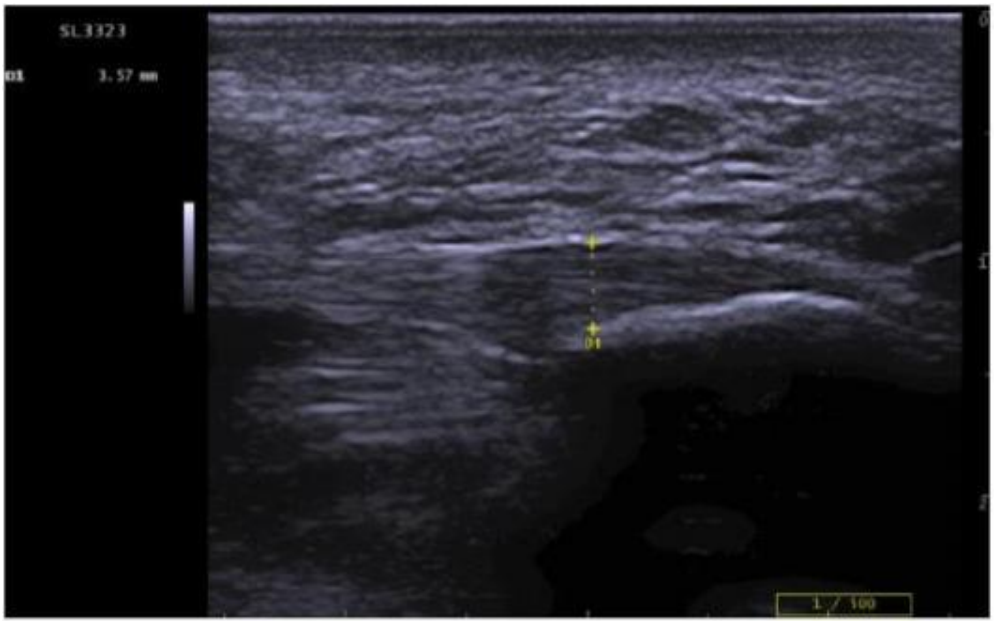

Figure 3. Medición de la fascia plantar al final de la línea brillante del calcáneo (línea hiperecoica).

Todas las aplicaciones de medicamento fueron guiadas por ultrasonido, considerando el punto de máximo dolor en la cara medial plantar del pie, colocando la aguja por arriba y cerca de la inserción de la fascia plantar y aplicando el medicamento en forma de abanico. Todas las mediciones de

dorsiflexión, evaluaciones ultrasonográficas y aplicación de tratamiento inyectado guiado fueron realizadas por el mismo investigador.

6.5 EVOLUCIÓN CLÍNICA

Las puntuaciones usadas para evaluar la función de los pacientes fueron la de la Sociedad de Ortopedia Americana de Pie y Tobillo (AOFAS), Puntuación Maryland para Pie y el Índice de Discapacidad de Pie y Tobillo (FADI). Además, se utilizó la Escala Visual Análoga de 10-cm (EVA) para evaluar dolor.(Anexo E)

La EVA evalúa el dolor en una escala del 0 al 10, donde 0 representa ausencia de dolor y el 10 representa el peor dolor. La escala de la AOFAS evalúa dolor en pie, función y alineación. El puntaje más alto es de 100, indicando bienestar, y el puntaje más bajo es 0, indicando la peor condición posible del paciente.[28] La puntuación Maryland para Pie está dividida en varias secciones que evalúan función y dolor del pie (actividades funcionales y movimiento), y una sección que evalúa la forma del pie. El mejor puntaje es 100, indicando ausencia de problemas en el pie, y el puntaje más bajo es 0.[41] La escala FADI evalúa actividades como mantenerse de pie, marcha en una superficie plana o irregular, marcha en superficies inclinadas, y el tiempo tolerado caminando sin dificultad. También incluye una sección de actividades deportivas y dolor en pie o tobillo (o en ambos). El puntaje más alto es 136 puntos, indicando la mejor situación clínica

posible (libre de dolor y limitaciones), mientras que el puntaje más bajo es 0.[33] Los puntajes clínicos fueron realizados por un médico cegado al tratamiento recibido por cada paciente.

6.6 Instrucciones al Paciente y Seguimiento

Todas las evaluaciones clínicas fueron registradas al inicio del estudio, a las 2, 4, 12 y 24 semanas. La medición de la dorsiflexión del tobillo y el ultrasonido para medir el grosor de la fascia plantar se realizaron al inicio y al final del estudio a las 24 semanas.

Todos los pacientes fueron informados sobre su patología y recibieron instrucciones para realizar diariamente ejercicios de estiramiento del tendón de Aquiles.[15] Se les indicó realizar los ejercicios sin inserto de zapato. Brevemente, los pacientes fueron instruidos a colocar la pierna afectada detrás de la pierna contralateral, apuntando los dedos de la pierna afectada hacia el talón del pie de enfrente, y apoyarse en una pared. Después, la rodilla frontal se dobla mientras la rodilla trasera sigue extendida, y el talón se mantiene firme en el piso por 20 segundos. El ejercicio se repetiría tres veces por sesión, con cuatro sesiones por día. Se les pidió a los pacientes llenar una cartilla marcando sus ejercicios diarios.

El ejercicio debería iniciarse dos días después de la aplicación del tratamiento inyectado.(Anexo D)

6.7 Manejo de la Información Faltante

En algunos casos no fue posible obtener los datos de todas las evaluaciones de los pacientes para nuestro estudio. Estos datos faltantes no seguían un patrón monótono (por ejemplo en algunos sujetos faltaba la información de la segunda semana o cuarta semana y luego regresaban a la semana doce o veinticuatro para su seguimiento), y el porcentaje de información faltante fue menor al 40%.[6] Se estableció que los datos faltantes eran al azar y sin un patrón,[24] y se usó una técnica de imputación multiple.[21,44] El modelo de imputación múltiple usó edad, sexo y todas las variables de resultado para imputar valores perdidos. Para evaluar la solidez del estudio, realizamos un análisis de sensibilidad basado en un análisis por intención de recibir tratamiento.

6.8 Análisis de Datos

Basados en resultados previos de nuestro grupo de estudio, usamos una fórmula para la diferencia de dos medias con un poder de 90% a una confianza de 95%, con un valor alfa bilateral de 1.96, dando como resultado que el número

de pacientes por grupo sea 18 para una diferencia significativa en la escala de Maryland de 15.2 puntos.[17] Las pruebas de Chi cuadrada se usaron para comparar los datos cualitativos entre grupos. Se utilizó el análisis de varianza unidireccional (One-way ANOVA) con la prueba de comparación múltiple de Bonferroni para comparar datos cuantitativos entre grupos. La comparación de los datos previos y posteriores al tratamiento se realizó mediante pruebas t pareadas. Los valores de p a dos colas <0.05 se consideraron estadísticamente significativos. El análisis estadístico de la información fue realizado usando el software GraphPad Prism 5.00 para Windows (GraphPad Software, San Diego, CA, USA).

CAPÍTULO VII

RESULTADOS

7.1 Estudio de Flujo y Demografía de Pacientes

Se evaluaron 78 pacientes para elegibilidad del estudio. Durante el proceso de selección, siete pacientes fueron excluidos ya que no reunían los criterios de inclusión (n=3) o se negaron a participar (n=4). Los 71 pacientes restantes fueron aleatorizados y durante el período de seguimiento 8 pacientes más se dieron de baja del estudio. Al final del estudio se evaluaron un total de 60 pacientes (Figura 4).

La demografía de los tres grupos de pacientes fue homogénea ($p>0.05$), incluyendo edad, sexo, pie afectado e índice de masa corporal. No se observaron diferencias significativas entre los grupos de tratamiento en lo que se refiere al dolor inicial y a los puntajes funcionales ($p>0.05$). La información inicial completa de todos los pacientes se encuentra en la Tabla 2.

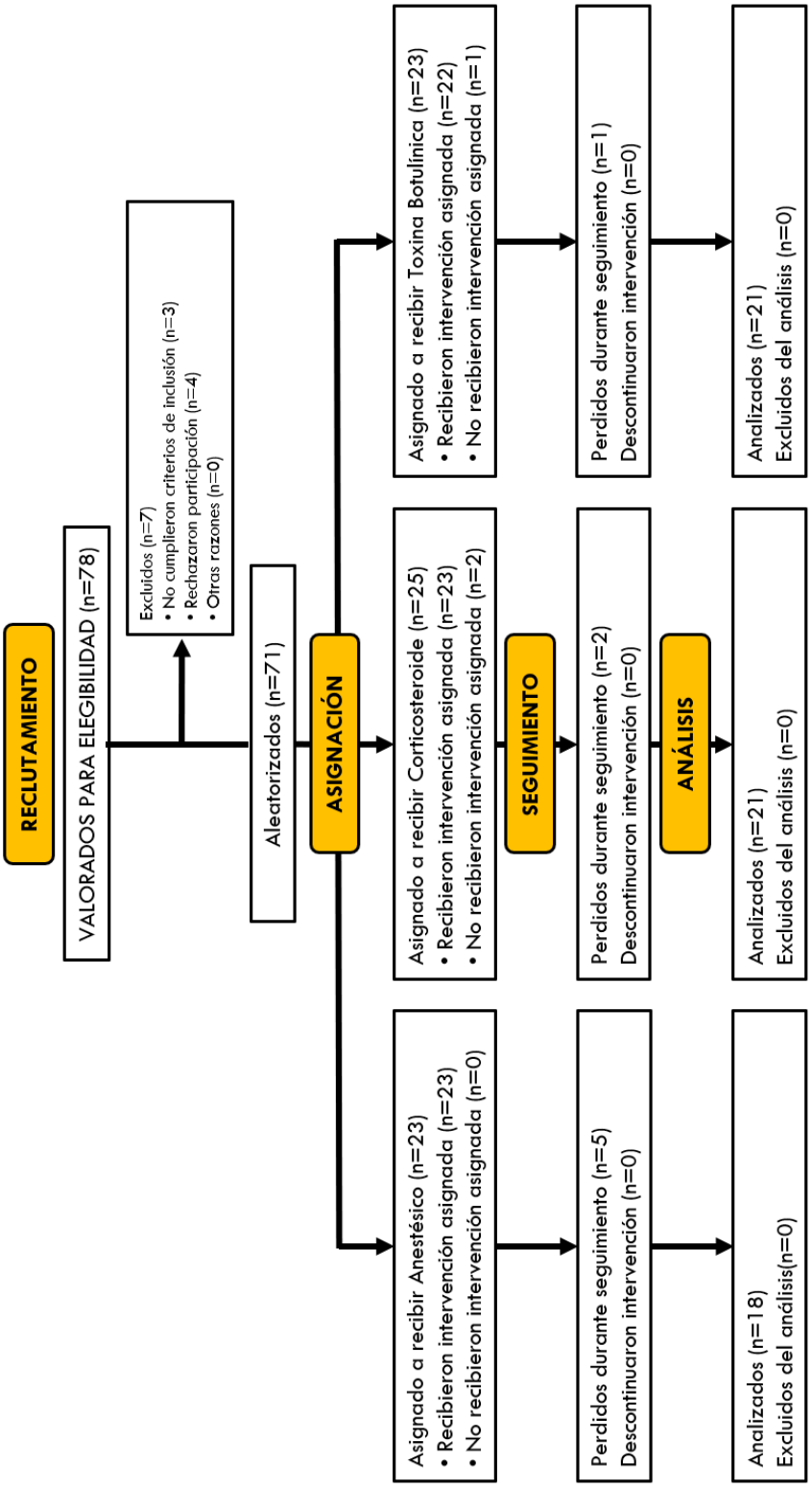

Figura 4. Flujo de estudio. Diagrama Consort.

Tabla 2. Comparación de las características demográficas iniciales de los pacientes incluidos en los grupos de estudio

	ANESTÉSICO	CORTICOSTEROIDE	T. BOTULÍNICA	VALOR *P*
PACIENTES (n)	23	25	23	
EDAD	49.3±10.6	46.4±11.0	44.0±12.5	0.2850*
SEXO (%)				
FEMENINO	13 (57)	19 (76)	13 (57)	
MASCULINO	10 (43)	6(24)	10 (47)	0.2661**
PIE AFECTADO (%)				
IZQUIERDO	14 (60.8)	13 (52)	12 (52.1)	
DERECHO	9 (39.2)	12 (48)	11 (47.9)	0.7847**
IMC, kg/m^2	30.2±2.9	29.7±4.8	31.4±5.5	0.5091*
EVA, cm (0-10)	7.9±1.2	7.7±1.9	8.0±1.5	0.6844*
FADI	72.2±24.2	78.0±27.6	77.9±25.7	0.6847*
AOFAS	70.4±14.65	70.4±15.8	66.7±15.4	0.6558*
MARYLAND	84.6±12.1	83.9±13.4	77.6±15.5	0.1864*

Los valores son presentados como media ± desviación estándar

IMC, Índice de Masa Corporal; EVA, Escala Visual Análoga; FADI, Índice de Discapacidad de Pie y Tobillo; AOFAS, Sociedad de Ortopedia Americana de Pie y Tobillo; MARYLAND, Escala de Pie y Tobillo Maryland

*Análisis de Varianza de Una Sola Vía (ANOVA)

**Prueba Chi Cuadrada

7.2 MEDICIÓN DE EVOLUCIÓN CLÍNICA

Hubo una mejoría sostenida en lo que se refiere a dolor y las evaluaciones de función (EVA, FADI, AOFAS y Maryland) en cada uno de los tres grupos de tratamiento después de 24 semanas (Tabla 3). La percepción del dolor en los pacientes (EVA) mejoró significativamente a partir de la semana 2 ($p<0.05$) y siguió mejorando durante el resto del estudio hasta la semana 24 ($p <0,001$). No se detectaron diferencias significativas entre los grupos a las 24 semanas ($p>0.05$).

En cuanto a los resultados funcionales (FADI, AOFAS y Maryland), se observó una tendencia similar, con una mejoría significativa en todas las puntuaciones evaluadas en la semana 24 en comparación con las puntuaciones basales ($p<0.05$). La única diferencia estadísticamente significativa para los resultados funcionales se detectó entre los grupos de anestésico y BoNT-A a las 24 semanas utilizando la puntuación de Maryland. En la Tabla 3 se puede observar el análisis completo de los resultados clínicos.

Tabla 3. Análisis de los resultados clínicos a lo largo del tiempo entre y dentro de los diferentes grupos de tratamiento

RESULTADO/TIEMPO	**ANESTÉSICO (n=18)**	**CORTICOSTEROIDE (n=21)**	**BoNT-A (n=21)**	**VALOR *p***
EVA (cm)				
BASAL	7.611 ± 0.2574	7.762 ± 0.4077	8.048 ± 0.3272	
2 SEMANAS	5.667 ± 0.3961^{+}	5.143 ± 0.3860^{++}	5.619 ± 0.5541^{+}	
4 SEMANAS	4.611 ± 0.6164^{+++}	5.048 ± 0.5140^{+++}	4.619 ± 0.6113^{+++}	
12 SEMANAS	3.444 ± 0.5127^{+++}	3.857 ± 0.4893^{+++}	3.429 ± 0.5756^{+++}	
24 SEMANAS	2.111 ± 0.3322^{+++}	2.571 ± 0.5281^{+++}	2.571 ± 0.5756^{+++}	0.7702
FADI				
BASAL	69.72 ± 5.566	78.24 ± 6.289	78.76 ± 5.668	
2 SEMANAS	87.61 ± 5.329	92.19 ± 5.947	93.71 ± 5.412	
4 SEMANAS	97.11 ± 6.608^{++}	99.57 ± 6.570	98.33 ± 5.723	
12 SEMANAS	106.5 ± 5.386^{++}	103.2 ± 5.850^{+}	101.1 ± 5.797	
24 SEMANAS	116.1 ± 3.733^{+++}	110.8 ± 4.721^{++}	106.5 ± 5.744^{++}	0.470
AOFAS				
BASAL	69.67± 3.666	70.95 ± 3.427	66.10 ± 3.370	
2 SEMANAS	79.11± 3.952	80.4 3± 2.316	82.14 ± 2.421^{++}	
4 SEMANAS	84.67± 2.943^{+}	81.95 ± 2.588^{+}	89.00 ± 2.970^{+++}	
12 SEMANAS	87.61± 2.288^{++}	87.81 ± 1.576^{+++}	85.43 ± 3.142^{+++}	
24 SEMANAS	90.33± 2.777^{+++}	90.67 ± 1.720^{+++}	86.29 ± 3.372^{+++}	0.4398
MARYLAND				
BASAL	82.28 ± 2.944	84.05 ± 2.897	77.10 ± 3.423	
2 SEMANAS	89.11 ± 2.988	87.95 ± 2.739	87.00 ± 2.548	
4 SEMANAS	90.28 ± 2.764	94.29 ± 1.304^{++}	93.86 ± 1.739^{+++}	
12 SEMANAS	93.28 ± 1.885^{+}	93.57 ± 1.307^{+}	88.29 ± 2.887	
24 SEMANAS	99.39 ± 1.553^{+++*}	96.05 ± 1.776^{++}	90.62 ± 3.207^{+*}	0.387

Los valores son presentados como media ± desviación estándar

EVA, Escala Visual Análoga; FADI, Índice de Discapacidad de Pie y Tobillo; AOFAS, Sociedad de Ortopedia Americana de Pie y Tobillo; MARYLAND, Escala de Pie y Tobillo Maryland

$^{+}$p<0.05; $^{++}$p<0.01; $^{+++}$p<0.001 contra valores basales

*Diferencia significativa entre grupos (p<0.05)

7.3 Medición Ecográfica del Grosor de la Fascia Plantar y Dorsiflexión del Tobillo

La medición ecográfica del grosor de la fascia plantar se registró al inicio y al final del estudio (Tabla 4). La única diferencia significativa con respecto al valor inicial se observó en el grupo del anestésico ($p<0.001$). Sin embargo, no se detectaron diferencias significativas entre los grupos a las 24 semanas ($p>0.05$). Con respecto a la dorsiflexión del tobillo, hubo un aumento de la amplitud de movimiento en los tres grupos (Tabla 4), pero solo el grupo BoNT-A registró un cambio significativo desde el inicio y hasta las 24 semanas ($p<0.001$). Otra vez, no se detectaron diferencias significativas entre los grupos ($p>0.05$). (Figura 5)

Tabla 4. Análisis del grosor de la fascia plantar y la dorsiflexión a lo largo del tiempo entre y dentro de los diferentes grupos de tratamiento

RESULTADO/ TIEMPO	**ANESTÉSICO (n=18)**	**CORTICOSTEROIDE (n=21)**	**BoNT-A (n=21)**	**VALOR *p***
GROSOR DE LA FASCIA (mm)				
BASAL	6.889 0.3782	6.143 0.3605	6.095 0.4018	
24 SEMANAS	5.994 0.3379^{+++}	5.905 0.2573	5.619 0.2966	0.6958
DORSIFLEXIÓN (GRADOS)				
BASAL	9.167 0.6530	6.238 1.019	6.190 0.7547	
24 SEMANAS	11.39 0.7547	10.10 0.7619	9.952 0.4999^{+++}	0.2829

Los valores son presentados como media ± desviación estándar

$^{+++}p<0.001$ contra valores basales

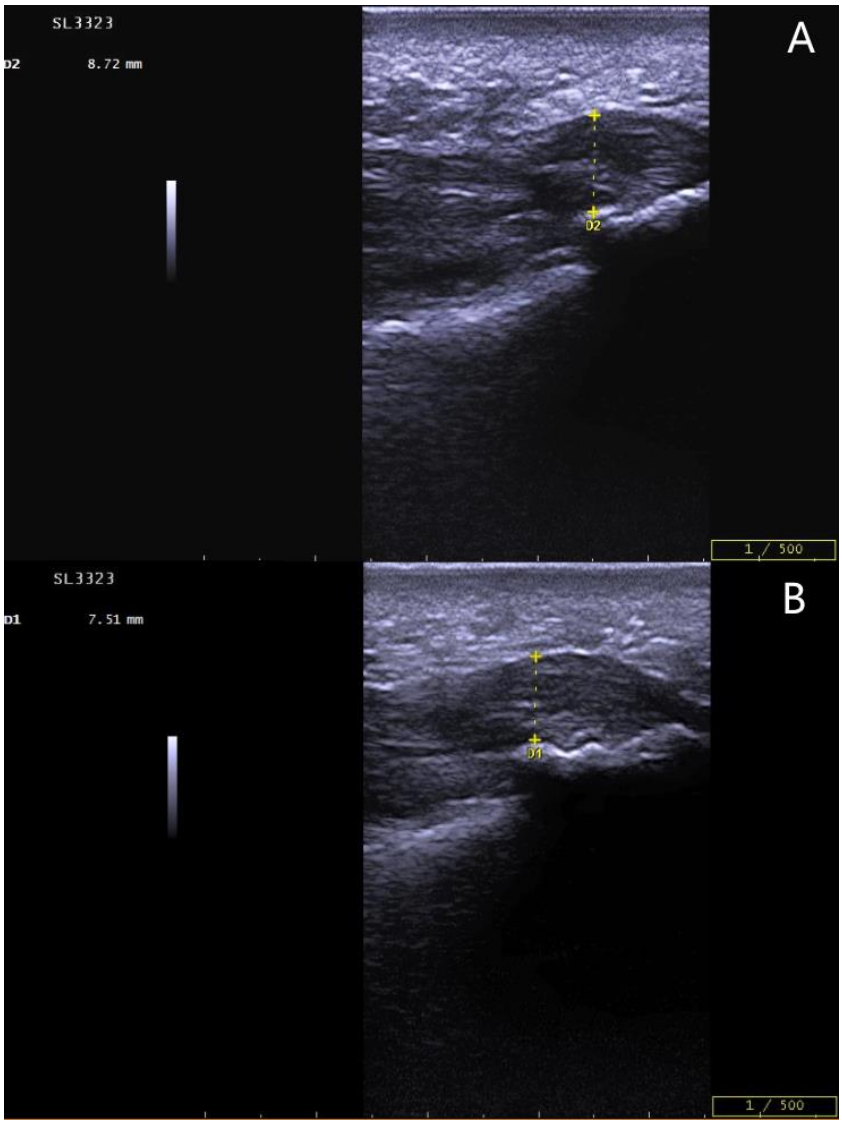

Figura 5. Medición de la fascia plantar. A) Imagen previa al tratamiento y B) Imagen posterior al tratamiento al finalizar el estudio

7.4 EFECTOS COLATERALES

No se reportó ningún efecto secundario severo.

CAPÍTULO VIII

DISCUSIÓN

La fascitis plantar es un problema autolimitado pero problemático del talón que generalmente se presenta con dolor. Las tres diferentes modalidades de tratamiento empleadas en este estudio mostraron mejoría significativa del dolor, mejores resultados funcionales y clínicos en el seguimiento, aumento en la dorsiflexión del tobillo, disminución en el grosor de la fascia plantar y ningún efecto secundario severo. Curiosamente, no se demostró una diferencia significativa entre el anestésico solo, el corticosteroide y la BoNT-A. Planteamos la hipótesis de que la toxina botulínica A iba a mostrar mejores resultados en el tratamiento de la fascitis plantar que el corticosteroide. El anestésico era sólo un grupo de control. Al no obtener el resultado esperado necesitamos reformular y explicar nuestros resultados.

La ropivacaína se considera un anestésico regional bien tolerado para el alivio del dolor postoperatorio. Una dosis adecuada de ropivacaína se asocia con una menor incidencia de bloqueo motor en comparación con la bupivacaína (a

través de la inhibición reversible del ion sodio en el nervio). Además, debido a que la ropivacaína tiene un potencial reducido de toxicidad en el sistema nervioso central y cardiotoxicidad, podría considerarse una buena opción para la anestesia regional y el manejo del dolor. La dosis inyectable recomendada es de 7.5 a 225 mg (1 a 30 mL).[29] En nuestro estudio utilizamos una preparación de 7.5 mg /mL, con una concentración total inyectada de 37.5 mg y en conjunto con los ejercicios de estiramiento y tal vez los llamados efectos de contexto o efectos no específicos, (en los que el paciente muestra un alivio de sus síntomas debido a la resolución natural, el efecto expectativa, o debido a la manera cálida, amigable y tranquilizadora del trato de su médico)[14] y/o el efecto paradoja, (en el cual el beneficio experimentado por el paciente después del tratamiento usualmente equivale a la respuesta general observada en el grupo de tratamiento)[48], podemos explicar la mejoría sostenida.(Figura 6)

Kalaci *et al*. informó de excelentes resultados clínicos con la inyección de corticosteroides (triamcinolona). Evaluaron a sus pacientes con una EVA y una puntuación modificada de Roles y Maudsley a las 3 semanas y a los 6 meses. Informaron mejores resultados con la inyección de corticosteroides utilizando la técnica de puntilleo. En este mismo estudio, otro grupo recibió anestésicos intralesionales utilizando la misma técnica, y aunque el dolor en estos pacientes disminuyó a los 3 y 6 meses, esto no fue estadísticamente significativo.[25] En un estudio doble ciego que evaluó tratamientos con placebo, corticosteroide (40 mg

Figura 6. Anestésico

de metilprednisolona) y plasma rico en plaquetas (PRP) durante 3 meses, el uso de corticosteroides o PRP fue más efectivo que el placebo en términos de dolor y puntuaciones funcionales (AOFAS).[32] Un estudio diferente comparó el uso de la inyección de corticosteroides con la movilización articular y los ejercicios de estiramiento. Ambos grupos de pacientes mostraron buenos resultados en la evaluación de seguimiento a 1 año. Los pacientes con inyección de esteroides obtuvieron mejores puntuaciones en las evaluaciones. La aplicación de esteroides

(40 mg de acetato de metilprednisolona) se realizó en el punto de máxima sensibilidad a la palpación sobre la cara medial del talón.[5] De manera similar a estos resultados, los pacientes tratados con corticosteroides en nuestro estudio mostraron una mejoría significativa en la percepción de dolor, así como en la función comparados con los valores iniciales, pero la mejoría fue similar a los otros dos grupos. (Figura 7)

Figura 7. Corticosteroide

Diaz-Llopis *et al*. compararon BoNT-A con un corticosteroide y encontraron mejores resultados en pacientes tratados con BoNT-A a los 6 meses[13] y a 1 añode seguimiento.[12] Se inyectó BoNT-A en dos sitios diferentes: 40 U se inyectaron en la inserción de la fascia plantar, y 30 U se inyectaron a 2.5 cm distal a la inserción talar de la fascia plantar. El corticosteroide utilizado fue betametasona (6 mg/ml) más anestésico local sobre la tuberosidad del calcáneo. Anteriormente, Babcock *et al*. utilizaron un enfoque de aplicación similar de 70 U de BTX-A aplicado a dos

sitios diferentes (40 U y 30 U) en comparación con placebo. Encontraron mejores resultados en pacientes que recibieron BoNT-A en la evaluación EVA y la puntuación de Maryland en un seguimiento de 3-8 ocho semanas.[4] También hay un estudio de aplicación de 100U de BoNT-A inyectada sobre el sitio de la lesión con terapia física supervisada adicional durante 6 semanas. Tanto el dolor como la función mejoraron en pacientes tratados con BoNT-A en comparación con los tratados con placebo.[1] Un estudio a corto plazo, aleatorizado, multicéntrico, doble ciego, controlado con placebo de 40 pacientes utilizando 200 U de BoNT-A (Dysport®) o inyecciones de placebo salino aplicadas localmente en forma de abanico a las 6 y 18 semanas. Se observó una disminución similar del dolor en torno al origen de la fascia plantar en ambos grupos de tratamiento.[34] Anteriormente reportamos la aplicación intralesional de corticosteroides (8 mg de dexametasona) comparado con aplicación de 250U de BoNT-A (Dysport®). BoNT-A se aplicó en el complejo gastro-soleo (200U a cada uno de los músculos de la pantorrilla y 50U al músculo soleo). Los pacientes tratados con BoNT-A tuvieron un mejor y más rápido alivio del dolor y mejoría en la función durante el seguimiento de 6 meses en comparación con los pacientes tratados con corticoesteroides.[17] En el estudio actual, realizamos una aplicación única intralesional de BoNT-A en el punto de máxima sensibilidad. Al igual que en los estudios anteriores el grupo BoNT-A mostró una mejoría significativa en el dolor y las puntuaciones funcionales durante el seguimiento, pero de nuevo no demostró una diferencia significativa entre los grupos.(Figura 8)

Figura 8. BoNT-A

En el caso de BoNT-A puede ser posible que sus efectos antiinflamatorios y de bloqueo de los mediadores del dolor se haya sobreestimado en los estudios antes comentados.[4,12,13,17] que reportaron mejores resultados comparándola con cortisona o placebo, los autores aplicaron la BoNT-A siguiendo la indicación de aplicarla en el vientre muscular observando así su función de bloqueo de la acetilcolina y disminución de la contractura.

En nuestro estudio inyectamos el tratamiento directamente en la inserción fibrosa de la fascia plantar esperando que su efecto antiinflamatorio y de bloqueo del dolor mejoraría la sintomatología de los pacientes. En estudios previos donde esto fue realizado[1,37] al igual que en el nuestro, reportaron mejoría en el dolor y la función al compararlo con los datos iniciales del estudio, pero no mostraron una

diferencia significativa entre los grupos a los 6 meses. Amhad et al.[1] reportó una mejoría significativa en el grupo tratado con BoNT-A, pero a los 12 meses de seguimiento usando Xeoming™. Sin embargo, algunos pacientes pudieron haber hecho ejercicios terapéuticos o usado ortosis más que otros, lo que puede afectar las tasas de éxito en este tratamiento. Igualmente, Huang et al., aplicando Botox™ contra placebo bajo guía ecográfica reportó mejoría significativa en el grupo de la toxina, pero en un diseño de estudio de 3 meses de seguimiento.[22]

Por otro lado, el grosor de la fascia plantar se midió antes del tratamiento y al final del estudio, mostrando una disminución del grosor en todos los pacientes, sin diferencia entre los grupos. El grosor promedio de la fascia plantar se ha reportado en 4.00 mm, y es considerado un indicador de enfermedad cuando es >4.00 mm, lo cual generalmente está relacionado con los síntomas del paciente.[3,34] Nuestros resultados revelan que todos los grupos de pacientes mostraron una reducción del grosor de la fascia después del tratamiento, pero aun así se encontraba por arriba de la media (5.7 mm). Aún con esta medida los pacientes mostraron una buena evolución clínica.

Nuestro estudio tiene ciertas limitaciones que merecen ser mencionadas. Primero, no hubo grupo placebo, o grupo que haya sido intervenido solamente con ejercicios de estiramiento, lo cual nos podría haber ayudado a entender mejor la respuesta de los tratamientos inyectados. Segundo, algunos pacientes no

completaron su seguimiento, lo cual se solucionó con un apropiado y robusto análisis de imputación. Finalmente, este estudio tuvo un período de seguimiento corto, y aunque sabemos que esta patología puede ser considerada autolimitada, un seguimiento más prolongado pudo haber ayudado a determinar los verdaderos efectos de cada tratamiento.

CAPÍTULO IX

CONCLUSIONES

En conclusión, no se observó una diferencia estadísticamente significativa entre las tres terapias inyectadas. Se observó una mejoría sostenida en los valores de dolor y función en todos los grupos a las 24 semanas. El resultado inesperado en el grupo del anestésico evidenció la falta de un grupo placebo dejándonos la pregunta si la mejoría fue debido a las terapias inyectadas o por el aumento en el rango de movilidad del tobillo y disminución en el grosor de la fascia plantar (ejercicios de estiramiento). Estudios futuros que aborden esta pregunta nos podrán confirmar si debemos o no ofrecer cualquier tipo de terapia inyectada a los pacientes con fascitis plantar.

La aplicación intralesional de toxina botulínica A no presentó mejores resultados que la aplicación intralesional de corticosteroide en el tratamiento de la fascitis plantar. Por lo tanto, la hipótesis no pudo ser comprobada.

CAPÍTULO X

REFERENCIAS

1. Ahmad J. Ahmad SH, Jones K. Treatment of plantar fasciitis with botulinum toxin: A randomized, controlled study. Foot and Ankle Int 2017;38(1):1-7. doi: 10.1177/1071100716666364.

2. Aoki KR. Review of a proposed mechanism for the antinociceptive action of botulinic toxin type A. Neurotoxicology 2005; 26:785-93

3. Argerakis NG, Positano RG, Positano RCJ, Boccio AK, Adler RS, Saboeiro GR, Dines JS. Ultrasound diagnosis and evaluation of plantar heel pain. J Am Pod Med Assoc 2015; 105(2):135-140. doi:10.7547/0003-0538-105.2.135.

4. Babcock MS, Foster L, Pasquina P, Jabbari B. Treatment of pain attributed to plantar fasciitis with botulinum toxin A: A short-term, randomized, placebo-controlled, double blind study. Am J Phys Med Rehabil 2005; 84:649-654. doi: 10.1097/01.phm.0000176339. 73591.d7.

5. Celik D, Kus G, Önder Simma S. Joint mobilization and stretching exercise vs steroid injection in the treatment of plantar fasciitis: A randomized controlled study. Foot Ankle Int 2016;37(2):150-56. doi: 10.1177/1071100715607619

6. Clark TG, Altman DG. Developing a prognostic model in the presence of missing data: an ovarian cancer case study. J Clin Epidemiol. 2003:56(1)128-37. doi: 10.1016/s0895-4356(02)00539-5.

7. Cornwall MW, McPoil TG. Plantar fasciitis: etiology and treatment. J Orthop Sports Phys Ther 1999; 29:756-60

8. Cui m, Khanijou S, Rubino J, Aoki KR. Subcutaneus administration of botulinum toxin A reduced formalin-induced pain. Pain 2004; 107:125-33

9. Chandler TJ, kibler WB. A biomechanical approach to the prevention, treatment and rehabilitation of plantar fasciitis. Sport Med 1993; 15:344-52

10. David JA, Sancarapandian V, Christopher PRH, Chatterjee A, Macaden AS. Injected corticosteroids for treating plantar heel pain in adults. Cochrane Database of Systematic Reviews 2017,6:CD009348. doi: 10.1002/14651858.CD009348.pub2.

11. Davis PF, Severud E, Baxter DE. Painful heel syndrome: results of nonoperative treatment. Foot Ankle Int 1994; 15:531-35. doi: 10.1177/107110079401501002.

12. Diaz-Llopis IV, Gómez-Gallego D, Mondéjar-Gómez FJ, López-García A, Climent-Barberá JM, Rodríguez-Ruiz CM. Botulinum toxin type A in chronic plantar fasciitis: clinical effects one year after injection. Clinical Rehabilitation 2013;27(8):681-685. doi: 10.1177/0269215512469217.

13. Díaz-Llopis IV, Rodríguez-Ruíz CM, Mulet Perry S, Mondéjar-Gómez FJ, Climent-Barberá JM, Cholbi-Llobel F. Randomized controlled study of the efficacy of the injection of botulinum toxin type A versus corticosteroids in chronic plantar fasciitis: results at one and six months. Clin Rehab 2011;26(7):594-606. doi: 10.1177/0269215511426159.

14. Di Blasi Z, Harkness E, Ernst E, Georgiou A, Kleijnen J. Influence of context effects on health outcomes: a systematic review. Lancet 2001; 357:757-62. doi: 10.1016/s0140-6736(00)04169-6.

15. DiGiovanni BF, Nawoczenski DA, Lintal ME, Moore EA, Murray JC, Wilding GE, Baumhauer JF. Tissue-specific plantar fascia-stretching exercise enhances outcomes in patients with chronic heel pain. A prospective,

randomized study. J Bone Surg Am 2003;85(7):1270-77. doi: 10.2106/00004623-200307000-00013.

16. Durham PL, Cady R, Cady R. Regulation of calcitonin gene-related peptide secretion from trigeminal nerve cells by botulinum toxin type A: implications for migraine therapy. Headache 2004; 44:35-42

17. Elizondo-Rodriguez J, Araujo-Lopez Y, Moreno-González JA, Cardenas-Estrada E, Mendoza-Lemus O, Acosta-Olivo C. A comparison of botulinum toxin A and intralesional steroids for the treatment of plantar fasciitis: A randomized, double-blind study. Foot Ankle Int 2013;34(1):8-14. doi: 10.1177/1071100712460215.

18. Ermutlu C, Aksakal M, Gümüstas A, Ozkaya G, Kovalak E, Ózkan Y. Thickness of plantar fascia is not predictive of functional outcome in plantar fasciitis treatment. Acta Orthop Traumatol Turc 2018; 52:442-446. doi: 10.1016/j.aott.2018.01.002

19. Gefen A. stress analysis of the standing foot following surgical plantar fascia release. J Biomech 2002; 35:629-37

20. Hick JH. The mechanics of the foot. II The plantar aponeurosis and the arch. J Anat 1954;88 (1):25-30

21. Horton NJ, Lipsitz SR. Multiple imputation in practice: comparison of software packages for regression models with missing variables. Am Stat. 2001;55(3):244–54.

22. Huang YC, Wei SH, Wang HK, Lieu FK. Ultrasonographic guided botulinum toxin type A treatment for plantar fasciitis: an outcome-based investigation for treating pain and gait changes. J Rehabil Med 2010;42(2):136-40. doi: 10.2340/16501977-0491.

23. Irving DB, Cook JL, Menz HB. Factors associated with chronic plantar heel pain: a systematic review. J Sci Med Sport 2006; 9:11-22

24. Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomized clinical trials – a practical guide with flowcharts. BMC Med Res Methodol 2017; 17:162. doi: 10.1186/s12874-017-0442-1.

25. Kalaci A, Cakici H, Hapa O, Yanat AN, Dogramaci Y, Sevinc TT. Treatment of plantar fasciitis using four different local injection modalities. A randomized prospective clinical trial. J Am Podiatric Med Assoc 2009;99(2):108-113. doi: 10.7547/0980108.

26. Kamel M, Eid H, Mansour R. Ultrasound detection of heel enthesitis: a comparison with magnetic resonance imaging. J Rheumatol 2003;30(4):774-78

27. Kim W, Voloshin AS. Role of plantar fascia in the load bearing capacity of the human foot. J Biomech 1995; 28:1025-33

28. Kitaoka HB, Alexander IJ, Adelaar RS, Nunley JA, Myerson MS, Sanders M. Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. Foot Ankle Int 1994;15(7):349-353. doi: 10.1177/107110079401500701.

29. Kuthiala G, Chaudhary G. Ropivacaine: a review of its pharmacology and clinical use. Indian J Anaesth 2011; 55:104-110. doi: 10.4103/0019-5049.79875.

30. Landorf KB, Radford JA, Hudson S. Minimally important difference (MID) of two commonly used outcome measure for foot problems. J Foot Ankle Res 2010;14; 3:7. doi: 10.1186/1757-1146-3-7

31. Landorf KB, Radford JA. Minimal important difference: Values for the foot health status questionnaire, foot function index and visual analogue scale. The Foot 2008; 18:15-19. doi: 10.1016/j.foot.2007.06.006

32. Mahindra P, Yamin M, Selhi HS, Singla S, Soni A. Chronic plantar fasciitis: Effect of platelet-rich plasma, corticosteroid, and placebo. Orthopedics 2016;39(2): e285-e289. doi: 10.3928/01477447-20160222-01.

33. Martin RL, Burdett RG, Irrgang JJ. Development of the foot and ankle disability index (FADI). J Orthop Sports Phys Ther 1999;29: A32-33. doi: 10.1177/107110070502601113.

34. McMillan AM, Landorf KB, Barrett JT, Menz HB, Bird AR. Diagnostic imaging for chronic plantar heel pain: a systematic review and meta-analysis. J Foot Ankle Res 2009; 2:32. doi: 10.1186/1757-1146-2-32.

35. Pacsek R, Dueretzbacger G, Buttgereit F, Mesiss L. treatment of chronic plantar fasciitis with botulinum toxin A: an open case series with a 1-year follow-up. Ann Rheum Dis 2005; 64:1659-1661

36. Patel A, DiGiovanni B. Association between plantar fasciitis and isolated contracture of the gastrocnemius. Foot Ankle Int 2011;32(1):5-8. doi: 10.3113/FAI.2011.0005.

37. Peterline CD, Funk JF, Hölscher A, Schuh A, Placzek R. Is botulinum toxin A effective for the treatment of plantar fasciitis. Clin J Pain 2012; 28:527-533. doi: 10.1097/AJP.0b013e31823ae65a.

38. Riddle DL, Pullsic M, Pidcoe P, Johnson RE. Risk factors for plantar fasciitis: a matched case-control study. J Bone Joint Surg Am 2003;85;872-877. doi: 10.2106/00004623-200305000-00015.

39. Riddle DL, Pulisic M, Sparrow K. Impact of demographic and impairment-related variables on disability associated with plantar fasciitis. Foot Ankle Int 2004; 25: 311-17

40. Rosenbaum AJ, DiPreta JA, Misener D. Plantar heel pain. Med Clin N Am 2014; 98:339-352. doi: 10.1016/j.mcna.2013.10.009.

41. Sanders R, Fortin P, DiPasquale T, Walling A. Operative treatment in 120 displaced intraarticular calcaneal fractures. Results using a prognostic computed tomography scan classification. Clin Orthop Relat Res 1993;(290):87-95

42. Seyler TM, Smith BP, Marker DR, Ma J, Shen J, Smith TL, Mont MA, Kolaski K, Koman AL. Botulinum neurotoxin as a therapeutic modality in orthopaedic surgery: more than twenty years of experience. J Bone Joint Surg Am 2008;90(Suppl 4):133-145. doi: 10.2106/JBJS.H.00901.

43. Singh D, Angel J, Bentley G, Trevino SG. Fortnightly review. Plantar fasciitis. BMJ 1997;315(7101):172-75. doi: 10.1136/bmj.315.7101.172.

44. Sterne JAC, White IR, Carlin JB, Spratt M, Royston P, Kenward MG, Wood AM, Carpenter JR. Multiple imputations for missing data in epidemiological and clinical research: potential and pitfalls. BMJ 2009;338: b2393. doi: 10.1136/bmj. b2393.

45. Tsikopoulos K, Vasiliadis HS, Mavridis D. Injection therapies for plantar fasciopathy ("plantar fasciitis"): a systematic review and network meta-analysis of 22 randomized controlled trials. Br. J Sports Med 2016; 50:1367-1375. doi: 10.1136/bjsports-2015-095437.

46. Wall JR, Harkness MA, Crawford A. Ultrasound diagnosis of plantar fasciitis. Foot Ankle Int 1993; 14:465-70. doi: 10.1177/107110079301400807.

47. Whittaker GA, Munteanu SE, Menz HB, Bonanno DR, Gerrard JM, Landorf KB. Corticosteroid injection for plantar heel pain: a systematic review and meta-analysis. BMC Musculoskeletal Disorders 2019; 20:378. doi: 10.1186/s12891-019-2749-z.

48. Zhang W, Doherty M. Efficacy paradox and proportional contextual effect (PCE). Clin Immunology 2018, 186:82-86. doi: 10.1016/j.clim.2017.07.018.

ANEXO A

APROBACIÓN POR EL COMITÉ DE ÉTICA EN INVESTIGACIÓN DE LA FACULTAD DE MEDICINA Y HOSPITAL UNIVERSITARIO DE LA UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN

UANL
UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN
FACULTAD DE MEDICINA Y HOSPITAL UNIVERSITARIO

DR. med. CARLOS ALBERTO ACOSTA OLIVO
Investigador Principal
Servicio de Traumatología y Ortopedia
Presente.-

Estimado Dr. Acosta:

Le informo que el Comité de Ética en Investigación de la Facultad de Medicina y Hospital Universitario de la Universidad Autónoma de Nuevo León, **ha evaluado y aprobado** el protocolo de investigación titulado **"Efecto terapéutico de la toxina botulínica A para el tratamiento de la fascitis plantar"** el cual quedó registrado en esta Subdirección con la clave **OR15-001**, participando además el Dr. Jorge Alberto Elizondo Rodríguez y el Dr. Jose Félix Vilchez Cavazos como Co-investigador.

De igual forma el siguiente documento:

- Protocolo en extenso, de fecha 29 de octubre del 2014.
- Consentimiento Informado de fecha 29 de octubre del 2014.

Le pedimos mantenemos informados del avance o terminación de su proyecto.

Sin más por el momento, me despido de usted.

Atentamente,
"Alere Flammam Veritatis"
Monterrey, Nuevo León 09 de Enero de 2015

SUB-DIRECCIÓN DE INVESTIGACIÓN
COMITÉ DE ÉTICA
COMITÉ DE INVESTIGACIÓN

DR. JOSE GERARDO GARZA LEAL
Secretario de Investigación Clínica
Presidente del Comité de Ética en Investigación

Comité de Ética en Investigación
Comité de Investigación
Av. Francisco I. Madero Pte. s/n y Av. Gonzalitos, Col. Mitras Centro, 64460 Monterrey N.L. México Apartado Postal 1-4409
Teléfonos (+52) 8329 4750 Ext. 2870 al 2874 Correo Electrónico: investigacionclinica@meduanl.com

ANEXO B

CONSENTIMIENTO INFORMADO

CONSENTIMIENTO INFORMADO

Titulo del Estudio	Efecto terapéutico de la toxina botulínica tipo A para el tratamiento de la fascitis plantar.
Nombre del Investigador Principal	Dr. Med. Carlos Alberto Acosta Olivo
Institución	Facultad de Medicina y Hospital Universitario "Dr. José Eleuterio González. Universidad Autónoma de Nuevo León"
Servicio/Departamento	Servicio de Ortopedia y Traumatología
Teléfono de Contacto	(81) 83476698
Persona de Contacto	Dr. Jorge Alberto Elizondo Rodríguez

Esta forma de consentimiento informado puede contener palabras que usted no entienda. Por favor pídale a su médico del estudio o al personal del estudio que le explique cualquier palabra o información que no le quede clara.
Su participación en este estudio es voluntaria. Es importante que lea y entienda la siguiente explicación de los procedimientos propuestos. Este documento describe el propósito, los procedimientos, beneficios, riesgos conocidos, molestias, precauciones del estudio incluyendo la duración y la naturaleza de su participación.
También describe las terapias o tratamientos alternativos conocidas que pueden estar disponibles y su derecho a retirarse del estudio en cualquier momento. No se pueden dar garantías respecto a los resultados del estudio de investigación.
Para ingresar al estudio, Usted como sujeto debe de firmar y fechar este documento con la presencia de dos testigos y finalmente recibirá una copia del mismo.

1.- PROPOSITO DEL ESTUDIO

La fascitis plantar es la causa más común de dolor en el talón. Es tan común en paises como Estados Unidos que cerca de dos millones de personas reciben tratamiento al año.
A pesar de que la fascitis plantar es un problema tan común, de que existen muchas formas de tratarla y de que sabemos que el 90% de los pacientes responden bien al tratamiento médico, no tenemos todavía el tratamiento ideal

que nos garantice que la mayoria de los pacientes se van a curar. Los tratamientos más comunes son los ejercicios de estiramiento y la aplicación de esteroides por medio de una inyección en el sitio de mayor dolor. Recientemente se ha visto que el uso de la tóxina botulínica ha tenido buenos resultados en el tratamiento de esta enfermedad. El objetivo de este estudio es comparar y valorar el uso de la toxina botulínica contra el tratamiento mas común que son los esteroides y un grupo control al que se le aplicará un anestésico local de larga duración. Todos con la aplicación en el mismo lugar y realizando ejercicios de estiramiento los cuales seran explicados por el médico antes de poner la inyección.

2.- CRITERIOS DE INCLUSION Y EXCLUSION

El médico del estudio verificará que Usted cumpla con los siguientes requisitos antes de considerar su ingreso al estudio de investigación.

Criterios de inclusión: -

Pacientes con dolor en el talón a nivel de la inserción de la fascia plantar en el hueso del talón. Pacientes que aceptaron formar parte del estudio y firmaron el consentimiento informado. Pacientes mayores de 18 años y menores de 60 y que tengan mas de dos semanas con la molestia y que no hayan tenido ningún tratamiento anterior.

Criterios de exclusión: -

Pacientes con alguna otra lesión en cualquier parte del cuerpo o enfermedades como osteoartritis, artritis reumatoidea, espondilitis anquilosante, etc. Pacientes con fascitis plantar en los dos pies. Pacientes con alguna cirugía previa en el pie afectado. Pacientes con alguna enfermedad psiquiátrica y pacientes embarazadas.

3.- MEDICAMENTO/DISPOSITIVO DE ESTUDIO

Ropivacaína (Naropín 7.5 mg/ml Astrazeneca).- 5 ml.
Dexametasona (Alín Depot 8 MG. / 2 ml. Chinoin).- 2 ml.
Toxina Botulínica A (Dysport 500 Uds.).- 125 Uds.

4.- PROCEDIMIENTOS

Este es un estudio en el que vamos a comparar el resultado del tratamiento de la fascitis plantar con tres diferentes medicamentos.
A cada paciente se le aplicará por medio de una inyección en el talón en el sitio de más dolor uno de los medicamentos estudiados y que será escogido a la suerte por medio de un sorteo. Usted no sabrá que medicamento se le va a

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COMITÉ DE INVESTIGACIÓN

aplicar. Todas las inyecciones de todos los pacientes serán aplicadas por el mismo médico.
Después de la aplicación se valorará la respuesta al tratamiento citándolo a la consulta a los 15 días, 1, 3 y 6 meses y se le harán preguntas muy sencillas las cuales serán las mismas cada vez que acuda a consultar.
Al completar el número de pacientes necesarios para el estudio se analizará la información para saber cuál de los medicamentos funcionó mejor y de esta forma saber cuál es el mejor tratamiento para nuestros pacientes.

5.- TERAPIAS ALTERNATIVOS
Terapia de ondas de choque extra-corporeas, cirugía de liberación de la fascia plantar.

6.- RIESGOS Y MOLESTIAS
Dolor local y enrojecimiento en el sitio de la punción, reacciones adversas al uso de medicamentos, infección, ruptura de la fascia plantar, ligera disminución de la fuerza de los músculos de la planta del pie.

7.- POSIBLES BENEFICIOS
Usted puede verse beneficiado por su participación en este estudio, aunque no hay garantías de que tenga un beneficio directo por participar en este estudio.

Mejoría del dolor, reincorporación a sus actividades laborales y deportivas, mejoría en la calidad de vida y su función.

8.- NUEVOS HALLAZGOS
El médico del estudio le informará a usted o a su representante legar acerca de cualquier hallazgo significativo que se desarrolle durante el transcurso de este estudio que pudiera afectar el deseo de seguir participando en este estudio. Usted tiene el derecho de conocerla y tomar la decisión si continúa o no en el estudio.

9.- RETIRO Y TERMINACIÒN
Su participación es estrictamente voluntaria. Si desea suspender su participación, puede hacerlo con libertad en cualquier momento. Si elige no participar o retirarse del estudio, su atención medica presente y/o futura no se verá afectada y no incurrirá en sanciones ni perderá los beneficios a los que usted tendría derecho de algún otro modo.
El médico podrá suspender su participación en el estudio, sin su consentimiento, por cualquiera de las siguientes circunstancias:

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1.- Que el patrocinador del estudio cancele el estudio.
2.- Que el médico considere que es lo mejor para Usted.
3.- Que necesita algún procedimiento o medicamento que interfiere con esta investigación.
4.- Su participación se suspende para cumplir con los requisitos del estudio.
5.- Que no ha seguido las indicaciones del médico lo que pudiera traer como consecuencias problemas en Usted.

Se Usted decide retirarse de este estudio, deberá realizar lo siguiente:
1.- Notificar a su médico tratante del estudio
2.- Deberá de regresar todo el material que su médico le solicite.

Si su participación en el estudio se da por terminada, cualquier que sea la razón, el médico por su seguridad, continuará con seguimientos clínicos, además de podrá utilizar la información médica que se recabó antes de su terminación.

10.- COSTOS, REEMBOLSOS Y PAGOS

Los medicamentos, procedimientos y pruebas relacionadas con el estudio no tendrán ningún costo.
Sin embargo puede incurrir en gastos propios a la atención que normalmente recibiría.
.

11.- CONFIDENCIALIDAD/EXPEDIENTE CLINICO

Si acepta participar en la investigación, el médico del estudio recabará y registrará información personal confidencial acerca de su salud y de su tratamiento. Esta información no contendrá su nombre completo ni su domicilio, pero podrá contener otra información acerca de Usted, tal como iniciales y su fecha de nacimiento. Toda esta información tiene como finalidad garantizar la integridad científica de la investigación. Su nombre no será conocido fuera de la Institución al menos que lo requiera nuestra Ley.

Usted tiene el derecho de controlar el uso de sus datos personales de acuerdo a la Ley Federal de Protección de datos Personales en Posición de Particulares, así mismo de solicitar el acceso, corrección y oposición de su información personal. La solicitud será procesada de acuerdo a las regulaciones de protección de datos vigentes. Sin embargo, cierta información no podrá estar

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disponible hasta que el estudio sea completado, esto con la finalidad de proteger la integridad del Estudio.

La Facultad de Medicina y Hospital Universitario así como el Investigador serán los responsables de salvaguardar la información de acuerdo con las regulaciones locales. Usted tiene el derecho de solicitar por escrito al medico un resumen de su expediente clínico.

La información personal acerca de su salud y de su tratamiento del estudio podrá procesarse o transferirse a terceros en otros países para fines de investigación y de reportes de seguridad, incluyendo Agencias reguladoras (Secretaria de Salud SSA) locales así como a comité de Ética en Investigación y de Investigación de nuestra Institución.

Para los propósitos de este estudio, autoridades sanitarias como Secretaria de Salud y Comité de Ética en Investigación y de Investigación de nuestra Institución podrán inspeccionar el expediente clínico, incluso los que fueron recabados antes de su inicio de participación, los cuales pueden incluir su nombre, domicilio y otra información personal. En caso necesario estas auditorías o inspecciones podrán hacer fotocopias de parto o de todo su expediente clínico. La razón de esto es asegurar que el estudio se está llevando a cabo apropiadamente con la finalidad de salvaguardar sus derechos como pacientes en investigación.

Los resultados de este estudio de investigación podrán presentarse en reuniones o en publicaciones.

La información recabada durante este estudio será recopilada en bases de datos del investigador, los cuales podrán ser usados en otros estudios en el futuro. Estos datos no incluirán información médica personal confidencial. Se mantendrá el anonimato.

Al firmar este documento, Usted así como su representante autorizan el uso y revelaciones de la información acerca de su estado de salud y tratamiento identificado en esta forma de consentimiento. No perderá ninguno de sus derechos legales como sujeto de investigación. Si hay cambios en el uso de su información, su médico le informará.

12.- INTERVENCIÓN DEL MEDICO FAMILIAR

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Se le informará a su médico de cabecera acerca de su participación en este estudio, enviándole la información médica pertinente si lo solicita así como cualquier información médica relevante.
Para que los médicos de la Institución conozcan de su participación en el estudio, los expedientes clínicos cuentan con un identificador para que el médico de cabecera se ponga en contacto con el Investigador.

13.- COMPENSACION Y TRATAMIENTO DE LESIONES
Si se enferma o se lesiona debido a una complicación o adversidad que sea resultado directo del uso del medicamento/dispositivo o procedimiento en estudio, deberá Usted notificar a su Médico para que el proporcione los cuidados necesarios para el tratamiento de dicha complicación. El tratamiento recibido no tendrá ningún costo y será cubierto por la Institución, así como la indemnización a la cual tendría derecho en caso de requerirla.

Si desea mayor información podrá contactar Lic. Antonio Zapata de la Riva al teléfono (81) 83294050 exts 2870 a 2874.

13.- DECLARACIÓN
Reconozco que me han dado la oportunidad de hacer preguntas relacionadas al estudio de investigación y que todas estas se me han respondido de manera clara y precisa.

Entiendo además si tengo preguntas relacionadas al estudio, así como en el caso de lesiones o complicaciones deberé de notificar de inmediato al investigador con la siguiente información de contacto.

Nombre del Investigador Principal	Dr. Med. Carlos Alberto Acosta Olivo
Teléfono de Contacto	(81) 83476698
Teléfono de emergencias	(81) 83471983

Además entiendo que el Comité de Ética en Investigación cuenta con un numero de emergencias para estos casos y que podré contactarlos para notificar de una complicación.

Urgencias Médicas. Comité de Ética en Investigación. Teléfono 044-8119085882

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En caso de tener alguna pregunta relacionada a mis derechos como sujeto de investigación de la Facultad de Medicina podre contactar al Comité de Ética en Investigación y de Investigación de nuestra Institución al Presidente, **Dr. José Gerardo Garza Leal,** o al Represente legal de los sujetos de Investigación al **Lic Antonio Zapata de la Riva.**

Comité de Ética en Investigación y de Investigación
Av. Francisco I Madero Pte. s/n y Av. Gonzalitos, Col. Mitras Centro, 66460 en Monterrey, Nuevo León México.
Teléfonos: 81-83294050 exts 2870 a 2874
www.investigacion-medunal.com
email. investigacionclinica@meduanl.com

Al firmar este consentimiento reconozco que mi participación es voluntaria y que puedo negarme a participar o suspender mi participación en cualquier momento sin sanciones ni perdidas de los beneficios a los que de otro modo tengo derechos.
Acepto además que mi información personal de mi salud puede utilizarse y transferirse para nuevos estudios de investigación clínica con la finalidad de brindar más información y así contar con nuevas opciones de tratamiento.
Entiendo que mi información puede ser auditada o inspeccionada por agencias reguladoras como la Secretaria de Salud así como por la misma Institución.
Se me entrega una copia del consentimiento informado.

13.- FIRMAS

Fecha	*Firma de la Sujeto*	*Nombre en letra de molde*
Fecha	*Firma del Primer Testigo*	*Nombre en letra de molde*
Relación del Primer Testigo con la Sujeto del Estudio	*Dirección*	
Fecha	*Firma del Segundo Testigo*	*Nombre en letra de molde*
Relación del Primer Testigo con la Sujeto del Estudio	*Dirección*	

COMITÉ DE ÉTICA
COMITÉ DE INVESTIGACIÓN

II. ASEGURAMIENTO DEL INVESTIGADOR O DEL MIEMBRO DEL EQUIPO

He discutido lo anterior con esta persona. A mi más leal saber y entender, el sujeto está proporcionando su consentimiento tanto voluntariamente como de una manera informada, y él/ella posee el derecho legal y la capacidad mental suficiente para otorgar este consentimiento.

_____	_____	_____
Fecha	*Firma de la Persona que Obtuvo el Consentimiento/Investigador Principal*	*Nombre en letra de molde*

ANEXO C

FICHA DE IDENTIFICACIÓN DEL PACIENTE

Ficha de identificación del paciente

Nombre:_____Fecha:_____

Género: (M) (F) Edad:____ Ocupación:_____ ___ Escolaridad:_____

Domicilio:_____

Teléfono casa:_____

Teléfono celular:_____ No. Exp HU:_____

Teléfono opcional:_____ No. Registro de protocolo:_____

Correo electrónico:_____

Estatura (mts):_____

Peso (kgs):_____

IMC:_____

Pie a tratar:_____

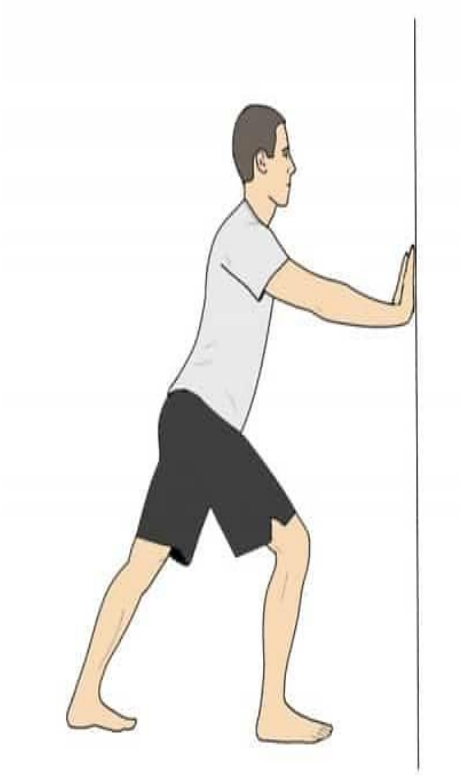
Aplicación y evaluaciones:

	Fecha	EVA	FADI	Maryland	AOFAS	Dorsiflexión	Grosor de fascia por US
Inicio							
14 días							
4semanas							
3 meses							
6 meses							

Uso de medicamentos o condiciones especiales durante el seguimiento:

ANEXO D

ESTIRAMIENTOS PARA FASCITIS PLANTAR



Instrucciones

1. Poner la pierna afectada detrás de la otra con los dedos apuntando hacia el talón de enfrente.
2. Doblar la rodilla de adelante mientras la de atrás se deja estirada y con los talones fijos en el piso por 20 segundos.
3. El ejercicio se repite 3 veces por sesión con cuatro sesiones al día.

Primera cita de seguimiento. (14 días después de tratamiento)

Lunes	Martes	Miércoles	Jueves	Viernes	Sábado	Domingo

Segunda cita de seguimiento. (4 semanas después de tratamiento)

Lunes	Martes	Miércoles	Jueves	Viernes	Sábado	Domingo

Tercera cita de seguimiento. (3 meses después de tratamiento)

Lunes	Martes	Miércoles	Jueves	Viernes	Sábado	Domingo

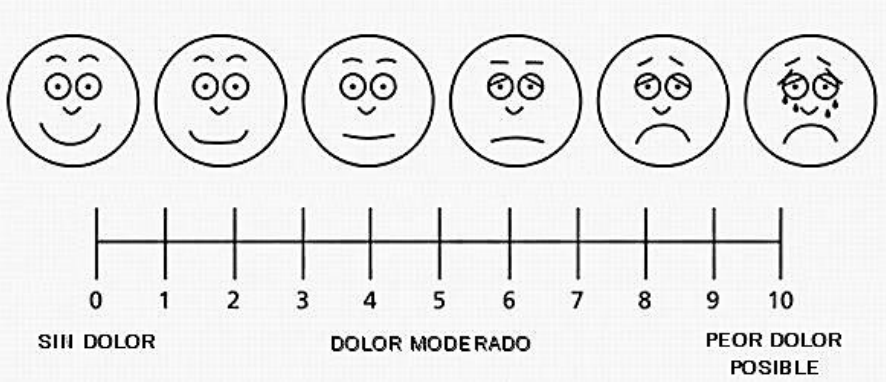
Cuarta cita de seguimiento. (6 meses después de tratamiento)

L	M	M	J	V	S	D	L	M	M	J	V	S	D

ANEXO E

ESCALAS

E.1 ESCALA VISUAL ANÁLOGA (EVA)



Escala Visual Analógica (EVA)

La **Escala Visual Analógica (EVA)** permite medir la intensidad del dolor que describe el paciente con la máxima reproducibilidad entre los observadores. Consiste en una línea horizontal de 10 centímetros, en cuyos extremos se encuentran las expresiones extremas de un síntoma. En el izquierdo se ubica la ausencia o menor intensidad y en el derecho la mayor intensidad. Se pide al paciente que marque en la línea el punto que indique la intensidad y se mide con una regla milimetrada. La intensidad se expresa en centímetros o milímetros.

Sin dolor _____ Máximo dolor

La **Escala numérica (EN)** es un conjunto de números de cero a diez, donde cero es la ausencia del síntoma a evaluar y diez su mayor intensidad. Se pide al paciente que seleccione el número que mejor indique la intensidad del síntoma que se está evaluando. Es el método más sencillo de interpretar y el más utilizado.

0	1	2	3	4	5	6	7	8	9	10
Sin dolor										Máximo dolor

E.2 ÍNDICE DE DISCAPACIDAD DEL TOBILLO (FADI)

The Foot and Ankle Disability Index (FADI) Score and Sports Module

Nombre del paciente: _____ Fecha: _____

Por favor responda cada pregunta con la respuesta que describa mas acertadamente su condición dentro de los últimos siete días marcando el número apropiado en el recuadro. Si la actividad en cuestión es limitada por algo externo a su pie o tobillo, marque N/A

0 Incapaz de realizar
1 Dificultad extrema
2 Dificultad moderada
3 Dificultad leve
4 Sin dificultad

Permanecer de pie		Caminar cuesta arriba	
Caminar en terreno regular		Caminar cuesta abajo	
Caminar en terreno regular sin calzado		Subir escaleras	
Caminar en terreno irregular		Bajar escaleras	
¿¿Stepping up and down curves??		Ponerse en cuclillas	
Dormir		Tocarse los dedos de los pies	
Dar primeros pasos después de estar en reposo		Caminar 5 minutos o menos	
Caminar por 10 minutos		Caminar 15 minutos o mas	
Atender actividades del hogar		Realizar actividades de la vida diaria	
Cuidado personal		Realizar trabajo leve/moderado (permanecer de pie, caminar)	
Trabajo pesado (empujar/jalar, escalar, cargar)		Realizar actividades recreativas	

Modulo de deporte:

Correr		Saltar	
Caer de pie		Realizar sentadillas o detenerse rápidamente	
Cortar, realizar movimientos laterales		Actividades de bajo impacto	
Habilidad de realizar actividades con técnica normal		Habilidad de participar en deporte de elección por el tiempo deseado	

Dolor relacionado a pie y tobillo:

0 Insoportable
1 Dolor severo
2 Dolor moderado
3 Dolor leve
4 Sin dolor

Nivel general de dolor		Dolor en reposo	
Dolor durante actividades cotidianas		Dolor al levantarse por las mañanas	

Office Use Only: Score: ____/136 points (FADI 104 points & SPORTS 32 points; No Disability 136)
Number of PT Sessions: _____ Gender: M F Age: _____
ICD-9 Code: PT Initials:

E.3 ESCALA DE LA SOCIEDAD AMERICANA DE PIE Y TOBILLO (AOFAS)

Fecha:_____

Ankle-Hindfoot Scale (100points Total)

I Dolor (40 puntos)

Nada	40
Leve, ocasional	30
Moderado, diario	20
Severo, casi siempre presente	0

II Función (50 puntos)

Limitación de actividades, requerimiento de soporte	
Sin limitaciones, sin soporte	10
Sin limitación de actividades diarias, limitación de actividades recreativas, sin soporte	7
Limitación de actividades diarias y recreativas, bastón	4
Limitación severa de actividades diarias y recreativas, andador, muletas, silla de ruedas, férula	0

Distancia máxima al caminar, cuadras	
Más de 6	5
4-6	4
1-3	2
Menos de 1	0

Caminar en superficies	
Sin dificultad en cualquier superficie	5
Alguna dificultad en terreno irregular, peldaños, pendientes, escaleras	3
Dificultad severa en terreno irregular, peldaños, pendientes, escaleras	0

Anormalidad de la marcha	
Ninguna, leve	8
Obvia	4
Marcada	0

Rango de movimiento sagital (flexión mas extensión)	
Normal o restricción leve (30° o más)	8
Restricción moderada (15° -29°)	4
Restricción severa (menos de 150)	0

Fecha:_____

Retropié, rango de movimiento (inversión mas eversión)	
Normal o restricción leve (75%-100% normal)	6
Restricción moderada (25%-74% normal)	3
Restricción marcada (menos de 25% normal)	0

Estabilidad de tobillo y retropié (anteroposterior, varus-valgus)	
Estable	8
Definitivamente inestable	0

III Alineación (10 puntos)

Buena, pie plantigrado, medio pie bien alineado	15
Favorable, pie plantigrado, algún grado de desalineación en mediopie, asintomático	8
Pobre, pie no plantigrado, desalineación severa, sintomático	0

Total_____100/Max.

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E.4 Escala de Pie y Tobillo de Maryland

Maryland Foot Score Fecha:_____

1. **Dolor**

Sin dolor (aún con deportes)	45
Mínimo (sin limitación para trabajar)	40
Mediano (algunas limitaciones para trabajar)	35
Moderado (disminución significante de la actividad)	30
Marcado (aún con mínima actividad)	15
Incapacitado (incapaz de caminar sin dolor)	5

2. **Función**
   a. **Marcha**

Distancia caminada	
Ilimitada	10
Limitación mínima	8
Limitación moderada	5
Limitación severa	2
Solo intramuros	0
Estabilidad	
Normal	4
Sensación de debilidad	3
Falseo ocasional	2
Falseo continuo	1
Utiliza ortesis	0
Soporte	
Ninguno	4
Bastón	3
Muletas	1
Silla de ruedas	0
Claudicación	
Ninguna	4
Leve	3
Moderada	2
Severa	1
Incapaz de caminar	0

ANEXO F

PUBLICACIONES PROPIAS SOBRE EL TEMA

- F.1 Comparison Of Botulinum Toxin A, Corticosteroid And Anesthetic Injection For Plantar Fasciitis

  2020

- F.2 Plantar Fasciitis—A Comparison Of Treatment With Intralesional Steroids Versus Platelet-Rich Plasma

  2017

- F.3 A Comparison Of Botulinum Toxin A And Intralesional Steroids For The Treatment Of Plantar Fasciitis: A Randomized, Double-Blinded Study

  2013

- F.4 Highlight Article: January-June 2013

  Editorial

Article

AMERICAN ORTHOPAEDIC FOOT & ANKLE SOCIETY

Foot & Ankle International®
1–9

DOI: 10.1177/1071100720961093
journals.sagepub.com/home/fai

Comparison of Botulinum Toxin A, Corticosteroid, and Anesthetic Injection for Plantar Fasciitis

Jorge Elizondo-Rodríguez, MD[1], Mario Simental-Mendía, PhD[1], Victor Peña-Martínez, PhD, MD[1], Félix Vilchez-Cavazos, PhD, MD[1], Yadira Tamez-Mata, MD[1], and Carlos Acosta-Olivo, PhD, MD[1]

Abstract

Background: Plantar fasciitis is the most common cause of heel pain, and injection therapies are part of the treatment modalities. This study aimed to compare 2 intralesional injection therapies for plantar fasciitis: corticosteroid and botulinum toxin A, compared with a third control group using a local anesthetic. The clinical evolution, as well as changes in the thickness of the plantar fascia and ankle dorsiflexion, was evaluated.

Methods: A randomized, controlled, double-blind trial design was used. Patients were divided into 3 groups: group 1, anesthetic only; group 2, corticosteroid; and group 3, botulinum toxin A (BoNT-A). We used an ultrasonographic evaluation to measure the plantar fascia thickness. The results were evaluated using the Maryland Foot Score and a 10-cm visual analog scale. Clinical scores were recorded at the beginning of the study, at 2 weeks, and at 1, 3, and 6 months. We evaluated 78 patients for study eligibility. The 3 intervention groups were homogeneous.

Results: All patients showed better clinical outcomes compared with their initial evaluations, without differences between groups at the end of follow-up. The thickness of plantar fascia diminished at the final evaluation, and ankle dorsiflexion was better compared with the initial values without difference between treatment groups.

Conclusion: Considering all the evaluated outcomes, no significant differences between treatment groups were observed. The pain relief and functional improvement obtained with the different treatments was maintained during the 6-month follow-up.

Level of Evidence: Level I, therapeutic study.

Keywords: plantar fasciitis, corticosteroid, botulinum toxin A, anesthetic

Introduction

Plantar fasciitis is diagnosed in approximately 80% of patients with heel pain.[26] It is triggered by collagen degeneration at the calcaneal origin of the plantar fascia attributed to repetitive microtears that occur in conjunction with a loss of collagen continuity and increase in connective tissue and vascularity.[29] Obesity is an independent risk factor for the development of plantar fasciitis and is present in up to 70% of these patients. Work-related weight-bearing activities are also associated with plantar fasciitis.[25] The diagnosis is usually clinical. Patients have pain to palpation of the anteromedial aspect of the heel and complain of pain that is worse with the first steps in the morning or when standing after prolonged sitting. It has been reported that there is an association between plantar fasciitis and gastrocnemius contracture, manifested as limited dorsiflexion of the ankle. The decreased dorsiflexion has been reported as the most important risk factor to develop plantar fasciitis.[23,25] These patients may also experience decreased pain as their activities progress, but the pain returns later in the day.[26] With the use of ultrasonography, which has become a common diagnostic tool, fascial thickening and soft tissue edema in the plantar heel can be identified. The plantar fascia thickness is regarded as an indicator of the extent of inflammation, in

[1]Ortopedia y Traumatología, Facultad de Medicina y Hospital Universitario "Dr José E. González," Universidad Autónoma de Nuevo León, Monterrey, Nuevo León, México

Corresponding Author:
Carlos Acosta-Olivo, PhD, MD, Orthopaedics and Traumatology, Universidad Autónoma de Nuevo León, Av. Madero y Gonzalitos, S/N. Mitras Centro, Monterrey, Nuevo León 64480, México.
Email: dr.carlosacosta@gmail.com

which increased thickness is consistent with more severe inflammation.[15] In the setting of plantar fasciitis, ultrasonography reveals a thickened and hypoechoic fascia.[18]

Multiple treatment modalities have been proposed for the management of this pathology, including nonsteroidal anti-inflammatory drugs, heel pads, orthoses, night splints, extracorporeal shock-wave therapy, a stretching exercise program (first-line treatment in many cases), and injection therapies.[26]

One of the most common injection therapies for plantar fasciitis patients is corticosteroids. However, this treatment has been shown to only slightly reduce heel pain for up to 1 month, and this reduction is not maintained for up to 6 months. Moreover, adverse events are related to the use of corticosteroids, although this was found at a relatively low rate (3 infections and 2 ruptures of the plantar fascia) in a review of 2492 patients.[6]

Reports concerning plantar fasciitis injection treatment are conflicting. A recent meta-analysis reported that corticosteroid injections had similar effectiveness to placebo injections for reducing both short-term (0-6 weeks) and medium-term (7-12 weeks) pain. In contrast, it was also concluded that corticosteroid injection was more effective than some therapies like autologous blood injection, platelet-rich plasma, or dry needling for the reduction of pain and the improvement of function in patients with plantar heel pain.[32] Another injection option is botulinum toxin A (BoNT-A), which has been increasingly considered as an alternative treatment for chronic musculoskeletal conditions such as multiple sclerosis, idiopathic toe walking, lateral epicondylitis, cerebral palsy, or torticollis.[28] Intralesional BoNT-A has been previously studied for the treatment of plantar fasciitis, showing significantly reduced pain intensity for 0-6 months.[31] A systematic review and meta-analysis reported that BoNT-A provided a significant short-term advantage over placebo for pain relief, and the effect was still present at 6 months.[31]

Trials reporting the use of injection therapies (especially corticosteroids) in combination with an anesthetic are widespread,[6] but reports including a treatment group with a control arm using anesthetic alone are scarce.[17] The majority of studies compare corticosteroid or BoNT-A with placebo. The purpose of this study was to compare 2 intralesional and ultrasound-guided injection therapies (corticosteroid or BoNT-A) for plantar fasciitis using a control anesthetic group. The clinical evolution (pain and functionality) as well as changes in the thickness of the plantar fascia and ankle dorsiflexion were evaluated. We hypothesized that patients with plantar fasciitis receiving intralesional BoNT-A would have more significant improvement in pain and function than those receiving intralesional corticosteroids.

Methods

We performed a randomized, controlled, double-blind (patients and clinical outcomes evaluator) trial. The study was approved by the Research Ethics Committee of our institution. All included patients were informed about the study and provided written informed consent before participation.

All the procedures included in this study were performed in the outpatient clinic. The inclusion criteria were heel pain at the origin of the plantar fascia (anteromedial calcaneal tuberosity), an age of 18-60 years old, at least 2 months of persisting pain, failure to respond to conventional treatment (orthotics, ice, stretching, and nonsteroidal anti-inflammatory drugs), and no previous injections in the affected zone. Patients were excluded if they had any anatomic or pathologic alterations in the knee, foot, or ankle; seronegative arthritis; rheumatoid arthritis; ankylosing spondylitis; Reiter syndrome; diabetes mellitus; a neurologic abnormality, psychiatric pathology, and psychomotor impairment; skin infections or a history of infection at the application site in the previous 3 months; previous surgery on the affected foot or ankle; pregnancy or breastfeeding. Patients who did not receive the intervention, those who had an incomplete follow-up (less than 3 visits), those who voluntarily declined to participate in the study, and those who presented adverse reactions to any of the medications used were eliminated.

Randomization and Intervention Groups

Using computer-generated randomization technology (www.randomization.com), patients were included into 1 of the treatment groups. The patients were blinded to the treatment applied. Patients in group 1 (anesthetic only) received a single application of 5 mL of ropivacaine (7.5 mg/mL; Naropin, AstraZeneca LP, Wilmington, DE), patients in the group 2 (corticosteroid) received a single application of 1 mL betamethasone sodium phosphate equivalent to 3 mg of betamethasone and betamethasone acetate equivalent to 2.71 mg of betamethasone injectable suspension (3 mg/mL; Celestone Soluspan, Schering-Plough Canada Inc, Kirkland, Canada), and patients in group 3 (BoNT-A) received a single application 200 U of BoNT-A (Dysport, IPSEN Ltd, Slough, UK) in a total volume of 2 mL. Asepsis of the heel region was achieved using an antiseptic (Avagard, 3M Health Care, St Paul, MN) for 2 minute prior to injection.

Ankle Dorsiflexion Measurements, Ultrasonographic Evaluation, and Injection

During the initial evaluation, the mobility of the subtalar joint was assessed with rear foot inversion/eversion maneuvers to detect functional alterations. We recorded the maximal dorsiflexion of the ankle using a goniometer with the knee fully extended. The dorsiflexion was graded in a positive or negative measure with respect to the neutral position of the foot (Figure 1).

Figure 1. Measure of ankle dorsiflexion using a goniometer.

All patients were evaluated by ultrasonographic imaging using a MyLab One system with an SL3323 transducer (Esaote Europe BV, Maastricht, the Netherlands). The thickness of the plantar fascia was measured at the end of the calcaneus bright line (hyperechoic line) at the anterior edge of the medial tubercle of the calcaneus (Figure 2).

All injections were applied under ultrasound guidance, at the maximal tenderness point into the medial plantar aspect of the foot, placing the needle just superior (subfascially) and near the insertion of the plantar fascia in a fan-shaped manner. All ankle dorsiflexion measurements, ultrasonographic evaluations, and guided injected therapies were performed by the same single investigator.

Clinical Outcomes

The clinical scores used to evaluate patient progression were the 10-cm visual analog scale (VAS) for pain and the Maryland Foot Score for function. The VAS assesses the pain level on a scale of 0 to 10 (0 = no pain, 10 = the worst pain). The Maryland Foot Score is divided into several sections that

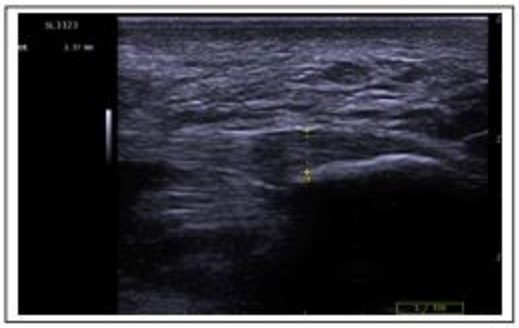

Figure 2. Measure of the plantar fascia at the end of the calcaneus bright line.

evaluate pain and function (motion and functional activities) and a section that evaluates the shape of the foot. The best score possible is 100, indicating no problem with the foot, and the lowest possible score is 0.[27] The clinical scores were performed by a physician blinded to the treatment given to each patient.

Follow-up and Patient Instructions

All clinical outcomes scores were recorded at the beginning of the study, 2 weeks thereafter, and at 1, 3, and 6 months. Ultrasonographic fascia thickness and ankle dorsiflexion measures were performed at the beginning and at the end of the study (6 months).

All patients were informed about their pathology and were instructed to perform daily stretching exercises of their Achilles tendon.[11] The patient was instructed to perform the exercise without a shoe insert. Briefly, the patients were instructed to place the affected leg behind the contralateral leg, with the toes of the affected foot pointing toward the heel of the front foot, and to lean into the wall. Then, the front knee was bent while the back knee was straight, and the heel was kept firmly on the floor for 20 seconds. The exercise was repeated 3 times per session, with 4 sessions per day. The patients were asked to fill in a chart recording their daily exercise. The exercise was planned to start 2 days after the injection.

Handling of Missing Data

Some data were missing for the different outcomes evaluated in our study. The missing data did not follow a monotonic pattern (eg, some subjects had missing data at 2 or 4 weeks and then returned at 12 or 24 weeks for follow-up), and the proportion of missing data was $<40\%$.[5] The missing values were determined to be missing at random,[16] and a multiple imputation technique was used.[14,30] The multiple

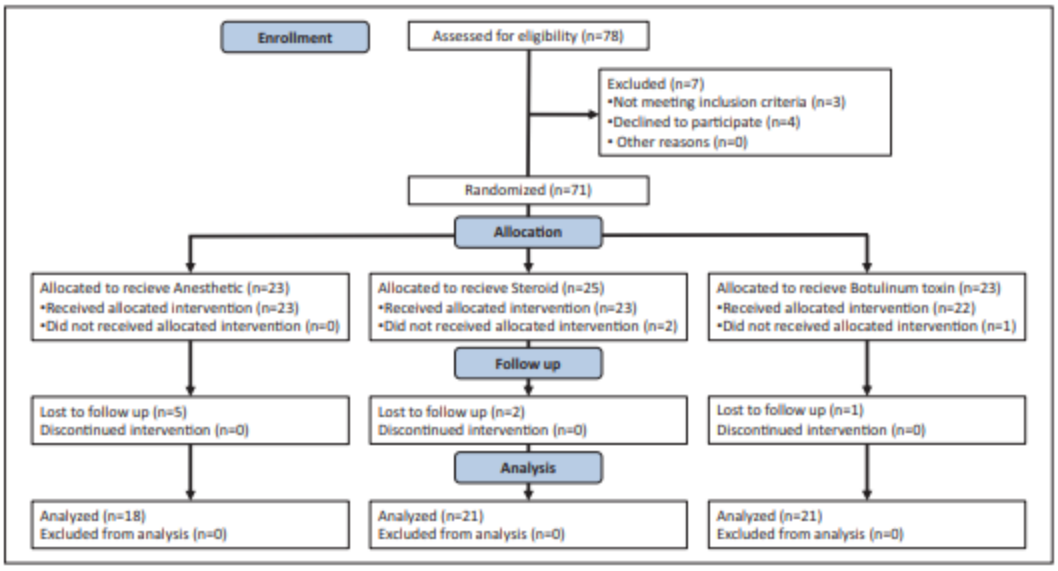

Figure 3. The Consolidated Standards of Reporting Trials (CONSORT) flow diagram of our current study.

imputation model used age, gender, and all outcome variables to impute missing values. To assess the robustness of the study, we conducted a sensitivity analysis based on an intention-to-treat analysis.

Study Flow and Patient Demographics

We evaluated 78 patients for study eligibility. During the selection process, 7 patients were excluded because they did not meet the inclusion criteria (n = 3) or they refused to participate (n = 4). The remaining 71 patients were randomized, and during the follow-up period, 8 more patients were lost. At the end of the study, we evaluated a total of 60 patients (Figure 3). The patient demographics of the 3 intervention groups were homogeneous ($P > .05$), including age, gender, affected foot, and body mass index. No significant differences between treatment groups were observed regarding baseline pain and functional scores ($P > .05$). The complete baseline information for all patients is reported in Table 1.

Data Analysis

Based on previous results from our study group, we used a formula for the difference of 2 means with a power of 90% at a confidence of 95%, with a bilateral α-value of 1.96, resulting in the number of patients per group being 18 for a meaningful difference in the Maryland Foot Score of 15.2 points.[12] Chi-square tests were used to compare the qualitative data between groups. One-way analysis of variance with Bonferroni multiple comparison test was used for comparing quantitative data within and between groups. Comparison of pre- and posttreatment data was performed using paired *t* tests and repeated measurement methods. Two-tailed *P* values $< .05$ were considered statistically significant. Statistical analysis of the data was performed using GraphPad Prism 5.00 software Windows (GraphPad Software, San Diego, CA).

Results

Clinical Outcome Measures

There was a sustained improvement in pain and functional outcomes (VAS and Maryland Foot Score) in each of the 3 treatment groups after 24 weeks (Table 2). Pain perception in patients (VAS) significantly improved from week 2 ($P < .05$) and reached a very slight intensity after 24 weeks compared with the baseline scores ($P < .001$). No significant differences were detected between the groups at 24 weeks ($P > .05$). Regarding the Maryland Foot Score, a similar trend was observed, with a significant improvement at week 24 compared with the baseline scores ($P < .05$). The only statistically significant difference was detected between the anesthetic and BoNT-A groups at 24 weeks. A complete analysis of the clinical outcomes is reported in Table 2.

Ultrasonographic Measure of Plantar Fascia Thickness and Ankle Dorsiflexion

Ultrasonographic measurement of the plantar fascia thickness was recorded at baseline and at the end of the study

Table 1. Comparison of the Initial Demographic Characteristics of the Patients Included in the Study Groups.[a]

	Anesthetic	Steroid	Botulinum toxin A	*P* value
Patients (n)	23	25	23	
Age, y	49.3±10.6	46.4±11.0	44.0±12.5	.2850[b]
Gender, (%)				.2661[c]
Female	13 (57)	19 (76)	13 (57)	
Male	10 (43)	6 (24)	10 (43)	
Affected foot (%)				.7847[c]
Left	14 (60.8)	13 (52)	12 (52.1)	
Right	9 (39.2)	12 (48)	11 (47.9)	
BMI	30.2±2.9	29.7±4.8	31.4±5.5	.5091[b]
VAS score, cm (0-10)	7.9±1.2	7.7±1.9	8.0±1.5	.6844[b]
Maryland Foot Score	84.6±12.1	83.9±13.4	77.6±15.5	.1864[b]

Abbreviations: BMI, body mass index; VAS, visual analog scale.
[a]Unless otherwise noted, values are mean ± standard deviation.
[b]One-way analysis of variance.
[c]Chi square test.

(Table 3). The only significant difference from the baseline was observed in the anesthetic group ($P < .001$). Nonetheless, no significant differences were detected between groups at 24 weeks ($P > .05$). Concerning ankle dorsiflexion, there was an increased range of motion in all 3 groups (Table 3), but only the BoNT-A group registered a significant change from the baseline at 24 weeks ($P < .001$). Again, no significant differences between groups were detected ($P > .05$) (Figure 4).

Side Effects

No significant side effects were reported by the patients or noticed by the investigators involved.

Discussion

Plantar fasciitis is a limited but troublesome heel problem that typically presents with pain. The 3 different treatment modalities employed in this study showed significant pain relief with respect to the baseline values and better clinical and functional outcomes in the follow-up. The improvement in pain was above the minimally important difference reported for plantar heel pain (0.8-1.9 cm on the 10-cm VAS)[20,21] in the 3 groups from week 2 and continued to improve up to week 24. To date, no minimally important difference has been reported for the Maryland Foot Score in plantar fasciitis. Interestingly, we did not observe a difference between the anesthetic alone, corticosteroid, and BoNT-A groups. We hypothesized that botulinum toxin A was going to show better results in the treatment of plantar fasciitis than cortisone. The anesthetic was just a control group. By not getting the expected outcome, we needed to reframe and try to explain our results.

Ropivacaine is considered a well-tolerated regional anesthetic for the relief of postoperative pain. An adequate dose of ropivacaine is associated with a lower incidence of motor block compared with bupivacaine. The recommended injected dose is 7.5-225 mg (1-30 mL).[19] In our study, we used a 7.5-mg/mL preparation, with a total injected concentration of 37.5 mg. Altogether with the stretching exercises and maybe the so-called context effects or nonspecific effects (in which the patient shows a relief of her or his symptoms because of natural resolution, expectancy effects, or because of the warm, friendly, and reassuring manner of the physician)[10] or/and the efficacy paradox (in which the treatment benefit experienced by the patient usually equates more with the overall treatment response seen in the treatment group),[33] we may explain the sustained improvement.

Kalaci et al[17] reported excellent clinical results using corticosteroid injection (triamcinolone). They evaluated their patients with a VAS and the modified Roles and Maudsley score at 3 weeks and at 6 months. They reported better results with corticosteroid injection using the peppering technique. In this same study, another group received intralesional anesthetics using the same technique, and although the pain in these patients decreased at 3 and 6 months, this was not statistically significant. A different study compared the use of corticosteroid injection (40 mg of methylprednisolone acetate) with joint mobilization and stretching exercises. Both groups of patients showed improved outcomes during the 1-year follow-up evaluation. The patients with steroid injection had better scores at the evaluation time points.[4] Similar to these results, the patients treated with corticosteroid in our study showed a significant improvement in pain and functional scales compared with the initial values, but the improvement was similar to the other 2 groups.

Table 2. Between and Within Analysis of Clinical Outcomes Over Time in the Different Treatment Groups.

	Anesthetic (n=18)		Steroid (n=21)		Botulinum toxin A (n=21)		
Outcome/Time	Mean ± SD	Mean difference (95% CI)	Mean ± SD	Mean difference (95% CI)	Mean ± SD	Mean difference (95% CI)	*P* value[a]
VAS score, cm							
Baseline	7.6 ± 0.26		7.8 ± 0.41		8.0 ± 0.33		
2 wk	5.7 ± 0.40[#]	−1.9 (−0.14, −3.75)	5.1 ± 0.39**	−2.6 (−0.72, −4.52)	5.6 ± 0.55*	−2.43 (−0.24, −4.62)	
4 wk	4.6 ± 0.62***	−3.0 (−1.20, −4.80)	5.0 ± 0.51***	−2.7 (−0.81, −4.62)	4.6 ± 0.61***	−3.43 (−1.24, −5.62)	
12 wk	3.4 ± 0.51***	−4.17 (−2.37, −5.97)	3.9 ± 0.49***	−3.9 (−2.00, −5.81)	3.4 ± 0.58***	−4.62 (−2.43, −6.81)	
24 wk	2.1 ± 0.33***	−5.5 (−3.70, −7.30)	2.6 ± 0.53***	−5.2 (−3.29, −7.09)	2.5 ± 0.58***	−5.48 (−3.29, 7.66)	.7702
Maryland Foot Score							
Baseline	82.3 ± 2.94		84.1 ± 2.90		77.1 ± 3.42		
2 wk	89.1 ± 2.99	6.8 (17.02, −3.35)	88.0 ± 2.74	3.9 (12.51, −4.70)	87.0 ± 2.55	9.9 (21.37, −1.56)	
4 wk	90.3 ± 2.77	8.0 (18.18, −2.18)	94.3 ± 1.30**	10.2 (18.84, 1.63)	93.9 ± 1.74***	16.8 (28.22, 5.30)	
12 wk	93.3 ± 1.89[#]	11.0 (21.18, 0.82)	93.6 ± 1.31*	9.5 (18.13, 0.92)	88.3 ± 2.89	11.2 (22.65, −0.27)	
24 wk	99.4 ± 1.55[b],***	17.1 (27.29, 6.93)	96.1 ± 1.78**	12.0 (20.60, 3.40)	90.6 ± 3.21[b],*	13.5 (24.99, 2.06)	**.0387**[c]

Abbreviation: VAS, visual analog scale.
[a]One-way analysis of variance, Bonferroni multiple comparison test between treatments at 24 weeks.
[b]Significant difference between groups ($P < .05$).
[c]Bold indicates significant difference.
[#]$P < .05$; **$P < .01$; ***$P < .001$ vs baseline values.

Table 3. Between and Within Analysis of Fascia Thickness and Dorsiflexion Over Time in the Different Treatment Groups.

Outcome/Time	Anesthetic, mean ± SD (n=18)	Steroid, mean ± SD (n=21)	Botulinum toxin A, Mean ± SD (n=21)	*P* value[a]
Fascia thickness (mm)				
Baseline	6.9 ± 0.4	6.1 ± 0.4	6.1 ± 0.4	
24 wk	5.9 ± 0.3***	5.9 ± 0.3	5.6 ± 0.3	.6958
Dorsiflexion (degrees)				
Baseline	9.2 ± 0.7	6.2 ± 1.0	6.2 ± 0.8	
24 wk	11.4 ± 0.8	10.1 ± 0.8	10.0 ± 0.5***	.2829

[a]One-way analysis of variance; Bonferroni multiple comparison test between treatments at 24 weeks.
***$P < .001$ vs baseline values.

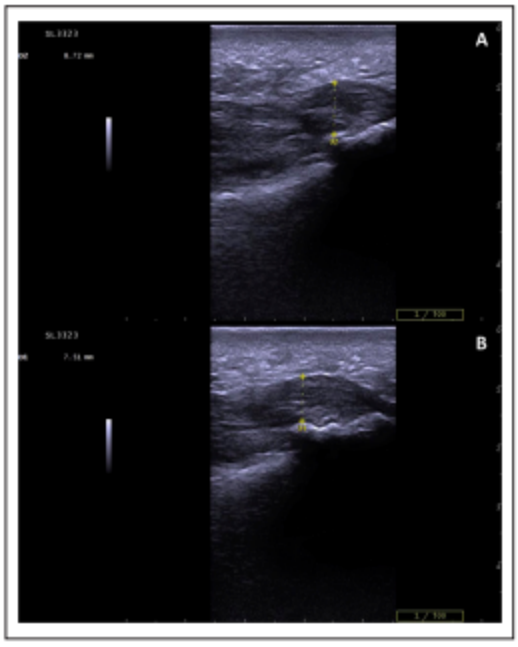

Figure 4. Plantar fascia measure showing the images (A) pretreatment and (B) posttreatment at the end of the study.

Díaz-Llopis et al[8] compared BoNT-A with a corticosteroid and found better results in patients treated with BoNT-A at 6 months[9] and at 1-year of follow-up. They injected BoNT-A in 2 different sites: 40 U were injected in the insertion of the plantar fascia, and 30 U were injected at 1-inch distal to the talar insertion of the plantar fascia. Previously, Babcock et al[3] used a similar application approach of 70 U of BTX-A applied to 2 different sites (40 and 30 U) compared with placebo. They found better results in patients who received BoNT-A in the evaluation of pain (VAS) and the Maryland Foot Score in a follow-up of 3-8 weeks. We previously reported the intralesional application of corticosteroid (8 mg of dexamethasone) compared with 250 U of BoNT-A (Dysport). BoNT-A was applied in the gastro-soleus complex (200 U to each one of the calf muscles and 50 U to the soleus muscle). The patients treated with BoNT-A had better and faster improvement in pain and functional scores during the 6-month follow-up compared with the patients treated with corticosteroid.[12] In the current study, we performed a single intralesional application of BoNT-A at the point of maximum tenderness. Similar to the other 2 groups, the patients in the BoNT-A group showed a significant improvement in pain and functional scores during the follow-up.

In the case of BoNT-A, it might be possible that its anti-inflammatory and pain mediator blockade effect was overestimated. In previously commented studies[3,8,9,12] which reported better results compared to cortisone or placebo, the authors applied the BoNT-A following the indication to apply it in the muscle belly, thus observing its blocking function of acetylcholine and possibly decrease the contracture.

In our trial, we injected the treatment directly in the fibrous insertion of the plantar fascia expecting that its anti-inflammatory and pain blocking properties would improve the symptomatology of the patients. In prior studies where this was done[1,24] and just like ours, reported improvement of pain and function compared to the baseline scores of the study but did not show significant difference at 6 months between comparative groups. Ahmad et al[1] reported a significant improvement in the BoNT-A group but at 6 months and was maintained at 12 months of follow-up using Xeoming. However, some patients may have used therapeutic exercise and/or orthotics more than others, which can affect the success rates with such treatment.[1] Likewise, Huang et al,[15] applying Botox vs placebo under ultrasonographic guidance, reported significant improvement of the toxin group but in a 3-month follow-up study design.

On the other hand, the thickness of the plantar fascia was measured before the treatment and at the end of the study, showing a diminished thickness in all patients, with no differences between groups. The mean normal thickness of the

plantar fascia has been reported as 4.0 mm, and it is considered an indicator of pathology when the thickness is >4.0 mm, which is related to the symptoms of the patient.[2,22] Our results revealed that all patient groups showed a reduction in plantar fascia thickness after the treatment, but the mean thickness was still above normal (5.7 mm). In spite of these results, the patients showed a good clinical evolution. Similar results were reported by Ermutlu et al,[13] where the functional recovery of the patients was not associated with a normal degree of fascia thinning after treatment.

It has been reported that rigidity in the gastrocnemius-soleus complex decreases the dorsiflexion movement of the foot, predisposing the individual to the development of chronic foot problems. Contracture of the gastrocnemius-soleus muscular complex, defined as a limitation in dorsiflexion of less or equal to 10 degrees, is present in up to 88% of patients.[11] All of the patients enrolled in the study were encouraged to carry out the Achilles tendon stretching described by DiGiovanni et al[11] and showed improvement in ankle dorsiflexion and function as well as pain. Most of the time, the outcome for individuals with acute plantar fasciitis is favorable. Approximately 90%, have resolution of the symptoms within 10 months.[7]

Our study has some limitations that deserve mentioning. First, there was a lack of a placebo group or a group of patients intervened with a stretching exercise program alone which might have helped to elucidate the therapeutic effect of the injected treatments. Second, some patients had an incomplete follow-up that was remedied with an appropriate and robust imputation analysis. Third, our study population was low-income and lack social security, so they sought a treatment option that would allow them to return to their job activities as quickly as possible. That was the reason why 2 months was decided as the cutoff period for failure of conventional treatment. We acknowledge that giving more time to the conservative management may have provided the patients the possibility to respond to traditional non-injection treatment. Finally, this study had a short follow-up, and even though this pathology can be considered a self-limited disease, a more prolonged follow-up could be helpful to determine the true effects of each treatment.

In conclusion, no significant differences between the 3 injection therapies were observed. There was a sustained improvement in pain and functional outcomes in each of the treatment groups after 24 weeks. The unexpected outcome in the anesthetic group highlights the lack of a control group. The question of whether the improvement was due to the injection therapies or because of the increased range of motion and the diminished thickness in the plantar fascia is unclear. Future studies addressing this question may confirm whether or not we should be providing any injection treatment.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. ICMJE forms for all authors are available online.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Carlos Acosta-Olivo, PhD, MD, https://orcid.org/0000-0002-2025-1865

References

1. Ahmad J, Ahmad SH, Jones K. Treatment of plantar fasciitis with botulinum toxin: a randomized, controlled study. *Foot Ankle Int*. 2017;38(1):1-7.
2. Argerakis NG, Positano RG, Positano RCJ, et al. Ultrasound diagnosis and evaluation of plantar heel pain. *J Am Podiatr Med Assoc*. 2015;105(2):135-140.
3. Babcock MS, Foster L, Pasquina P, Jabbari B. Treatment of pain attributed to plantar fasciitis with botulinum toxin A: a short-term, randomized, placebo-controlled, double-blind study. *Am J Phys Med Rehabil*. 2005;84(9):649-654.
4. Celik D, Kus G, Önder Sirma S. Joint mobilization and stretching exercise vs steroid injection in the treatment of plantar fasciitis: a randomized controlled study. *Foot Ankle Int*. 2016;37(2):150-156.
5. Clark TG, Altman DG. Developing a prognostic model in the presence of missing data: an ovarian cancer case study. *J Clin Epidemiol*. 2003;56(1):28-37.
6. David JA, Sankarapandian V, Christopher PRH, Chatterjee A, Macaden AS. Injected corticosteroids for treating plantar heel pain in adults. *Cochrane Database Syst Rev*. 2017;6(6):CD009348.
7. Davis PF, Severud E, Baxter DE. Painful heel syndrome: results of nonoperative treatment. *Foot Ankle Int*. 1994;15(10):531-535.
8. Díaz-Llopis IV, Gómez-Gallego D, Mondéjar-Gómez FJ, López-García A, Climent-Barberá JM, Rodríguez-Ruiz CM. Botulinum toxin type A in chronic plantar fasciitis: clinical effects one year after injection. *Clin Rehabil*. 2013;27(8):681-685.
9. Díaz-Llopis IV, Rodríguez-Ruíz CM, Mulet Perry S, Mondéjar-Gómez FJ, Climent-Barberá JM, Cholbi-Llobel F. Randomized controlled study of the efficacy of the injection of botulinum toxin type A versus corticosteroids in chronic plantar fasciitis: results at one and six months. *Clin Rehabil* 2011;26(7):594-606.
10. Di Blasi Z, Harkness E, Ernst E, Georgiou A, Kleijnen J. Influence of context effects on health outcomes: a systematic review. *Lancet*. 2001;357(9258):757-762.
11. DiGiovanni BF, Nawoczenski DA, Lintal ME, et al. Tissue-specific plantar fascia-stretching exercise enhances outcomes in patients with chronic heel pain. A prospective, randomized study. *J Bone Joint Surg Am*. 2003;85(7):1270-1277.
12. Elizondo-Rodriguez J, Araujo-Lopez Y, Moreno-González JA, Cardenas-Estrada E, Mendoza-Lemus O, Acosta-Olivo C. A comparison of botulinum toxin A and intralesional steroids for the treatment of plantar fasciitis: a randomized, double-blind study. *Foot Ankle Int*. 2013;34(1):8-14.
13. Ermutlu C, Aksakal M, Gümüstas A, Ozkaya G, Kovalak E, Özkan Y. Thickness of plantar fascia is not predictive of

functional outcome in plantar fasciitis treatment. *Acta Orthop Traumatol Turc*. 2018;52(6):442-446.
14. Horton NJ, Lipsitz SR. Multiple imputation in practice: comparison of software packages for regression models with missing variables. *Am Stat*. 2001;55(3):244-254.
15. Huang YC, Wei SH, Wang HK, Lieu FK. Ultrasonographic guided botulinum toxin type A treatment for plantar fasciitis: an outcome-based investigation for treating pain and gait changes. *J Rehabil Med*. 2010;42(2):136-140.
16. Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomised clinical trials—a practical guide with flowcharts. *BMC Med Res Methodol*. 2017;17(1):162.
17. Kalaci A, Cakici H, Hapa O, Yanat AN, Dogramaci Y, Sevinc TT. Treatment of plantar fasciitis using four different local injection modalities. A randomized prospective clinical trial. *J Am Podiatr Med Assoc*. 2009;99(2):108-113.
18. Kamel M, Eid H, Mansour R. Ultrasound detection of heel enthesitis: a comparison with magnetic resonance imaging. *J Rheumatol*. 2003;30(4):774-778.
19. Kuthiala G, Chaudhary G. Ropivacaine: a review of its pharmacology and clinical use. *Indian J Anaesth*. 2011;55(2):104-110.
20. Landorf KB, Radford JA. Minimal important difference: values for the foot health status questionnaire, foot function index and visual analogue scale. *Foot*. 2008;18(1):15-19.
21. Landorf KB, Radford JA, Hudson S. Minimally important difference (MID) of two commonly used outcome measure for foot problems. *J Foot Ankle Res*. 2010;3:7.
22. McMillan AM, Landorf KB, Barrett JT, Menz HB, Bird AR. Diagnostic imaging for chronic plantar heel pain: a systematic review and meta-analysis. *J Foot Ankle Res*. 2009;2:32
23. Patel A, DiGiovanni B. Association between plantar fasciitis and isolated contracture of the gastrocnemius. *Foot Ankle Int*. 2011;32(1):5-8.
24. Peterline CD, Funk JF, Hölscher A, Schuh A, Placzek R. Is botulinum toxin A effective for the treatment of plantar fasciitis. *Clin J Pain*. 2012;28(6):527-533.
25. Riddle DL, Pullsic M, Pidcoe P, Johnson RE. Risk factors for plantar fasciitis: a matched case-control study. *J Bone Joint Surg Am*. 2003;85(5):872-877.
26. Rosenbaum AJ, DiPreta JA, Misener D. Plantar heel pain. *Med Clin North Am*. 2014;98(2):339-352.
27. Sanders R, Fortin P, DiPasquale T, Walling A. Operative treatment in 120 displaced intraarticular calcaneal fractures. Results using a prognostic computed tomography scan classification. *Clin Orthop Relat Res*. 1993;290:87-95.
28. Seyler TM, Smith BP, Marker DR, et al. Botulinum neurotoxin as a therapeutic modality in orthopaedic surgery: more than twenty years of experience. *J Bone Joint Surg Am*. 2008;90(suppl 4):133-145.
29. Singh D, Angel J, Bentley G, Trevino SG. Fortnightly review. Plantar fasciitis. *BMJ*. 1997;315(7101):172-175.
30. Sterne JAC, White IR, Carlin JB, et al. Multiple imputations for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ*. 2009;338:b2393.
31. Tsikopoulos K, Vasiliadis HS, Mavridis D. Injection therapies for plantar fasciopathy ("plantar fasciitis"): a systematic review and network meta-analysis of 22 randomised controlled trials. *Br J Sports Med*. 2016;50(22):1367-1375.
32. Whittaker GA, Munteanu SE, Menz HB, Bonanno DR, Gerrard JM, Landorf KB. Corticosteroid injection for plantar heel pain: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2019;20(1):378.
33. Zhang W, Doherty M. Efficacy paradox and proportional contextual effect (PCE). *Clin Immmunol*. 2018;186:82-86.

Plantar Fasciitis—A Comparison of Treatment with Intralesional Steroids versus Platelet-Rich Plasma

A Randomized, Blinded Study

Carlos Acosta-Olivo, MD, PhD*
Jorge Elizondo-Rodriguez, MD*
Ricardo Lopez-Cavazos, MD*
Felix Vilchez-Cavazos, MD, PhD*
Mario Simental-Mendia, BsSc*
Oscar Mendoza-Lemus, MD, PhD*

Background: Many treatment options for plantar fasciitis currently exist, some with great success in pain relief. The objective of our study was to compare the use of intralesional steroids with platelet-rich plasma (PRP), using pain scales and functional evaluation, in patients with plantar fasciitis who did not respond to conservative treatment.

Methods: A controlled, randomized, blinded clinical assay was performed. Patients were assigned to one of the two groups by selecting a sealed envelope. The steroid treatment group received 8 mg of dexamethasone plus 2 mL of lidocaine as a local anesthetic. The PRP treatment group received 3 mL of PRP activated with 0.45 mL of 10% calcium gluconate. All of the patients were evaluated at the beginning of the study, and at 2, 4, 8, 12, and 16 weeks post-treatment with the Visual Analog Scale (VAS), Foot and Ankle Disability Index (FADI), and American Orthopedic Foot and Ankle Society (AOFAS) scale.

Results: The right foot was the most frequently affected foot (63%). The average age of the patients was 44.8 years (range, 24–61 years). All scales used (VAS, FADI and AOFAS) showed that the difference was not statistically significant between the two groups.

Conclusions: We can conclude that the use of PRP is an effective treatment method for patients with plantar fasciitis who do not respond to conservative treatment because PRP demonstrates an efficacy equal to that of steroids. However, the cost and the time for preparation the PRP are two of the disadvantages of this treatment. (J Am Podiatr Med Assoc 107(6): 490-496, 2017)

The pathology that is usually present in the medial heel region has traditionally been known as plantar fasciitis. However, recently, the term *plantar fasciosis* has been used to dismiss the inflammatory component and emphasize the degenerative nature that is observed histologically in the insertion zone in the calcaneus.[1] Regardless of its inflammatory or degenerative nature, this pathology is usually described as heel pain in the medial calcaneal tuberosity.[2] It is estimated that 1 in 10 people may experience heel pain at some point in their lives.[3] Up to one third of cases may be bilateral[4] and are usually observed in patients of working age, between 40 and 60 years old, patients with intense physical activity, or in patients whose body mass index is >30 kg/m^2.[4-7]

The most common initial treatment includes the use of analgesics, stretching exercises, and rest. However, in cases where conservative treatment is ineffective, infiltration with intralesional steroids is often used. This procedure is usually effective in patients with acute pain but produces only short-

*Department of Orthopedics and Traumatology, Universidad Autonoma de Nuevo Leon, Nuevo Leon, Mexico.

Corresponding author: Carlos Acosta-Olivo, MD, PhD, Department of Orthopedics and Traumatology, Universidad Autonoma de Nuevo Leon, Ave Madero y Gonzalitos S/N 4th Floor, Monterrey, Nuevo Leon, 64480, Mexico. (E-mail: dr.carlosacosta@gmail.com)

term pain relief.[8] Customarily, these treatments are accompanied by exercises for stretching the gastrocnemius and soleus muscles and the plantar fascia itself.[2,9] One of the most used treatment methods is infiltration with steroids, which relieves the pain rapidly, and reports have demonstrated its effectiveness for treating plantar fasciitis.[2] However, complications have also been described with its use, such as application site infections, heel fat pad atrophy, and plantar fascia rupture. Although the rupture of the fascia may help to resolve the pain, it usually affects the biomechanics of the foot.[10,11]

Recently, platelet-rich plasma (PRP) has been used as a therapeutic alternative for obtaining relief and resolution of symptoms. There are various modalities of PRP preparation, which result in greater or lesser concentrations of leukocytes according to the number of centrifugations used and the revolution velocity employed. There are currently several trademarked products on the market that can be used. The biotechnology now in use has reportedly been successfully used for muscle and tendon injuries.[12] Additionally, its safety and potential for reducing pain has previously been proven in patients with plantar fasciitis.[13,14]

In its simplest definition, PRP is a blood derivative with a higher number of platelets than those found in peripheral blood.[15] Currently, PRP can be obtained through a process of two-phase centrifugation known as plasmapheresis in which the liquid and solid components of the anticoagulated blood are separated. The first phase is carried out at a lower centrifugation speed (1,200–1,500 rpm), and it separates the plasma and platelets from the white and red cells. The second phase is performed at a higher centrifugation speed (4,000–7,000 rpm) to increase the concentrations of PRP and platelet-poor plasma.[15] The PRP formulation may vary in cellular content, which may influence its effects on tissue healing. Thus, two principal types of PRP are produced: leukocyte-rich PRP (LR-PRP), which includes white blood cells, and leukocyte-poor PRP (LP-PRP), which contains a minimal amount of white blood cells. The increase in the number of platelets is also a variable in these samples.[12] The white cells, as well as monocytes and neutrophils, can trigger localized inflammatory effects. These effects may suggest that these cells are critical to the repair process; however, some reports have found that neutrophils may impede healing.[16]

Once the PRP is obtained, it can be applied with an activating agent, such as thrombin, gluconate, or calcium chloride, to release growth factors rapidly, or it can be infiltrated directly and thereby produce a slower release when activated by the collagen in the area.[17,18]

In addition to the variations previously described, other patient factors, such as age and comorbidities, may also cause variations in the cellular content and the growth factors in the PRP.[19] However, the optimal amount of platelets and growth factors required for the healing of tendons or muscles is not yet known. According to Marx,[20] clinical effectiveness was obtained with a concentration of at least four times that of the normal platelet concentration. However, efficacy studies have been performed with preparations of lower concentrations,[21,22] including a study by Giusti et al,[23] who proposed that the most effective platelet concentration for stimulation of angiogenesis was 1.5×10^6 platelets per microliter in an in vitro study.

The objective of our study was to compare the use of intralesional steroids against intralesional PRP, using pain scales and functional evaluation, in patients with plantar fasciitis who did not respond to conservative treatment.

Patients and Methods

A controlled, randomized, blinded clinical assay was performed (Fig. 1). All of the patients included in our study were diagnosed with plantar fasciitis in the outpatient clinic by the same orthopedist (J.E.R.). All of the patients underwent conventional radiographs of the foot and magnetic resonance imaging (MRI) to rule out stress fractures and associated bone lesions. The inclusion criteria consisted of skeletally mature patients with heel pain at the insertion of the plantar fascia (anteriormedial calcaneal tuberosity), failure of conservative treatment for 3 months (orthotics and nonsteroidal anti-inflammatory drugs, without stretching exercise), and no previous infiltrations. The exclusion criteria consisted of patients with associated pathologies, such as alterations in the ipsilateral ankle and knee, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome, neurological abnormalities, skin infections, or a history of infection at the application site in the previous 3 months. The ethics committee of our institution approved this study. All of the included patients were informed regarding their condition. Likewise, the purpose of the study was explained to them, and all agreed to participate by signing an informed consent form. Patients were assigned to one of the two groups in a randomized manner by selecting a sealed envelope. All procedures were applied by the same researcher (R.L.C.), who was blinded to the

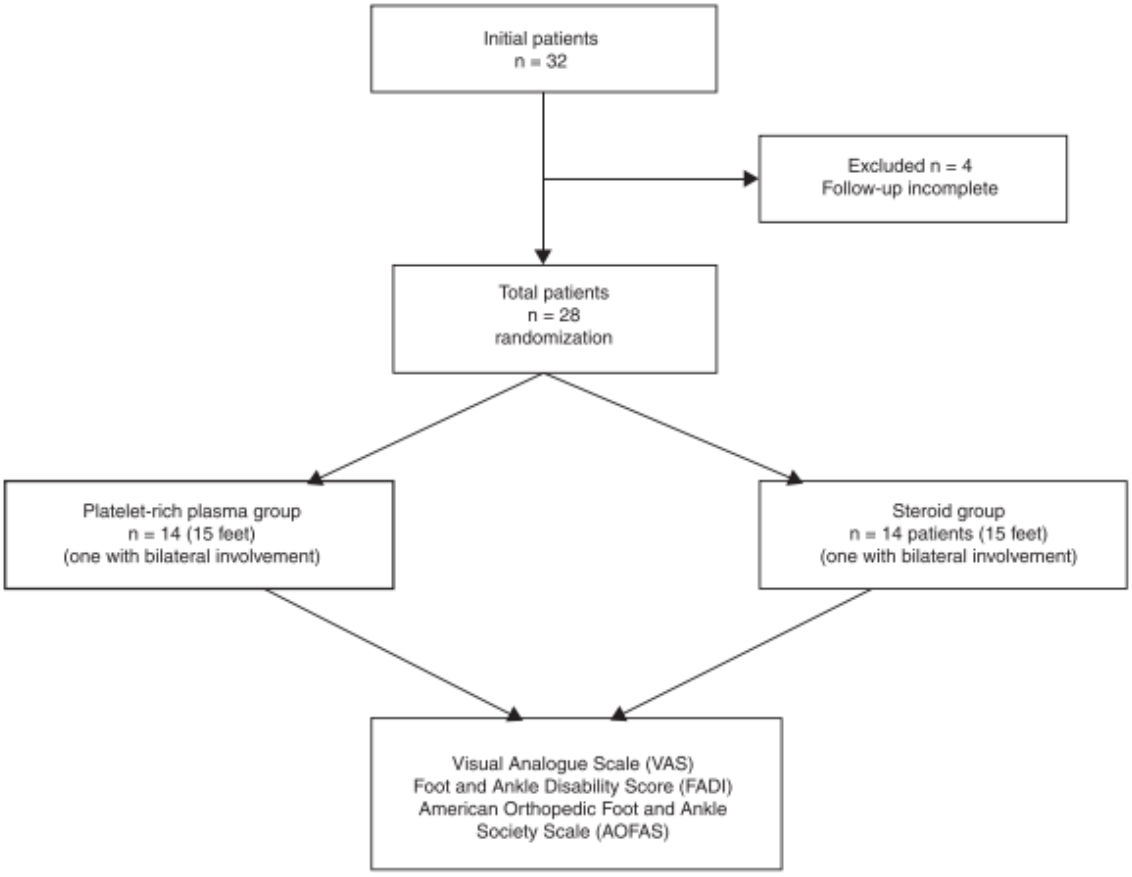

Figure 1. Flow chart of patient selection, randomization, treatment, and evaluation.

application through the use of covered syringes; further assessments were performed by another investigator (J.E.R.) blinded to the treatment.

Steroid Application

The steroid treatment group received 8 mg of dexamethasone (Alin Depot; Chinoin, Aguascalientes, Mexico) plus 2 mL of lidocaine as a local anesthetic. Asepsis of the heel region was performed with antiseptic sanitizer (Avagard; 3M, St. Paul, Minnesota) for 2 minutes. The drug was administered afterward by an infiltration in the anteromedial zone of the calcaneus (zone of greatest pain).

Preparation and Application of PRP

A 40-mL volume of whole blood was taken from the basilic or antecubital vein of the upper limb in sterile tubes and vacuum sealed with 3.8% sodium citrate as an anticoagulant (BD Vacutainer; Becton, Dickinson and Company, New Jersey). The samples were transported to the tissue engineering laboratory of the bone and tissue bank where they were centrifuged for 10 minutes at 1,800 rpm (Heraeus Megafuge 1.0R; Fisher Scientific, Waltham, Massachusetts) to separate the cellular parts corresponding to the erythrocytes and leukocytes. The upper plasma layer was removed from each of the tubes (taking care not to remove the buffy coat) and collected into a 50-mL sterile conical polypropylene tube (Falcon; Fisher Scientific, Corning, New York) for a second centrifugation step for 12 min at 3,400 rpm. The plasma supernatant, or platelet poor plasma (PPP), was removed, leaving a volume of 3 mL in which the platelets were resuspended. The 3 mL of PRP obtained was transferred to a sterile glass tube and vacuum sealed without anticoagulant (BD Vacutainer). An aliquot of the final PRP was

sent to the laboratory to quantify the number of platelets. Manipulation of the samples was performed in a sterile environment within a class II biosafety cabinet (Logic 3440801; Labconco, Kansas City, Missouri). Prior to the administration of PRP to the patient, activation of the platelets was induced by adding 0.45 mL of 10% calcium gluconate and inverting the sample several times to ensure a homogeneous mixture. Then, the activated PRP was aspirated with a 5-mL syringe for application to the patient using the technique described above after asepsis and the application of 2 mL of lidocaine into the application site.

Analysis of Whole Blood and PRP Samples

Additionally, for all patients, a blood sample was obtained in a tube that contained EDTA as an anticoagulant (BD Vacutainer). An analysis of the baseline platelet content (in the whole blood) and the platelet content in each of the PRP samples that were generated was performed.

Post-Treatment Monitoring and Management of Patients

All of the patients were given an explanation and instructions for the exercise program, which consisted of stretching the plantar fascia with the patient seated while performing an extension of the toes with his or her hand, and crossing the affected leg on the opposite thigh. The patients were instructed to perform 10 repetitions of each exercise three times a day and to maintain the exercise for 10 sec during each repetition, according to DiGiovanni et al.[9]

All of the patients were evaluated at the beginning of the study (pretreatment) and at 2, 4, 8, 12, and 16 weeks post-treatment with the Visual Analog Scale (VAS),[24] Foot and Ankle Disability Index (FADI),[25] and American Orthopedic Foot and Ankle Society (AOFAS) scale.[26] The VAS assesses the pain level by assigning a score from 0 to 10, with 0 representing no pain and 10 representing the worst pain level. The FADI scale assesses activities such as standing, walking on flat or uneven surfaces, walking on inclines, and the length of time of walking without difficulty. It also includes a section for sports activities and ankle or foot pain (or both). The highest score is 136 points, indicating the best clinical situation, free of pain and limitations, while the lowest score is 0. The AOFAS scale evaluates foot pain, function, and alignment. The best score is 100 and indicates wellness, while the lowest score is 0, indicating the worst possible condition of the patient.

Statistical Analysis

Using a formula to test hypothesis and two media difference, with a value of $z\alpha$ of 1.96 with significance level of 95 for two tails, and a value $z\beta$ of 1.24 with power 90, a sample of 13 participants for each of the groups was obtained. The results were reported in contingency tables, frequency tables, percentages, measures of central tendency and dispersion. Quantitative variables were analyzed with a Student t test for independent samples with a significance level of 95 with their respective confidence intervals. A P-value of <0.05 was considered statistically significant. Statistical analysis was performed with IBM SPSS version 20 (SPSS, Inc, Armonk, New York).

Results

Demographic data

We included a total of 32 patients divided into two groups of 16 patients each and excluded two patients in each group (four total) for not completing the follow-up. The final number of patients included was 28, which consisted of 14 patients in the steroid group (one patient with bilateral involvement) and 14 patients in the PRP group (one patient with bilateral involvement), with a total of 30 treated feet. The right foot was the most frequently affected foot (63%). The average age of the patients was 44.8 (range, 24–61) years, and 80% of the patients were female, while 20% were male. The patients did not experience any treatment-related complications in either group. The mean $\pm$ SD of the platelet number in the peripheral blood and PRP was 270.4 $\pm$ 71.1 $\times$ 10e3/μL and 678.8 $\pm$ 198.7 $\times$ 10e3/μL, respectively, meaning there were 2.5 times more platelets in PRP than in whole blood.

Visual Analog Scale

Before the infiltration, the pain experienced by the patients included in the steroid-treated group was more intense and showed statistical significance. During patient follow-up, an improvement in pain (decrease in the VAS score) was found in both groups. The difference was not statistically significant between the two groups. At the end of the study, the VAS value in the steroid group was 0.47

Table 1. Results of Visual Analog Scale

Time, wk	Steroid Group	PRP Group	*P* Value
Pretreatment	5.67 ± 1.54	4.53 ± 1.12	0.02
2	3.33 ± 1.67	3.33 ± 1.04	0.89
4	2.21 ± 1.69	2.42 ± 1.45	0.73
8	1.27 ± 1.53	1.13 ± 1.33	0.79
12	0.53 ± 1.06	0.62 ± 0.73	0.84
16	0.47 ± 1.34	0.33 ± 0.72	0.73

Note: Data are provided as mean ± SD.
Abbreviation: PRP, platelet-rich plasma.

(± 1.3), while the value of the PRP group was 0.33 (± 0.72) (Table 1).

Foot and Ankle Disability Index

During the initial evaluation, no statistically significant difference between the two groups was found for the FADI score. During follow-up consultations (2, 4, 8, 12, and 16 weeks), a progressive increase in the FADI score was observed in both groups of patients, reflecting clinical improvement. However, the difference in improvement between the two groups during the follow-up consultations was not statistically significant (Table 2).

American Orthopedic Foot and Ankle Society Scale

At the beginning of the evaluation, no statistically significant differences between groups were presented. Throughout the evaluation period, clinical improvement in the patients was evident, but no significant difference between the two study groups was observed (Table 3).

Discussion

In recent years, the use of PRP has increased in diverse clinical situations such as biological and autologous therapeutic alternatives. For the VAS,

Table 2. Results of Foot Ankle Disability Index (FADI)

Time, wk	Steroid Group	PRP Group	*P* Value
Pretreatment	66.8 ± 12.2	76.2 ±19.2	0.07
2	100.2 ± 20.5	96.6 ±19.5	0.62
4	116.2 ±17.8	108.2 ± 22.1	0.28
8	123.4 ±18.6	126.6 ± 14.0	0.6
12	132.9 ± 7.2	133.9 ± 2.7	0.62
16	130.9 ±15.2	134.8 ± 2.7	0.34

Note: Data are provided as mean ± SD.
Abbreviation: PRP, platelet-rich plasma.

Table 3. Results of AOFAS

Time, wk	Steroid Group	PRP Group	*P* Value
Pretreatment	67.6 ± 10.7	72.3 ± 9.1	0.22
2	82.6 ± 9.7	80.8 ± 6.0	0.54
4	86.8 ± 9.8	85.9 ± 6.7	0.76
8	91.4 ± 10.0	96.1 ± 10.1	0.21
12	96.8 ± 5.4	94.4 ± 5.7	0.25
16	97.2 ± 8.4	96.2 ± 6.0	0.73

Note: Data are provided as mean ± SD.
Abbreviation: PRP, platelet-rich plasma.

we found that at the beginning of the evaluation, the patients treated with steroids had significantly greater pain than those in the group that received PRP (Table 1). However, during all subsequent evaluations, both groups presented improvement, and no differences between the groups were found at the end of the study. For the evaluation of the FADI and AOFAS functional ankle scales, at the beginning of the study both groups were similar, with no differences between them, and all patients improved throughout the duration of the study (Tables 2–3). At the end of the study, no significant differences were observed between the two groups. One of the key components for the treatment of the chronic plantar fasciitis involves fascia and gastrocsoleus complex stretching exercises, as described above by DiGiovanni et al.[9] Therefore, we think that the intralesional infiltration may be used with steroids or PRP as an adjuvant for the rapid alleviation of pain and to initiate the stretching exercises.

In particular, clinical studies[14,27] have reported the use of PRP as a safe and effective treatment for plantar fasciitis. In one of these studies, 14 consecutive patients were treated with three injections of PRP for 12 months. They were assessed using the modified Roles and Maudsley score as well as the VAS, and good results were shown in nine patients (64%). The VAS score decreased significantly from 7.1 (± 1.1) before treatment to 1.9 (± 1.5) at the final follow-up evaluation ($P < 0.01$).[14] Double centrifugation PRP was applied to 23 consecutive patients who were the subjects of a retrospective study, and they were assessed using the VAS, Medical Outcomes Study Short Form 12 Health Survey, and Foot and Ankle Outcome Score (FAOS). A mean improvement of the VAS score from 7 to 4 was found. The FAOS scores for the pain, symptomatology, and quality of life scales improved significantly during the follow-up period.[27] In a cohort-type study with two treatment methods (either steroids or PRP) using a commer-

cial system and evaluated with the VAS, FADI, and AOFAS, a significant improvement was found in all scales after 3 months for patients treated with PRP.[28]

A prospective evaluation of the use of double centrifugation PRP in plantar fasciitis was performed using the VAS pre- and post-application in addition to an assessment of the plantar fascia thickness by ultrasound. It was found that the VAS score decreased from 9.1 prior to the injection to 1.6 following the application. The rate of patient satisfaction was 88%, and significant changes in the thickness of the plantar fascia were observed during the study period. In addition, no complications were presented during the evaluation.[13]

Sixty patients with failure of conservative treatment were divided into two groups. The first 30 patients received 40 mg of methylprednisolone, and the other 30 patients received double centrifugation PRP. The patients were evaluated with the modified Roles and Maudsley criteria and the VAS at 3 weeks and 6 months after injection. No differences in the VAS were observed between the groups at the end of the study, but the scores were significantly lower in both groups compared to the values at the initiation of the study. Likewise, no differences were found between the groups when they were evaluated using the Roles and Maudsley criteria. It was concluded that both methods are effective for the treatment of the plantar fascia. In addition, the use of PRP appears to be advantageous, considering the possible complications from steroids.[29]

The weaknesses of our study include the short follow-up period of the patients, the low number of patients studied, and the inclusion of more epidemiological data such as IMC, which has been linked to an increase in the incidence of this condition.[30] The strengths of our study include the use of validated and standardized scales for this type of pathology and the absence of complications with any of the two types of infiltration. Additionally, we used our double centrifugation technique of PRP preparation, which has a lower cost than the commercial method.

We used double centrifugation to obtain the PRP with the lowest possible amount of white blood cells; the cells are usually activated with 10% calcium gluconate. With this procedure, activation of the PRP is usually achieved between 10 and 15 min after its incorporation, and to date, no application difficulty has been reported. We can conclude that the use of PRP is an effective treatment method for patients with plantar fasciitis who do not respond to conservative treatment because PRP demonstrates an efficacy equal to that of steroids, without presenting, so far, the complications associated with steroid use that were not present during the time of this study. On the other hand, PRP is more expensive than a steroid infiltration; the process to obtain the PRP requires more time for the patient and the physician. In addition, the regenerative properties of PRP on soft tissues, such as muscles and tendons, could represent an additional benefit to patients by reducing inflammation and promoting the regeneration of damaged tissue.[31] Plantar fasciitis treatment with PRP seems promising; however, more studies with level 1 evidence are needed to determine the real beneficial effects of this therapy.

Financial Disclosure: None reported.
Conflict of Interest: None reported.

References

1. Lemont H, Ammirati KM, Usen N: Plantar fasciitis: a degenerative process (fasciosis) without inflammation. JAPMA **93:** 234, 2003
2. Thomas JL, Christensen JC, Kravitz SR, et al: The diagnosis and treatment of heel pain: A clinical practice guideline-revision 2010. J Foot Ankle Surg **49:** S1, 2010.
3. Crawford F, Thomson C: Interventions for treating plantar heel pain. Cochrane Database Syst Rev **3:** CD000416, 2003.
4. Buchbinder R: Clinical practice: Plantar fasciitis. N Engl J Med **350:** 2159, 2004.
5. Riddle DL, Schappert SM: Volume of ambulatory care visits and patterns of care for patients diagnosed with plantar fasciitis: A national study of medical doctors. Foot Ankle Int **25:** 303, 2004.
6. Gill LH, Kiebzak GM: Outcome of nonsurgical treatment for plantar fasciitis. Foot Ankle Int **17:** 527, 1996.
7. Riddle DL, Pulisic M, Pidcoe P, et al: Risk factors for plantar fasciitis: A matched case-control study. J Bone Joint Surg Am **85:** 872, 2003.
8. Tatli YZ, Kapasi S: The real risks of steroid injection for plantar fasciitis, with a review of conservative therapies. Curr Rev Musculoskelet Med **2:** 3, 2009.
9. DiGiovanni BF, Nawoczenski DA, Malay DP, et al: Plantar fascia-specific excercise improves outcomes in patients with chronic plantar fasciitis. A prospective clinical trial with two-year follow-up. J Bone Joint Surg Am **88:** 1775, 2006.
10. Acevedo JI, Beskin JL: Complications of plantar fascia rupture associated with corticosteroid injection. Foot Ankle Int **19:** 91, 1998.
11. Sellman JR: Plantar fasciitis ruptura associated with corticosteroid injection. Foot Ankle Int **15:** 376, 1994.
12. Harmon KG, Rao AL: The use of platelet-rich plasma in the nonsurgical management of sports injuries: hype or

hope? Hematology Am Soc Hematol Educ Program **2013:** 620, 2013.
13. Ragab EM, Othman AM: Platelets rich plasma for treatment of chronic plantar fasciitis. Arch Orthop Trauma Surg **132:** 1065, 2012.
14. Martinelli N, Marinozzi A, Carni S, et al: Platelet-rich plasma injections for chronic plantar fasciitis. Int Orthop **37:** 839, 2013.
15. Mazzocca AD, McCarthy MB, Chowaniec DM, et al: Platelet-rich plasma differs according to preparation method and human variability. J Bone Jone Srug Am **94:** 308, 2012.
16. DeLong JM, Russell RP, Mazzocca AD: Platelet-rich plasma: The PAW classification system. Arthroscopy **28:** 998, 2012
17. Mishra A, Pavelko T: Treatment of chronic elbow tendinosis with buffered platelet rich plasma. Am J Sport Med **34:** 1774, 2006.
18. Fufa D, Shealy B, Jacobson M, et al: Activation of platelet-rich plasma using soluble type I collagen. J Oral Maxillofac Surg **66:** 684, 2008.
19. Mazzucco L, Balbo V, Cattana E, et al: Not every PRP-gel is born equal: Evaluation of growth factor availability for tissues through four PRP-gel preparation. Fibrinet, RegenPRP-Kit, Plateltex and one manual procedure. Vox Sang **97:** 110, 2009.
20. Marx RE: Platelet-rich plasma: Evidence to support its use. J Oral Maxillofac Surg **62:** 489, 2004.
21. Eppley BL, Woodell JE, Higgins J: Platelet quantification and growth factor analysis from platelet-rich plasma: Implications for wound healing. Plast Reconstr Surg **114:** 1502, 2004.
22. Sanchez M, Anitua E, Azofra J, et al: Comparison of surgically repaired Achilles tendon tears using platelet-rich fibrin matrices. Am J Sports Med **35:** 245, 2007.
23. Giusti I, Rughetti A, D'Ascenzo S, et al: Identification of an optimal concentration of an optimal concentration of platelet gel for promoting angiogenesis in human endotelial cells. Transfusion **49:** 771, 2009.
24. Huskisson EC: Measurement of pain. Lancet **2:** 1127, 1974.
25. Martin RL, Burdett RG, Irrgang JJ: Development of the foot and ankle disability index (FADI). J Orthop Sports Phys Ther **29:** A32, 1999.
26. Kitaoka HB, Alexander IJ, Adelaar RS, et al: Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. Foot Ankle Int **15:** 349, 1994.
27. O'Malley MJ, Vosseller JT, Gu Y: Successful use of platelet-rich plasma for chronic plantar fasciitis. HSS J **9:** 129, 2013.
28. Shetty VD, Dhillon M, Hegde C, et al: A study to compare the efficacy of corticosteroid therapy with platelet-rich plasma therapy in recalcitrant plantar fasciitis: A preliminary report. Foot Ankle Surg **20:** 10, 2014.
29. Aksahin E, Dogruyol D, Yüksel HY, et al: The comparison of the effect of corticosteroids and platelet-rich plasma (PRP) for the treatment of plantar fasciitis. Arch Orthop Trauma Surg **132:** 781, 2012.
30. Irving DB, Cook JL, Menz HB: Factors associated with chronic plantar heel pain: a systematic review. J Sci Med Sport **9:** 11, 2006.
31. Mishra A, Woodall J Jr, Vieira A: Treatment of tendon and muscle using platelet-rich plasma. Clin Sports Med **28:** 113, 2009.

AMERICAN ORTHOPAEDIC FOOT & ANKLE SOCIETY

Foot & Ankle International
34(1) 8–14

DOI: 10.1177/1071100712460215
http://fai.sagepub.com

A Comparison of Botulinum Toxin A and Intralesional Steroids for the Treatment of Plantar Fasciitis: A Randomized, Double-Blinded Study

Jorge Elizondo-Rodriguez, MD[1], Yariel Araujo-Lopez, MD[1], J. Alberto Moreno-Gonzalez, MD[1], Eloy Cardenas-Estrada, MD, PhD[1], Oscar Mendoza-Lemus, MD, PhD[1], and Carlos Acosta-Olivo, MD, PhD[1]

Abstract

Background: The objective of this study was to compare intramuscularly applied botulinum toxin A (BTX-A) in the gastroc-soleus complex with intralesional steroids for the treatment of plantar fasciitis.

Methods: The patients were randomly divided into 2 groups according to the treatment received. The patients were evaluated over 6 months. The evaluation scores included the Visual Analog Scale (VAS), Maryland Foot and Ankle, Foot and Ankle Disability Index (FADI), and American Orthopaedic Foot and Ankle Society (AOFAS) score. Moreover, patients were instructed to perform plantar fascia stretching exercises over the course of the study. The final number of patients was 36, of whom 19 received BTX-A (10 men and 9 women) and 17 (6 men and 11 women) received steroids.

Results: When compared to patients who received steroids, the patients who received BTX-A exhibited more rapid and sustained improvement over the duration of the study.

Conclusion: A combination of BTX-A and plantar fascia stretching exercises yielded better results for the treatment of plantar fasciitis than intralesional steroids.

Level of Evidence: Level I, therapeutic studies.

Keywords: botulinum toxin A, intralesional steroids, plantar fasciitis, stretching exercise, randomized, double-blind study

Plantar fasciitis is the most frequent cause of chronic heel pain. This pathology generally presents in patients who are 40 years of age or older, overweight, sedentary, or engage in intense physical activity.[14,32] Because of its anatomic orientation and its tensile strength, the plantar fascia functions to prevent foot collapse. It is a piece of thick connective tissue that originates at the base of the calcaneus and extends distally to the phalanges. Stretching of the plantar fascia prevents the displacement of the calcaneus and the metatarsals and helps to maintain the medial longitudinal arch. The plantar fascia simulates a cable between the calcaneus and the metatarsophalangeal joints. The windlass mechanism described by Hicks[13] for the action of the plantar fascia explains that during dorsiflexion of the toes, the length of the plantar fascia is effectively shortened, causing an elevation of the arch. Extension of the toes increases the arc of tension with the metatarsophalangeal joints, similar to an axis or anchor point. Shortening of the plantar fascia that results from dorsiflexion of the hallux is the essence of the reel mechanism. When a complete fasciotomy is performed, this mechanism is lost, decreasing the stability of the arch and interfering with stability during the terminal stance phase.[4,10,13,16,20,29,33]

Historically, the development of plantar fasciitis was attributed to biomechanical defects, such as hyperpronation, contributing to excessive mobility of the foot, which in turn increases the stress applied to musculofascial structures and soft tissues via an elongation of the plantar fascia.[3,5,6,18] Other studies have demonstrated that one of the principal causes of plantar fasciitis is mechanical overload.[11,13,14,16,25]

A great variety of therapies have been reported for the treatment of this pathology: intralesional application of steroids, platelet-rich plasma, intralesional botulinum toxin A (BTX-A), extracorporeal shock waves, and all of these treatments in combination with stretching exercises of the gastrocnemius, soleus muscles, or the plantar fascia.[8,12,24,26,28,30,31,34]

BTX-A has been employed for the treatment of musculoskeletal pathology, and it has recently been used for the

[1]Universidad Autonoma de Nuevo Leon, Mexico

Corresponding Author:
Carlos Acosta-Olivo, Departamento de Ortopedia y Traumatologia, Hospital Universitario "Dr. Jose E. Gonzalez," Universidad Autonoma de Nuevo Leon, Ave. Madero y Gonzalitos, 4to piso, Mitras Centro, Monterrey, N.L., Mexico, CP 64480
Email: dr.carlosacosta@me.com

treatment of plantar fasciitis via intralesional application. The mechanism of action of this toxin involves blocking the release of acetylcholine at the neuromuscular junctions, but not the storage or flow of Ca^{++}, resulting in muscular paralysis. Moreover, this treatment causes proteolysis of the SNARE proteins, which are involved in the release of various neurotransmitters, including acetylcholine. Due to these autonomic and noncholinergic effects, introducing a toxin into noncholinergic nerve terminals permits its use for the treatment of both hypersecretory states and painful pathologies.[30]

Another very common form of treatment for plantar fasciitis is the application of intralesional steroids. However, there are reports of complications associated with these medications. One of the principal complications is the rupture of the plantar fascia, which occurs in 2.4% to 5.7% of patients. Despite relief of the pain resulting from the rupture, it has been associated with instability of the lateral column and calcaneocuboid joint pain.[1,15]

The purpose of this study was to compare the use of intramuscularly applied BTX-A in the gastroc-soleus muscle complex and the intralesional application of steroids. Both of these methods were combined with education regarding the disorder and a plantar fascia stretching program.

Methods

This study was a prospective, experimental, randomized, double-blinded, and controlled clinical trial. The patients who came to our clinic were recruited for the study and signed informed consent forms, which were previously approved by the ethics committee of the medical research department at our hospital.

The inclusion criteria were the following: skeletally mature, with heel pain at the insertion of the plantar fascia or in the anteromedial tuberosity of the calcaneus; failure of conservative treatment for 3 months, which consisted of pads in ordinary shoe and NSAID; and no previous injections. We excluded patients with associated pathologies, such as knee or ankle dysfunction, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, Reiter's syndrome, neurological abnormalities, mental retardation or psychiatric abnormalities, cutaneous infection, or a history of infection in the previous 3 months, at the application site. We also excluded patients with adverse reactions to the applied components, those who voluntarily asked to leave the study, and those who did not complete the follow-up appointments.

The patients were divided into 2 groups: group A, who received BTX-A, and group B, who received injections with steroids (dexamethasone isonicotinate). Stretching exercises for the plantar fascia were demonstrated to both groups[7] and consisted of the patient crossing the affected leg over the contralateral leg, then the patient pulled the toes back toward the shin until a stretch was felt in the arch or in the plantar fascia; moreover, patients received information regarding their disorder. The patients were randomly assigned into either group using the Alea-T-7/33 program. All of the patients attended the 6 visits. During the initial evaluation, we completed a physical examination, the informed consent forms were signed, and initial clinical scale measurements were made using the Visual Analog Scale (VAS), the Maryland Foot and Ankle scale, the American Orthopaedic Foot and Ankle Society (AOFAS), and the Foot and Ankle Disability Index (FADI). The assigned medication was also applied at the initial evaluation. The patients were evaluated 15 days following the application of the medication and at 1, 2, 4, and 6 months. The clinical measures were assessed at all visits. The measurements were made by a blinded investigator who was unaware of the patient group assignments.

A total of 40 patients were enrolled in this study. Of these, 4 were eliminated due to loss to follow-up (1 in the toxin group and 3 in the steroid group). The final number of patients was 36, of whom 19 received BTX-A (10 men and 9 women) and 17 (6 men and 11 women) received steroids. The mean age of those who were administered the toxin was 41.6 years (29-53 years), and the mean age of the steroid group was 44.5 years (32-54 years). With the numbers available, no significant difference could be detected between the 2 groups with respect to age. The 4 patients who were lost did not come back for follow-up after treatment.

Scales Used for Evaluation

We decided to use several scales to evaluate foot and ankle pathology to obtain improved information and to perform a detailed analysis of the evolution of the patients who received either treatment. The VAS evaluated pain on a numerical scale from 0 to 10, where 0 signified no pain and 10 signified the worst pain experienced by the patient. This scale was complemented by a color scale, on which green signified no pain and bright red signified the most intense pain that the patient had experienced. We also used the Maryland Foot Score,[22] which was divided into several sections that evaluated pain (a score of 45 signified no pain, and 0 indicated an incapacity to work). Among the sections of this scale were function, which was divided into two additional sections (motion and functional activities), and a section that evaluated the shape of the foot. The best score possible was 100, indicating no problem with the foot, and the lowest score was 0. The AOFAS included a scale for the hindfoot, which evaluated the broad categories of foot pain, function, and alignment. Similar to the other scales, the highest score for the AOFAS was 100.[17] We decided to include the FADI score because plantar fasciitis presents in patients who actively participate in sports, and this pathology can cause them to become disabled. The FADI scale

evaluated several metrics, including activities such as standing up, walking on flat or irregular surfaces, walking on inclined planes, and the amount of time one could walk without difficulty. Moreover, this scale included a module for sports activities and foot and ankle pain. The highest score possible was 136 points.[21]

Application of Botulinum Toxin A

The patients were placed in the prone position with the feet raised off the examination table, relaxing the calf musculature. The sites of application were 2 points (medial and lateral) at the site of greatest thickness of each calf muscle, perpendicular to the muscular mass of each calf. One hundred units of toxin were applied to each muscle belly, and 1 application of 50 U was administered to the soleus, for a total of 250 U; all applications were guided by anatomical landmarks (postero-medial into the calf). Following the treatment, dorsiflexion and plantarflexion of the affected foot were performed. The stretching exercises were initiated up to 7 days following the application of the toxin, permitting the patient to perform activities of daily living with ease. The patients were not immobilized.

Application of Steroids

The patients in group B received the medication via injection into the medial plantar surface of the foot, placing the needle just superior to the plantar fascia. A combination of 2% lidocaine (2 mL) and 8 mg of dexamethasone (2 mL) was used. Similar to the other group, plantar fascia stretching exercises were initiated at 7 days following the injection, permitting easy performance of normal activities of daily living. The patients were not immobilized.

Data Analyses

For parametric distributions, we used the Student's t test; for nonparametric distributions, the Wilcoxon rank test was used. We used analysis of variance (ANOVA) tests to analyze intergroup variability and considered $P \leq .05$ to be statistically significant. Electronic data processing and descriptive and inferential statistics were performed using the STATA-IC-10-2008 program.

Results

No significant differences were identified in the initial evaluation between the 2 groups with respect to the results obtained for pain using the VAS (7.1 ± 1.75 toxin group vs 7.7 ± 1.32 steroid group). At the second patient visit, we observed a decrease in pain perception in both groups, but there was no difference between the VAS scores (3.0 ± 1.56 for the toxin group vs 4.0 ± 1.37 for the steroid group). Beginning with the third visit, the group receiving BTX-A exhibited a significant improvement compared to the steroid group; we found that the toxin group scored 1.9 ± 1.51 points on the VAS, whereas the steroid group scored 3.4 ± 1.24 points. At visits 4 and 5, the patients receiving BTX-A scored 1.6 ± 2.07 and 1.5 ± 2.17 points, respectively, whereas for the same visits, the steroid group scored 3.6 ± 1.94 and 3.7 ± 1.96, respectively. At the end of the study, the patients receiving BTX-A averaged 1.1 ± 1.5 points, whereas for the steroid group, the final average was 3.8 ± 1.15 points (Table 1). For group A (BTX-A), the Wilcoxon rank tests indicated statistically significant differences in pain scores at visit 1 compared to visits 2, 3, 4, 5, and 6. The scores for visit 2 differed significantly from those for visits 1, 3, 4, 5, and 6. The scores for visit 3 differed significantly from those for visits 1, 2, and 6. The scores for visit 4 differed statistically from those for visits 1, 2, and 6. For group B (steroids), the scores for visit 1 differed from those for visits 2, 3, 4, 5, and 6. The scores for visit 2 differed from those for visits 1 and 3 (Table 1).

At the initial evaluation, no differences were observed in the mean Maryland Foot and Ankle score between the patient groups; however, following the second visit and until the final evaluation, the BTX-A group exhibited significantly better results than those of the steroid group (Table 2). Using the ANOVA analyses, we observed that group A (BTX-A) exhibited statistically significant differences in the scores for visit 1 compared to visits 2, 3, 4, 5, and 6. The scores for visit 2 were significantly different from those for visits 1, 3, 4, 5, and 6. For group B (steroids), the scores for visit 1 were different from those for visits 2, 3, 4, 5, and 6. The scores for visit 2 were different from those for visits 1 and 3 (Table 2).

At the beginning of the study, the two groups did not exhibit differences between their AOFAS scores (46.0 ± 14.83 for the toxin group vs 46.8 ± 11.23 for the steroid group); however, at the second visit, a significant improvement was observed in the toxin group (85.2 ± 10.66 points) versus the steroid group (72.8 ± 8.01). Moreover, in the following visits, significant differences were observed in favor of the toxin group (Table 3). For group A, ANOVA tests indicated statistically significant differences in the scores for visit 1 compared to visits 2, 3, 4, 5, and 6. The scores for visit 2 were significantly different from those for visits 1, 3, 4, 5, and 6. The scores for visit 3 were different from those for visits 1, 2, 4, 5, and 6. The scores for visit 4, 5, and 6 were significantly different from those for visits 1, 2, and 3. For group B, the scores for visit 1 were different from those for visits 2, 3, 4, 5, and 6. The scores for visit 2 were different from those for visits 1 and 3 (Tables 1 and 2).

The initial FADI scores were similar for the 2 groups (75.4 ± 6.92 points for the toxin group and 77.0 ± 3.21

Table 1. Comparison Between Groups Evaluating Visual Analogue Scale (VAS), With $P \leq .05$

	Group A		Group B		
	Value	SD	Value	SD	*P*
Initial	7.1	±1.75	7.7	±1.32	*ns*
Visit 2	3.0	±1.56	4.0	±1.37	.02
Visit 3	1.9	±1.51	3.4	±1.24	.0004
Visit 4	1.6	±2.07	3.6	±1.94	.0009
Visit 5	1.5	±2.17	3.7	±1.96	.0005
Final	1.1	±1.50	3.8	±1.15	.0005

			ANOVA			
	Wilcoxon Rank Test (VAS)		FADI		AOFAS	
Visit	Group A	Group B	Group A	Group B	Group A	Group B
1 vs 2	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$
1 vs 3	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$
1 vs 4	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$
1 vs 5	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$
1 vs 6	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$	$P \leq .0001$
2 vs 3	$P \leq .0001$	$P = .025$	$P \leq .0001$	$P = .005$	$P = .002$	$P = .017$
2 vs 4	$P \leq .0001$	*ns*	$P \leq .0001$	$P = .49$	$P = .001$	*ns*
2 vs 5	$P = .001$	*ns*	$P \leq .0001$	*ns*	$P \leq .0001$	*ns*
2 vs 6	$P = .001$	*ns*	$P \leq .0001$	*ns*	$P \leq .0001$	*ns*
3 vs 4	*ns*	*ns*	$P = .056$	*ns*	$P = .039$	*ns*
3 vs 5	*ns*	*ns*	$P = .032$	*ns*	$P = .20$	*ns*
3 vs 6	$P = .004$	*ns*	*ns*	*ns*	$P = .003$	*ns*
4 vs 5	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*
4 vs 6	$P = .033$	*ns*	*ns*	*ns*	*ns*	*ns*
5 vs 6	*ns*	*ns*	*ns*	*ns*	*ns*	*ns*

FADI = Foot and Ankle Disability Index; AOFAS = American Orthopaedic Foot and Ankle Society.

points for the steroid group). We observed a significant improvement in the FADI scores beginning with the second visit, and this improvement was maintained through the end of the study, clearly indicating a significant improvement for the group treated with BTX-A (Table 4). For group A, the ANOVA test indicated statistically significant differences between the scores for visit 1 compared to those for visits 2, 3, 4, 5, and 6. The scores for visit 2 differed significantly from those for visits 1, 3, 4, 5, and 6. The scores for visit 3 differed significantly from those for visits 1, 2, and 5. The scores for visit 4 differed significantly from those for visits 1 and 2. The scores for visit 5 differed significantly from those for visits 1, 2, and 3. The scores for visit 6 differed significantly from those for visits 1, 2, and 3. For group B, the scores for visit 1 differed from those for visits 2, 3, 4, 5, and 6. The scores for visit 2 differed from those for visits 1 and 3 (Tables 1 and 2).

We did not have any adverse reaction with the treatments.

Discussion

Babcock et al[2] performed a double-blinded, randomized, placebo-controlled study with 27 patients with plantar fasciitis. The authors administered 70 U of BTX-A into 2 sites per foot (medially on the heel near the calcaneal tuberosity and in the plantar arch of the foot, 1 inch anterior and medial). The control group received saline solution. This study evaluated VAS scores, Maryland Foot scores, and pressure algometry measurements; these metrics were evaluated following the injection and at 3 and 8 weeks. The authors observed significant changes in all of these metrics in the group treated with BTX-A. In our study, we observed that VAS scores were improved in both groups of patients; however, this difference was statistically significant only

Table 2. Comparison Between Groups With Maryland Foot Ankle Score, With $P \leq .05$

	Group A		Group B		
	Value	SD	Value	SD	*P*
Initial	62.1	±9.84	60.0	±11.87	ns
Visit 2	87.8	±11.18	76.3	±15.41	.002
Visit 3	92.8	±8.40	84.6	±15.05	.02
Visit 4	94.3	±10.58	83.5	±16.05	.004
Visit 5	94.3	±10.62	79.2	±17.15	.0002
Final	94.4	±10.64	79.2	±14.96	.0001

	Maryland Foot Score	
Visit	Group A	Group B
1 vs 2	$P \leq .0001$	$P \leq .0001$
1 vs 3	$P \leq .0001$	$P \leq .0001$
1 vs 4	$P \leq .0001$	$P \leq .0001$
1 vs 5	$P \leq .0001$	$P \leq .0001$
1 vs 6	$P \leq .0001$	$P \leq .0001$
2 vs 3	$P = .002$	$P = .030$
2 vs 4	$P = .004$	*ns*
2 vs 5	$P = .004$	*ns*
2 vs 6	$P = .003$	*ns*
3 vs 4	*ns*	*ns*
3 vs 5	*ns*	$P = .042$
3 vs 6	*ns*	$P = .35$
4 vs 5	*ns*	*ns*
4 vs 6	*ns*	*ns*
5 vs 6	*ns*	*ns*

Table 3. Comparison Between Groups With American Orthopaedic Foot and Ankle Society (AOFAS) Score, With $P \leq .05$

	Group A		Group B		
	Value	SD	Value	SD	*P*
Initial	46.0	±14.83	46.8	±11.2	*ns*
Visit 2	85.2	±10.66	72.8	±8.01	.00006
Visit 3	89.4	±9.92	77.1	±9.85	.00008
Visit 4	92.3	±11.03	76.8	±13.73	.00006
Visit 5	92.8	±10.52	74.4	±13.34	.000006
Final	93.2	±9.31	74.8	±10.29	.00000006

for patients treated with BTX-A. In the visit-by-visit analysis, we observed a rapid and sustained improvement in the patients treated with BTX-A compared to the steroid group.

In a randomized study, DiGiovanni et al[8] evaluated 82 patients using 1 of 2 types of stretching programs: one group performed a plantar fascia stretching program, and the other group performed an Achilles tendon stretching program. The different programs were evaluated using the Foot Function Index. All exhibited improvement with the exercises, but based on evaluation with the pain subscale, the patients performing the plantar fascia stretching program improved on item 1 (the highest degree of pain felt) and item 2 (the first steps in the morning). The principal goal of the plantar fascia stretching program is to recreate the windlass (reel) mechanism and to limit the repetitive microtrauma and chronic inflammation that occurs prior to the first steps in the morning or following prolonged periods of inactivity.

Table 4. Comparison Between Groups With Foot and Ankle Disability Index (FADI) Score, With $P \leq .05$

	Group A		Group B		
	Value	SD	Value	SD	*P*
Initial	75.4	±6.92	77.0	±3.20	*ns*
Visit 2	90.6	±7.34	82.4	±5.51	.00007
Visit 3	94.0	±7.30	85.5	±5.22	.00007
Visit 4	94.9	±7.52	84.7	±6.53	.00003
Visit 5	95.2	±7.64	82.8	±6.67	.000004
Final	95.0	±7.27	83.0	±6.41	.000004

Placzek et al[24] examined 9 patients diagnosed with chronic plantar fasciitis for a mean duration of 14 months. The patients were treated with 200 U of BTX-A; at the evaluation conducted 6 months following the procedure, all patients exhibited a 50% reduction in pain when supporting their body weight. This effect was maintained over the 14 weeks of treatment. One study reported that changes occur in the elasticity of the plantar fascia during plantar fasciitis, decreasing the mobility of the foot, reducing contracture, and resulting in the development of heel pain.[27] Our study focused on recovering the windlass mechanism, as described by Hicks et al,[13] by relaxing the musculature of the gastroc-soleus complex via intramuscular application of BTX-A. We observed greater and more sustained improvement in patients who received BTX-A; the patients also reported significant improvement in their symptomatology and in their activities of daily living. The same results were obtained with respect to the scales used to measure pain and functionality (ie, AOFAS, FADI, and Maryland Foot and Ankle scores). Both groups exhibited improvement at the second visit; however, this improvement was greater and more sustained in the group receiving BTX-A.

In one study, it was reported that exercises stretching the plantar fascia result in a limited short-term benefit; however, it was also noted that this effect might have reflected a significant longer term improvement. Moreover, with respect to the use of BTX-A, this study reports both

short-term and long-term improvement. The use of steroids, however, appears to generally result in short-term patient improvement, along with the described complications.[31] Investigators have also reported that rigidity in the gastrocsoleus complex decreases the dorsiflexion movement of the foot, predisposing the individual to the development of chronic foot problems. Contracture of the gastrocnemius-soleus muscular complex, defined as a limitation in dorsiflexion of less than or equal to 10 degrees, is present in as many as 88% of patients.[9]

An increase in hamstring muscle tension can increase the chance of developing plantar fasciitis by up to 8.7-fold; moreover, a body mass index (BMI) greater than 35 increases the risk of plantar fasciitis by 2.4.[19] It has been reported that there is an association between plantar fasciitis and gastrocnemius contracture, which presents as limited dorsiflexion in the majority of patients.[23] We did not evaluate BMI in our study; however, it is a factor that needs to be z: considered when evaluating patients with this type of pathology.

In conclusion, we found that a combination of BTX-A applications into the gastroc-soleus complex and plantar fascia stretching exercises yielded better results for the treatment of plantar fasciitis than intralesional steroids. It is important to note that patients must perform plantar fascia stretching exercises to obtain a rapid and sustained improvement of plantar fasciitis.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Acevedo JI, Beskin JL. Complications of plantar fascia rupture associated with corticosteroid injection. *Foot Ankle Int*. 1998;19(2):91-97.
2. Babcock M, Foster L, Pasquina P, Jabbari B. Treatment of pain attributed to plantar fasciitis with botulinum toxin A: a short term, randomized, placebo-controlled, double-blind study. *Am J Phys Med Rehabil*. 2005;84(9):649-654.
3. Backstrom KM, Moore A. Plantar fasciitis. *Phys Ther Case Rep*. 2000;3:154-162.
4. Bolgla LA, Malone TR. Plantar fasciitis and the windlass mechanism: a biomechanical link to clinical practice. *J Athl Train*. 2004:39(1):77-82.
5. Chandler TJ, Kibler WB. A biomechanical approach to the prevention, treatment and rehabilitation of plantar fasciitis. *Sport Med*. 1993;15:344-352.
6. Cornwall MW, McPoil TG. Plantar fasciitis: etiology and treatment. *J Orthop Sports Phys Ther*. 1999;29:756-760.
7. DiGiovanni B, Nawoczenski D, Lintal M, et al. Tissue-specific plantar fascia-stretching exercise enhances outcomes in patients with chronic heel pain. *J Bone Joint Surg*. 2003;85-A(7):1270-1277.
8. DiGiovanni BF, Nawoczenski DA, Malay DP, et al. Plantar fascia-specific stretching exercise improves outcomes in patients with chronic plantar fasciitis. A prospective clinical trial with two-year of follow-up. *J Bone Joint Surg Am*. 2006;88:1775-1781.
9. DiGiovanni CW, Kuo R, Tejwani N, et al. Isolated gastrocnemius tightness. *J Bone Joint Surg Am*. 2002;84:962-970.
10. Fuller EA. The windlass mechanism of the foot: a mechanical model to explain pathology. *J Am Podiatr Med Assoc*. 2000;90:35-46.
11. Gefen A. Stress analysis of the standing foot following surgical plantar fascia release. *J Biomech*. 2002;35:629-37.
12. Glazer JL. An approach to the diagnosis and treatment of plantar fasciitis. *Phys Sportsmed*. 2009;37(2):74-79.
13. Hicks JH. The mechanics of the foot. II. The plantar aponeurosis and the arch. *J Anat*. 1954;88(1):25-30.
14. Irving DB, Cook JL, Menz HB. Factors associated with chronic plantar heel pain: a systematic review. *J Sci Med Sport*. 2006;9:11-22.
15. Kim C, Cashdollar MR, Mendicino RW, Catanzariti AR, Fuge L. Incidence of plantar fascia ruptures following corticosteroid injection. *Foot Ankle Spec*. 2010;3(6):335-337.
16. Kim W, Voloshin AS. Role of plantar fascia in the load bearing capacity of the human foot. *J Biomech*. 1995;28:1025-1033.
17. Kitaoka HB, Alexander IJ, Adelaar RS, Nunley JA, Myerson MS, Sanders M. Clinical rating systems for the ankle-hindfoot, midfoot, hallux, and lesser toes. *Foot Ankle Int*. 1994;15(7):349-353.
18. Kwong PK, Kay D, Voner PT, White MW. Plantar fasciitis: mechanism and pathomechanics of treatment. *Clin Sport Med*. 1988;7:119-126.
19. Labovitz J, Yu J, Kim C. The role of hamstring tightness in plantar fasciitis. *Foot Ankle Spec*. 2011;4(3):141-144 [Published online March 2, 2011].
20. Lombardi CM, Silhanek AD, Connolly FG, Dennis LN. The effect of first metatarsophalangeal joint arthrodesis on the first ray and the medial longitudinal arch: a radiographic study. *J Foot Ankle Surg*. 2002;41:96-103.
21. Martin RL, Burdett RG, Irrgang JJ. Development of the foot and ankle disability index (FADI). *J Orthop Sports Phys Ther*. 1999;29:A32-33.
22. Myerson MS, Fisher RT, Burgess AR, Kenzora JE. Fracture dislocations of the tarsometatarsal joints; end results correlated with pathology and treatment. *Foot Ankle*. 1986;6:225-242.
23. Patel A, DiGiovanni B. Association between plantar fasciitis and isolated contracture of the gastrocnemius. *Foot Ankle Int*. 2011;32(1):5-8.

24. Placzek R, Deuretzbacher G, Meiss AL. Treatment of chronic plantar fasciitis with botulinum toxin A: preliminary clinical results. *Clin J Pain*. 2006;22(2):190-192.
25. Riddle DL, Pulisic M, Sparrow K. Impact of demographic and impairment-related variables on disability associated with plantar fasciitis. *Foot Ankle Int*. 2004;25:311-317.
26. Rompe JD, Cacchio A, Well L Jr, et al. Plantar fascia-specific stretching versus radial shock-wave therapy as initial treatment of plantar fasciopathy. *J Bone Joint Surg Am*. 2010;92(15):2514-2522.
27. Sahin N, Öztürk A, Atici T. Foot mobility and plantar fascia elasticity in patients with plantar fasciitis. *Acta Orthop Traumatol Turc*. 2010;44(5):385-391.
28. Sampson S, Gerhardt M, Mandelbaum B. Platelet rich plasma injection grafts for musculoskeletal injuries: a review. *Curr Rev Musuculoskelet Med*. 2008;1(3-4):165-174.
29. Sarrafian SK. Functional characteristics of the foot and plantar aponeurosis under tibiotalar loading. *Foot Ankle*. 1987;8:4-18.
30. Seyler TM, Smith BP, Marker DR, et al. Botulinum neurotoxin as a therapeutic modality in orthopaedic surgery: more than twenty years of experience. *J Bone Joint Surg Am*. 2008;90:133-145.
31. Soomekh DJ. Using platelet-rich plasma in the foot and ankle. *Foot Ankle Spec*. 2010;3(2)88-90.
32. Tatli Y, Kapasi S. The real risks of steroid injection for plantar fasciitis, with a review of conservative therapies. *Curr Rev Musculoskelet Med*. 2009;2:3-9.
33. Taunton JE, Ryan MB, Clement DB, McKenzie DC, Lloyd-Smith DR, Zumbo BD. A retrospective case-control analysis of 2002 running injuries. *Br J Sports Med*. 2002; 36:95-101.
34. Tsai WC, Hsu CC, Chen CP, Chen MJ, Yu TY, Chen YJ. Plantar fasciitis treated with local steroid injection: comparison between sonographic and palpation guidance. *J Clin Ultrasound*. 2006;34(1):12-16.

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Foot & Ankle International
34(11) 1471

DOI: 10.1177/1071100713508735
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Highlight Article: January–June 2013

With our new publisher, we have had many more online article downloads. One measure of the impact of an article is the number of downloads it has received. For January to June 2013, the clear leader was "A Comparison of Botulinum Toxin A and Intralesional Steroids for the Treatment of Plantar Fasciitis: A Randomized, Double-Blinded Study."[1] We are highlighting this article here to draw attention to some of the more important work being published by the journal.

This study had a sound scientific design with its double-blind format. In addition, it evaluated a novel treatment for plantar fasciitis, botulinum toxin injection. In the study, 19 patients received an injection of botulinum toxin into each head of the gastrocnemius with plantar fascia stretching exercises and 17 patients received an injection with dexamethasone and lidocaine into the plantar fascia origin with plantar fascia stretching exercises. At the 1-, 2-, 4-, and 6-month follow-up visits, the patients in the botulinum treatment group had significantly lower pain VAS scores and better FADI and Maryland Foot and Ankle Scores.

A previous study had evaluated injecting the botulinum toxin into the plantar fascia origin and arch musculature with some success. In the featured article, the treatment method of injecting the gastrocnemius is more consistent with gastrocnemius recession surgery but without the need for surgery. However the results were preliminary, with only 6 months of follow-up, but they were clearly superior to those of the steroid injection group.

As evident with this article, *Foot and Ankle International* publishes the latest, most important research involving care of the foot and ankle. We look forward to continuing to present the most important work being done in our field.

David B. Thordarson, MD
Editor in Chief
Foot and Ankle International

Reference

1. Elizondo-Rodriguez J, Araujo-Lopez Y, Moreno-Gonzalez JA, Cardenas-Estrada E, Mendoza-Lemus O, Acosta-Olivo C. A comparison of botulinum toxin A and intralesional steroids for the treatment of plantar fasciitis: a randomized, double-blinded study. *Foot Ankle Int*. 2013;34:8-14.