Clin Drug Investig (2013) 33:497–503
DOI 10.1007/s40261-013-0090-0

ORIGINAL RESEARCH ARTICLE

Treatment of Morton Neuroma with Botulinum Toxin A: A Pilot Study

José M. Climent · Francisco Mondéjar-Gómez · Carmen Rodríguez-Ruiz · Ismael Díaz-Llopis · Diego Gómez-Gallego · Patricia Martín-Medina

Published online: 6 June 2013

Abstract
Background and Objective Morton neuroma is a common cause of metatarsalgia of neuropathic origin. Systematic reviews suggest that insufficient studies have been performed on the efficacy of the different treatments available. OnabotulinumtoxinA has shown a degree of usefulness in other conditions associated with neuropathic pain. The aim of this study was to investigate the therapeutic potential of onabotulinumtoxinA in Morton neuroma.
Patients and Methods We present an open-label, pilot study with 17 consecutive patients with Morton neuroma and pain of more than 3 months' duration that had not responded to conservative treatment with physical measures or corticosteroid injection. Patients received one onabotulinumtoxinA injection in the area of the neuroma. The main outcome measure was the variation in the pain on walking evaluated using a visual analogue scale (VAS) before treatment and at 1 and 3 months after treatment. The secondary outcome was the change in foot function, which was assessed using the Foot Health Status Questionnaire.
Results In the overall group, the mean initial VAS score on walking was 7. This mean score had fallen to 4.8 at 1 month after treatment and to 3.7 at 3 months. Twelve patients (70.6 %) reported an improvement in their pain and five patients (29.4 %) reported no change; exacerbation of the pain did not occur in any patient. Improvements were also observed in two of the dimensions of the Foot Health Status Questionnaire: foot pain, which improved from a mean of 38.88 before treatment to 57 at 3 months, and foot function, which improved from a mean of 42.27 before treatment to 59.9 at 3 months. Clinical variables including age, sex, site and size of the lesion, standing activity, weekly duration of walking, footwear, foot type and footprint had no influence on the outcome. No adverse effects were reported.
Conclusions In this pilot study, injection with onabotulinumtoxinA was shown to be of possible usefulness to relieve the pain and improve function in Morton neuroma. This finding opens the door to further clinical research.

J. M. Climent (✉) · I. Díaz-Llopis · D. Gómez-Gallego
Department of Physical Medicine and Rehabilitation, Hospital General Universitario, Maestro Alonso 109, 03010 Alicante, Spain
e-mail: jclimentba@gmail.com

F. Mondéjar-Gómez
Department of Physical Medicine and Rehabilitation, Hospital Virgen del Castillo, Yecla, Spain

C. Rodríguez-Ruiz
Department of Physical Medicine and Rehabilitation, Hospital San Jaime, Torrevieja, Spain

P. Martín-Medina
MR Department, Erescanner Salud, Hospital General Universitario, Alicante, Spain

1 Introduction

Morton neuroma is a common cause of metatarsalgia. It is characterized by a thickening at the bifurcation of the plantar digital nerve, typically developing in the third intermetatarsal space and, less frequently, in the second intermetatarsal space [1]. Histology usually reveals endoneural and perineural fibrosis at the level of the heads of the metatarsals [2], and it is therefore considered to be an entrapment neuropathy in which the intermetatarsal ligament could play a key role [3]. Morton neuroma has been associated with various overload mechanisms and

particularly with the use of inadequate footwear. Previous studies have reported a prevalence of Morton neuroma of around 30–33 % [4]. Morton neuroma is eight to ten times more common in women than in men; this may be related to the use of shoes with high heels or with a constricting toe box [5, 6].

Morton neuroma is named after Thomas G. Morton [7] who described it in 1876, though earlier descriptions exist [8]. The symptoms are characterized by plantar pain of neuropathic characteristics in the forefoot, typically between the third and fourth toes. The pain is more intense during standing and walking and is exacerbated by the use of footwear with a high heel or narrow toe. It is described as a stabbing pain that radiates to the medial and lateral borders of the affected toes in the territory supplied by the plantar digital nerves.

On physical examination there is usually a tender point on the dorsal aspect of the corresponding intermetatarsal space. There may be altered sensation, with the hyperaesthesia characteristic of neuropathic pain, which can be provoked by testing light touch sensation over the medial and lateral surfaces of the affected toes.

Clinical diagnosis can be confirmed by sensory nerve conduction studies of the interdigital nerve, ultrasound or magnetic resonance imaging (MRI) (Fig. 1) [9]. An MRI increases the range of detectable differential diagnoses, which include intermetatarsal bursitis, arthritis, synovitis, osteomyelitis, foreign body granuloma, stress fracture, Freiberg disease and metatarsophalangeal subluxation [4].

Treatment of Morton neuroma can be conservative or surgical [10]. Patients are often instructed to use footwear that does not enclose the forefoot. Metatarsal offloading orthoses have also been used. In addition, corticosteroid injection and nerve blocks with local anaesthetic [5] or alcohol [11] are recommended. The principal surgical option indicated for cases refractory to conservative treatment is neurectomy [12]. Systematic reviews suggest that insufficient studies have been performed to demonstrate the efficacy of the different treatments employed or whether any one treatment is superior to the others [5].

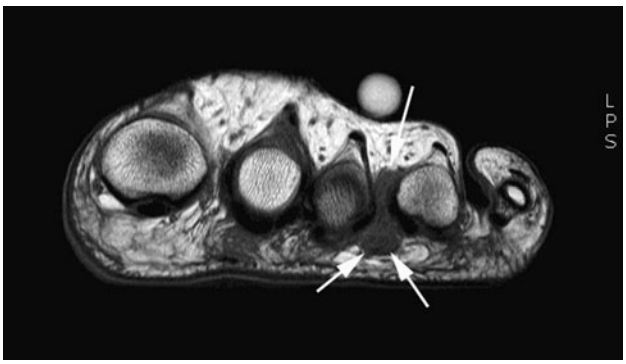

Fig. 1 Magnetic resonance image of a Morton neuroma (*arrows*)

Botulinum toxin A is a peptide formed by a light and a heavy chain linked by a disulphide bridge. It acts as a protease at the presynaptic nerve terminal, blocking acetylcholine release at the motor endplate. Because of this it has been used for decades in the treatment of disorders characterized by muscle hyperactivity, such as spasticity or dystonia [13]. Its analgesic potential was also observed when, in addition to decreasing the hyperactivity, it was found to improve the pain in patients with dystonia [14]. This initial finding was later confirmed when its analgesic therapeutic effect was observed in other conditions such as epicondylitis, low back pain, piriformis syndrome [15], migraine [16] and plantar fasciitis [17].

In recent years, this analgesic effect has also been investigated in the field of neuropathic pain [18–27]. The analgesic effect of the toxin may be related to inhibition of neuropeptide release in the nociceptive terminals [28].

The objective of the present study was to investigate the effect of treatment with onabotulinumtoxinA on the neuropathic pain of Morton neuroma.

2 Patients and Methods

We present an open pilot study performed on patients with Morton neuroma who attended the Rehabilitation and Orthopaedics Outpatients Clinic of Alicante University General Hospital, Alicante, Spain, and in whom the symptoms had not improved after treatment involving footwear modification and orthoses. The following inclusion criteria were applied: diagnosis of Morton neuroma, pain of more than 3 months' duration and with a pain intensity on walking $\geq$5 on a visual analogue scale (VAS). The diagnosis of Morton neuroma was confirmed by MRI or ultrasound in all patients. Seventeen consecutive patients who satisfied these criteria were included in the study. All patients received detailed information about the nature of the study, its objective and the therapeutic procedures involved. They all agreed voluntarily to participate in the study and signed an informed consent form. This research has received the approval of the ethics committee of Alicante General Hospital.

The following clinical variables were studied: body mass index, type of footwear (narrow-toed or broad-toed), occupational activity requiring standing, number of hours walking per week (more or less than 3 h per week), previous treatment with corticosteroid injections, type of footprint, foot morphology, web space affected and nocturnal pain.

The primary outcome measure was pain intensity on walking, evaluated using a VAS with a score range from 0

to 10 points. Secondary variables were studied using the Foot Health Status Questionnaire, for which there is a validated version in Spanish [29]. This questionnaire offers four domains related to foot health: foot pain, foot function, general foot health and footwear [30]. Optimum foot health is considered to be a score of 100 points and lower values indicate the percentage deterioration in the dimension being evaluated.

All patients received a single injection of onabotulinumtoxinA (Botox®, Allergan, Irvine, CA, USA) in the area of the neuroma. The site of injection was selected by anatomical skin marking based on the findings of the MRI scan and concordance with the site of pain. All patients received a dose of 50 units of onabotulinumtoxinA dissolved in 0.5 mL of normal saline.

The statistical study was performed using the SPSS software package version 15.0 (SPSS Inc., Chicago, IL, USA). Before data analysis, the Shapiro–Wilk test was employed to test for a normal distribution of the dependent variable. The values of the dependent variables before treatment and at 1 and 3 months after treatment were compared using repeated measures ANOVA. The possible influence of the clinical variables was studied by calculating the percentage of patients in whom the pain had improved at 3 months after treatment in each subgroup defined by the clinical variables; the percentages were then compared using contingency tables and the Chi-square test to determine the influence of each clinical variable on outcome. The Pearson coefficient was calculated to determine the relationship between quantitative variables.

3 Results

Seventeen patients [ten women (59 %) and seven men (41 %)] with a mean (standard deviation) age of 59.29 (2.65) years were included in the study.

The clinical characteristics of the patients are summarized in Table 1. Analysis of the results of the overall group (Table 2) showed a significant improvement in pain on walking measured using the VAS (Fig. 2) and in the foot pain and foot function (Fig. 3) dimensions of the Foot Health Status Questionnaire; the improvements in the other dimensions evaluated by the questionnaire (general foot health and footwear) did not reach statistical significance.

In terms of pain relief at 3 months after treatment, 12 patients (70.6 %) showed improvement and 5 patients (29.4 %) obtained no relief of their symptoms. The percentage improvement in each of the different subgroups of the sample is shown in Table 3. None of the clinical variables studied (body mass index, footwear, standing occupational activity, walking more than 3 h per week, previous treatment with corticosteroid injections, type of footprint, foot morphology, interdigital space affected or nocturnal pain) was found to have a significant influence on the initial pain intensity or on the outcome of treatment measured using the primary or secondary outcome variables.

The size of the neuroma also had no effect on the percentage of patients who presented an improvement in the pain score on the VAS 3 months after treatment. The largest and smallest diameters of the neuromas showed correlations of 0.16 and 0.19, respectively, with the outcome measure. Nor was treatment outcome related to patient age (correlation, $r = 0.15$).

Table 1 Characteristics of the sample ($n = 17$ patients)

Characteristic	*n* (%)	Mean (±SD)
Age (y)		58.19 (2.56)
Sex		
Female	7 (41.2)	
Male	10 (58.8)	
Body mass index (kg/m^2)		
≤25	5 (29.4)	
>25	12 (70.6)	
Site of the neuroma		
Second intermetatarsal space	6 (35.3)	
Third intermetatarsal space	11 (64.7)	
Standing activity		
Prolonged	9 (52.95)	
Normal	8 (47.1)	
Footwear		
Narrow toes	4 (23.5)	
Broad toes	13 (76.5)	
Walking activity (h/week)		
≥3	12 (70.6)	
<3	5 (29.4)	
Previous corticosteroid injection		
Yes	3 (17.5)	
No	14 (82.4)	
Footprint		
Normal	6 (35.3)	
Pes cavus	9 (52.9)	
Pes planus	2 (11.8)	
Foot type		
Greek	6 (35.3)	
Egyptian	11 (64.7)	
Nocturnal pain		
Yes	7 (41.8)	
No	10 (58.8)	
Largest diameter of the neuroma (mm)		14.1 (0.87)
Smallest diameter of the neuroma (mm)		4.8 (0.36)

SD standard deviation

Table 2 Treatment outcome evaluated using the visual analogue scale and the dimensions of the Foot Health Status Questionnaire

Parameter	Pre-treatment	Post-treatment		*P* value[a]
		1 month	3 months	
Pain at rest (VAS score)	2.28 (2.39)	0.95 (1.49)	0.95 (1.61)	0.02
Pain on walking (VAS score)	7 (1.4)	4.89 (3.04)	3.74 (3.52)	<0.001
FHSQ foot pain	38.88 (24.23)	54.14 (25.47)	57 (27.45)	0.005
FHSQ foot function	42.27 (27.99)	52.20 (35)	59.94 (37.19)	0.03
FHSQ footwear	26.46	28.91	26.95	0.7
FHSQ foot health	28.82	19.97	37.17	0.3

Values are given as mean (SD)

FHSQ Foot Health Status Questionnaire, *VAS* visual analogue scale

[a] Significance level comparing pre-treatment values with values at 3 months

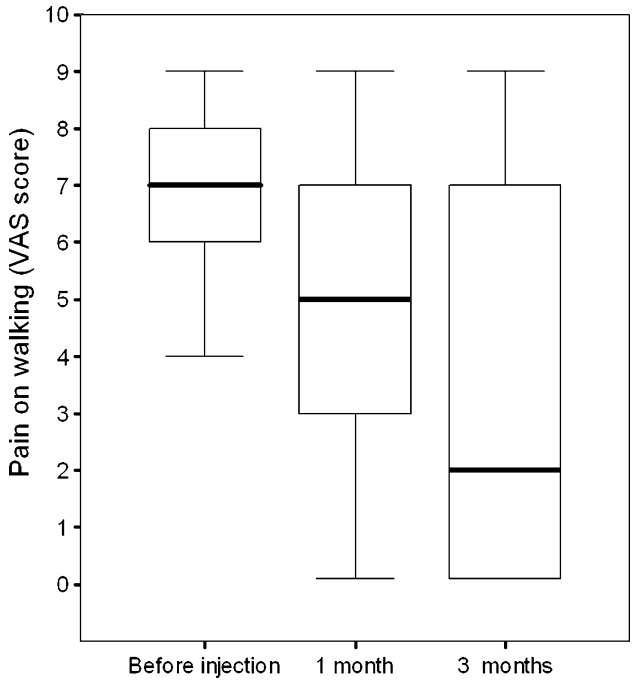

Fig. 2 Boxplot of the changes in pain on walking as measured on the visual analogue scale (VAS) before injection and at 1 and 3 months after treatment ($n = 17$ patients). The *box* represents 25th, 50th and 75th percentiles and the *whisker* represents the range

None of the patients reported any local, distant or generalized adverse effects after the injection.

4 Discussion

This is the first study of the effect of onabotulinumtoxinA on the symptoms of Morton neuroma. The data obtained show an improvement in pain at rest and on walking and an improvement in foot function; these improvements were detectable at 1 month after treatment and persisted at significant levels until the end of the study (3 months) in the sample analysed.

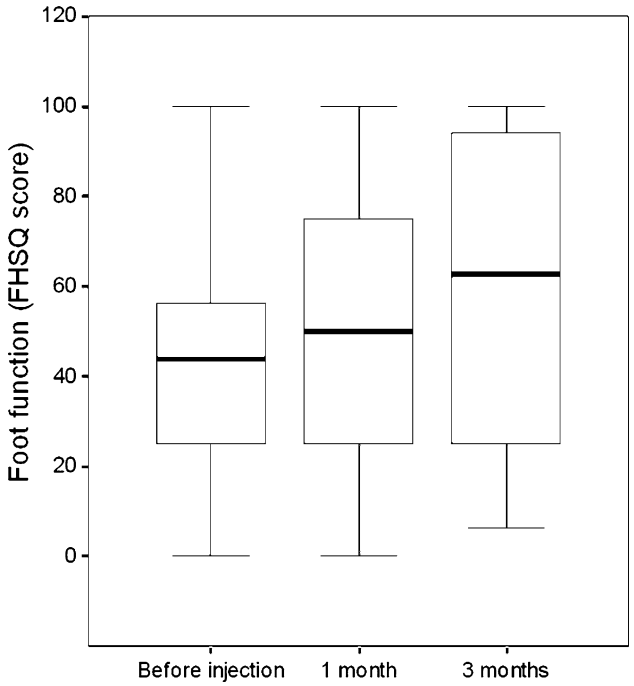

Fig. 3 Boxplot of the changes in foot function measured using the Foot Health Status Questionnaire (FHSQ) before injection and at 1 and 3 months after treatment ($n = 17$ patients). The *box* represents 25th, 50th and 75th percentiles and the *whisker* represents the range

Local corticosteroid injection is usually indicated when the first-line treatment of Morton neuroma by footwear modification and the use of orthoses does not achieve adequate control of symptoms. Favourable results have been reported in 76 % of cases 1 week after corticosteroid injection [3]. These good immediate results have not always been confirmed after a longer follow-up of months or years—the percentage of patients with continued improvement varied between 30 and 66 %, depending on the series [2, 31, 32]. One classic series reported improvement in only 40 % of patients despite repeating the injection on up to four occasions [6]. The injection of an alcohol solution into the Morton neuroma has also been proposed; published series have reported improvements in 69–84 % of patients [11, 33–35]. In some studies, the infiltration was repeated on up to four occasions. It should be noted that this procedure can lead to an increase in symptoms in the initial weeks in up to 16 % of patients [36].

A number of studies have been published in which onabotulinumtoxinA has been shown to have analgesic activity in conditions associated with neuropathic pain,

Table 3 Distribution of the patients who had improved at 3 months, according to different subgroups

Characteristic	Improvement, *n* (%)	No improvement, *n* (%)	*P* value
Sex			
Female	8 (80)	2 (20)	0.3
Male	4 (57.1)	3 (42.9)	
Body mass index (kg/m^2)			
≤25	8 (66.7)	4 (33.3)	0.5
>25	4 (80)	1 (20)	
Site of the neuroma			
Second intermetatarsal space	4 (66.7)	2 (33.3)	0.7
Third intermetatarsal space	8 (72.7)	3 (27.3)	
Standing activity			
Prolonged	6 (66.7)	3 (33.3)	0.5
Not prolonged	6 (75)	2 (25)	
Footwear			
Narrow toes	2 (50)	2 (50)	0.3
Broad toes	10 (76.9)	3 (23.1)	
Walking activity (h/week)			
≥3	9 (75)	3 (25)	0.4
<3	3 (60)	2 (40)	
Previous corticosteroid injection			
Yes	3 (100)	0 (0)	0.3
No	9 (64.3)	5 (35.7)	
Footprint			
Normal	5 (83.3)	1 (16.7)	0.6
Pes cavus	6 (66.7)	3 (33.3)	
Pes planus	1 (50)	1 (50)	
Foot type			
Greek	3 (50)	3 (50)	0.2
Egyptian	9 (81.8)	2 (18.2)	
Nocturnal pain			
Yes	5 (71.4)	2 (28.3)	0.6
No	7 (70)	3 (30)	
Overall sample	**12 (70.6)**	**5 (29.4)**	

such as postherpetic neuralgia [22], carpal tunnel syndrome [23], occipital neuralgia [24], diabetic polyneuropathy [25], trigeminal neuralgia [26] and phantom limb syndrome [37]. Morton neuroma, a well-known cause of neuropathic pain, is a localized lesion that can be observed on imaging studies, and it therefore represents a good model to study the possible beneficial effect of the local injection of different drugs. In this open pilot study, onabotulinumtoxinA improved the foot pain and foot function scores both at 1 month and at 3 months; this would suggest a potential beneficial therapeutic effect on the symptoms of Morton neuroma. The mechanism of action of onabotulinumtoxinA in neuropathic pain must be considered in the context of its activity as a protease of the cytoplasmic transport proteins. This activity could lead to a reduction in the concentration of some of the nociceptive neurotransmitters such as substance P, glutamate and calcitonin gene-related peptide [28]. It is also possible that it could inhibit the transport proteins of the membrane receptors. This blockade of neurotransmitter release could alter sensitization phenomena, interrupting the cascade of local events that precipitates the situation that perpetuates the pain [38]. This modulation of sensitization may also be implicated when botulinum toxin is used in the treatment of myofascial pain syndrome [39–44].

The results of this study show that 29.4 % of the sample showed no benefit whatsoever from the treatment. This result contrasts with the marked and sustained improvement in 70.6 % of the patients. An analysis of the clinical variables studied did not identify a specific profile of the patients who did not respond, as it was not possible to find any variable that was predictive of the success or failure of treatment. Nor was there a correlation between the size of the neuroma and the outcome. As the injections were directed by anatomical skin marking, it is possible that the therapeutic target may not have been adequately reached in all patients. For this reason, further studies of this treatment should be performed with ultrasound guidance in order to reduce the risk of treatment failure due to an incorrect site of injection of the drug [3].

Another aspect that must be considered is the suitability of a dose of 50 U. This dose is the same as has been used at each site of blockade in other series on the treatment of neuralgia [45]. The percentage of therapeutic success would suggest that this dose could be appropriate, although it is not currently known whether any variation in the dose might improve the results.

Another issue concerns the onset, peak and disappearance of the analgesic effect of onabotulinum toxin. In movement disorders, the clinical onset of action of botulinum toxin typically occurs between 12 and 72 h after injection; the effect peaks between 1 and 3 weeks and this is followed by a plateau phase that for lasts for 1–2 months. Patients therefore often require re-injection approximately every 3 months [46]. However, our patients presented better results at 3 months than at 1 month. This long-term improvement is not uncommon in pain treatment and improvements have even been reported at up to 6 months [16]. Apart from its analgesic action, botulinum toxin is effective in reducing fibrosis. This has been observed in patients with neurogenic bladder, as those who received treatment with abobotulinumtoxin injection presented less bladder wall fibrosis than those who received other treatments [47].

In addition to pain reduction, botulinum toxin treatment may also produce a decrease in the size of neuroma. We plan to study changes in Morton neuroma size after botulinum toxin injection in the future.

An interesting finding was the absence of adverse effects in this series. The treatment was well tolerated and an exacerbation of symptoms was not observed in any case. A further relevant consideration is that these results were achieved after a single injection, whereas other injectable treatments have required repetition of the procedure on up to four occasions.

The fundamental limitation of this study is the absence of a control group and the data presented cannot therefore be extrapolated to other populations. This was an initial clinical investigation in the form of an open pilot study, the main aim of which was to open a new line of investigation for the treatment of neuropathic pain in Morton neuroma. The small sample size and the lack of objective outcome measures can be rectified in further studies. These limitations should be taken into account when designing future prospective research.

5 Conclusion

The injection of onabotulinumtoxinA in Morton neuroma has been shown to be useful to relieve pain and improve function in a 3-month open pilot study. This finding opens the door to further clinical research to determine the optimal dose, possible improvements in the outcome through the use of ultrasound-guided injection, and comparison of the results of this new procedure with other procedures commonly used in Morton neuroma. It would also be interesting to determine the possible effects of treatment on the size and characteristics of the neuroma.

To establish the role of onabotulinumtoxinA in Morton neuroma, it will be necessary to perform clinical trials that compare this new therapeutic option with the established management options in order to determine its superiority or inferiority, its profile of adverse effects and its relative cost. Such studies would enable us to determine whether onabotulinumtoxinA offers any advantage over the other known injectable treatments.

Acknowledgments We would like to thank Dr Philip Bazire for the translation of this article from Spanish into English.

Funding There was no external funding for the conduct of this study. The translation into English was financed by Allergan. Allergan was not informed of the undertaking of the study until after its completion and after the analysis of results. The company did not exert any control over the preparation of the manuscript or the presentation of the results.

Conflicts of Interest The authors declare that they have no other conflicts of interests.

References

1. Hassouna H, Singh D. Morton's metatarsalgia: pathogenesis, aetiology and current management. Acta Orthop Belg. 2005;71(6):646–55.
2. Bennett GL, Graham CE, Mauldin DM. Morton's interdigital neuroma: a comprehensive treatment protocol. Foot Ankle Int. 1995;16:760–3.
3. Sofka CM, Adler RS, Ciavarra GA, et al. Ultrasound-guided interdigital neuroma injections: short-term clinical outcomes after a single percutaneous injection: preliminary results. HSS J. 2007;3(1):44–9.
4. Zanetti M, Weishaupt D. MR imaging of the forefoot: Morton neuroma and differential diagnoses. Semin Musculoskelet Radiol. 2005;9(3):175–86.
5. Thomson CE, Gibson JN, Martin D. Interventions for the treatment of Morton's neuroma. Cochrane Database Syst Rev. 2004;(3):CD003118.
6. Greenfield J, Rea J Jr, et al. Morton's interdigital neuroma. Indications for treatment by local surgery. Clin Orthop Relat Res. 1984;185:142–4.
7. Morton TG. The classic. A peculiar and painful affection of the fourth metatarso-phalangeal articulation. Thomas G. Morton, M.D. Clin Orthop Relat Res. 1979;142:4–9.
8. Pasero G, Marson P. Filippo Civinini (1805–1844) and the discovery of plantar neuroma [in Italian]. Reumatismo. 2006;58(4):319–22.
9. Lee MJ, Kim S, Huh YM, et al. Morton neuroma: evaluated with ultrasonography and MR imaging. Korean J Radiol. 2007;8(2):148–55.
10. Saygi B, Yildirim Y, Saygi EK, et al. Morton's neuroma: comparative results of two conservative methods. Foot Ankle Int. 2005;26:556–9.
11. Dockery GL. The treatment of intermetatarsal neuromas with 4% alcohol sclerosing injections. J Foot Ankle Surg. 1999;38:403–8.
12. Singh SK, Ioli JP, Chiodo CP. The surgical treatment of Morton's neuroma. Curr Orthop. 2005;19:379–84.
13. Brin MF. Botulinum toxin: chemistry, pharmacology, toxicity, and immunology. Muscle Nerve. 1997;Suppl 6:146–68.
14. Costa J, Espírito-Santo C, Borges A, et al. Botulinum toxin type A therapy for cervical dystonia. Cochrane Database Syst Rev. 2004;(4):CD004315.
15. Jabbari B, Machado D. Treatment of refractory pain with botulinum toxins: an evidence-based review. Pain Med. 2011;12(11):1594–606.
16. Lipton RB, Varon SF, Grosberg B, et al. Onabotulinum toxin A improves quality of life and reduces impact of chronic migraine. Neurology. 2011;77(15):1465–72.
17. Díaz-Llopis IV, Rodriguez-Ruiz CM, Mulet-Perry S, et al. 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. 2012;26(7):594–606.
18. Argoff C. The emerging use of botulinum toxins for the treatment of neuropathic pain. Pain Med. 2010;11(12):1750–2.
19. Ranoux D. Botulinum toxin and peripheral neuropathies: what should be expected? Rev Neurol (Paris). 2011;167(1):46–50.
20. Dworkin RH, O'Connor AB, Audette J. Recommendations for the pharmacological management of neuropathic pain: an

overview and literature update. Mayo Clin Proc. 2010;85(3 Suppl):S3–14.
21. Sim WS. Application of botulinum toxin in pain management. Korean J Pain. 2011;24(1):1–6.
22. Ruiz-Huete C, Bermejo PE. Toxina botulínica tipo A en el tratamiento del dolor neuropático en un caso de neuralgia postherpética. Neurología. 2008;23(4):259–62.
23. Tsai CP, Liu CY, Lin KP, et al. Efficacy of botulinum toxin type A in the relief of Carpal tunnel syndrome: a preliminary experience. Clin Drug Investig. 2006;26(9):511–5.
24. Vanelderen P, Lataster A, Levy R, et al. Occipital neuralgia. Pain Pract. 2010;10(2):137–44.
25. Yuan RY, Sheu JJ, Yu JM, et al. Botulinum toxin for diabetic neuropathic pain: a randomized double-blind crossover trial. Neurology. 2009;72(17):1473–8.
26. Ngeow WC, Nair R. Injection of botulinum toxin type A (Botox) into trigger zone of trigeminal neuralgia as a means to control pain. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2010;109(3):e47–50.
27. Piovesan EJ, Teive HG, Kowacs PA, et al. An open study of botulinum-A toxin treatment of trigeminal neuralgia. Neurology. 2005;65:1306–8.
28. Aoki KR. Review of a proposed mechanism for the antinociceptive action of botulinum toxin type A. Neurotoxicology. 2005;26(5):785–93.
29. Sirera-Vercher MJ, Sáez-Zamora P, Sanz-Amaro MD. Traducción y adaptación transcultural al castellano y al valenciano del Foot Health Status Questionnaire. Rev Esp Cir Ortop Traumatol. 2010;54(4):211–9.
30. Bennett PJ, Patterson C, Wearing S, et al. Development and validation of a questionnaire designed to measure foot-health status. J Am Podiatr Med Assoc. 1998;88:419–28.
31. Hassouna H, Singh D, Taylor H, et al. Ultrasound guided steroid injection in the treatment of interdigital neuralgia. Acta Orthop Belg. 2007;73(2):224–9.
32. Markovic M, Crichton K, Read JW, et al. Effectiveness of ultrasound-guided corticosteroid injection in the treatment of Morton's neuroma. Foot Ankle Int. 2008;29(5):483–7.
33. Mozena JD, Clifford JT. Efficacy of chemical neurolysis for the treatment of interdigital nerve compression of the foot: a retrospective study. J Am Podiatr Med Assoc. 2007;97(3):203–6.
34. Magnan B, Marangon A, Frigo A, et al. Local phenol injection in the treatment of interdigital neuritis of the foot (Morton's neuroma). Chir Organi Mov. 2005;90(4):371–7.
35. Fanucci E, Masala S, Fabiano S, et al. Treatment of intermetatarsal Morton's neuroma with alcohol injection under US guide: 10-month follow-up. Eur Radiol. 2004;14(3):514–8.
36. Hughes RJ, Ali K, Jones H, et al. Treatment of Morton's neuroma with alcohol injection under sonographic guidance: follow-up of 101 cases. Am J Roentgenol. 2007;188(6):1535–9.
37. Wu H, Sultana R, Taylor KB, et al. A prospective randomized double-blinded pilot study to examine the effect of botulinum toxin type A injection versus Lidocaine/Depomedrol injection on residual and phantom limb pain: initial report. Clin J Pain. 2012;28(2):108–12.
38. Aoki KR, Francis J. Updates on the antinociceptive mechanism hypothesis of botulinum toxin A. Parkinsonism Relat Disord. 2011;17(Suppl 1):28–33.
39. Acquadro MA, Borodic GE. Treatment of myofascial pain with botulinum A toxin [letter]. Anesthesiology. 1994;80:705–6.
40. Cheshire WP, Abashian SW, Mann JD. Botulinum toxin in the treatment of myofascial pain syndrome. Pain. 1994;59:65–9.
41. Kuan T-S, Chen J-T, Chen S-M, Chien C-H, Hong C-Z. Effect of botulinum toxin on endplate noise in myofascial trigger spots of rabbit skeletal muscle. Am J Phys Med Rehabil. 2002;81:512–20.
42. Gobel H, Heinze A, Reichel G, Hefter H, Benecke R. Efficacy and safety of a single botulinum type A toxin complex treatment (Dysport) for the relief of upper back myofascial pain syndrome: results from a randomized double-blinded placebo-controlled multicentre study. Pain. 2006;125(1–2):82–8.
43. Wheeler AH, Goolkasian P, Gretz SS. A randomized, double-blind, prospective pilot study of botulinum toxin injection for refractory, unilateral, cervicothoracic, paraspinal, myofascial pain syndrome. Spine. 1998;23:1662–7.
44. Yue SK. Initial experience in the use of botulinum toxin A for the treatment of myofascial related muscle dysfunctions. J Musculoskelet Pain. 1995;3(Suppl 1):22.
45. Kapural L, Stillman M, Kapural M, et al. Botulinum toxin occipital nerve block for the treatment of severe occipital neuralgia: a case series. Pain Pract. 2007;7(4):337–40.
46. Tilton AH. Injectable neuromuscular blockade in the treatment of spasticity and movement disorders. J Child Neurol. 2003;18(Suppl 1):S50–66.
47. Compérat E, Reitz A, Delcourt A, Capron F, Denys P, Chartier-Kastler E. Histologic features in the urinary bladder wall affected from neurogenic overactivity: a comparison of inflammation, oedema and fibrosis with and without injection of botulinum toxin type A. Eur Urol. 2006;50(5):1058–64.