Cochrane Library

Cochrane Database of Systematic Reviews

Interventions for the treatment of Morton's neuroma (Review)

Thomson CE, Gibson JNA, Martin D

Thomson CE, Gibson JNA, Martin D.
Interventions for the treatment of Morton's neuroma.
Cochrane Database of Systematic Reviews 2004, Issue 3. Art. No.: CD003118.
DOI: 10.1002/14651858.CD003118.pub2.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Interventions for the treatment of Morton's neuroma

Colin E Thomson[1], JN Alastair Gibson[2], Denis Martin[3]

[1]School of Health Sciences, Queen Margaret University, Edinburgh, UK. [2]Orthopaedic Surgery, The Royal Infirmary of Edinburgh, Little France, Edinburgh, UK. [3]Institute of Health and Social Care, Teesside University, Middlesbrough, UK

Contact address: Colin E Thomson, School of Health Sciences, Queen Margaret University, Edinburgh, East Lothian, EH21 6UU, UK. cthomson@qmu.ac.uk.

Editorial group: Cochrane Neuromuscular Group.
Publication status and date: Edited (no change to conclusions), published in Issue 4, 2011.

Citation: Thomson CE, Gibson JNA, Martin D. Interventions for the treatment of Morton's neuroma. *Cochrane Database of Systematic Reviews* 2004, Issue 3. Art. No.: CD003118. DOI: 10.1002/14651858.CD003118.pub2.

ABSTRACT

Background

Morton's neuroma is a common, paroxysmal neuralgia affecting the web spaces of the toes, typically the third. The pain is often so debilitating that patients become anxious about walking or even putting their foot to the ground. Insoles, corticosteroid injections, excision of the nerve, transposition of the nerve and neurolysis of the nerve are commonly used treatments. Their effectiveness is poorly understood.

Objectives

To examine the evidence from randomised controlled trials concerning the effectiveness of interventions in adults with Morton's neuroma.

Search methods

We searched the Cochrane Neuromuscular Disease Group trials register (searched January 2003), MEDLINE (January 1966 to January Week 2 2003), EMBASE (January 1980 to February Week 2 2003), and CINAHL (January 1982 to February Week 1 2003).

Selection criteria

Randomised or quasi-randomised (methods of allocating participants to an intervention which were not strictly random e.g. date of birth, hospital record, number alternation) controlled trials of interventions for Morton's neuroma were selected. Studies where participants were not randomised into intervention groups were excluded.

Data collection and analysis

Two reviewers selected trials for inclusion in the review, assessed their methodological quality and extracted data independently.

Main results

Three trials involving 121 people were included. There is, at most, a very limited indication that transposition of the transected plantar digital nerve may yield better results than standard resection of the nerve in the long term. There is no evidence to support the use of supinatory insoles. There are, at best, very limited indications to suggest that dorsal incisions for resection of the plantar digital nerve may result in less symptomatic post-operative scars when compared to plantar excision of the nerve.

Authors' conclusions

There is insufficient evidence with which to assess the effectiveness of surgical and non-surgical interventions for Morton's neuroma. Well designed trials are needed to begin to establish an evidence base for the treatment of Morton's neuroma pain.

PLAIN LANGUAGE SUMMARY

There is insufficient evidence from randomised controlled trials to assess efficacy of surgical and non-surgical interventions for Morton's neuroma. More research is needed.

Morton's neuroma is a common, painful condition affecting the web spaces of the toes. Limited evidence from one randomised controlled trial indicated that surgery involving cutting the relevant nerve and implanting it into a muscle tendon may yield better long-term results than standard surgical removal of the nerve. There is little evidence from randomised controlled trials to support the use of insoles. There were no randomised controlled trials reporting the effect of corticosteroid injections. Adverse events following surgery were common. Well-designed trials are needed to guide clinical practice.

BACKGROUND

Morton's neuroma is a common, paroxysmal neuralgia affecting the web spaces of the toes, typically the third (Thomson 2001). The pain is significant and often debilitating to the extent that patients become apprehensive and anxious about walking or even putting their foot to the ground. The source of the problem is associated with pathology of the plantar digital nerve as it divides to supply the adjacent sides of the toes. The precise cause is still not clear. One study has reported that there was no difference in histological examination of the nerves of asymptomatic control subjects and of patients with Morton's neuroma with respect to nerve enlargement, endoneurial vessel hyalinisation, perineurial and endoneurial fibrosis. The authors concluded that the changes are degenerative, non-specific and present in nerves in asymptomatic patients and are not responsible for the symptoms of Morton's neuroma (Bourke 1994). Ultrasound is a sensitive and reliable aid to diagnosis and preoperative scans are established practice in many centres (Oliver 1998). Whilst still considered the gold standard of diagnosis, histomorphological examination of resected nerves is a matter of contention.

The magnitude of the problem is unknown. To our knowledge, no study has identified the incidence or prevalence of this condition. Hospital activity analysis reveals that in the year 1999/2000, there were 139 inpatient and day case discharges following operations for this condition for hospitals in Scotland (population approximately 5,200,000 (GRO Scotland 1999)). These figures do not include those patients who received non-surgical interventions. When extrapolated to the rest of the UK this figure represents a significant proportion of patients presenting to orthopaedic clinics.

The literature does reveal that the mean age of presentation is between the years of 45 and 50 and, overwhelmingly, females are affected by this condition more than males (Thomson 2001). Both feet are affected equally but bilateral presentation is relatively uncommon, as is the occurrence of more than one lesion in the same foot. The complaint is that of a severe, sharp, sometimes lancing pain that occurs suddenly while walking. At onset, the patient must stop to remove their shoe and relief of pain can be aided by massaging the foot or manipulating the toes. In the worst cases, pain becomes debilitating and patients are apprehensive about walking. Incipient cases describe milder symptoms of burning or tingling sensations. The third web space is most frequently involved followed by the second. Only rarely do symptoms occur in the first or fourth web spaces.

Many patients undergo surgery under general anaesthetic to remove the pathological plantar digital nerve. In addition to the obvious cost associated with surgery, its clinical effectiveness has been consistently questioned with reports of high failure rates and associated complications (Okafor 1997). It is generally assumed that recurrence of symptoms is due to the formation of a terminal stump that results from neural regeneration. However, several studies indicate a satisfactory outcome of surgical management ranging from 96 per cent (Bennett 1995) to 80 per cent (Mann 1983). In the Bennett study, the outcome of surgery was evaluated using a patient's symptoms grading system post-operatively. The Mann study employed subjective (patient questionnaire) and objective evaluation (local tenderness, numbness in toes and plantar skin) pre-operatively and post-operatively.

Surgical alternatives to excision of the pathological nerve are emerging. Neurolysis involves releasing the nerve from intramuscular fibrosis and fascial slips crossing the nerve (Dellon 1992; Gauthier 1979; Okafor 1997; Price 1992). Finney (Finney 1989) has described percutaneous electrocoagulation and Barrett (Barret 1994) have pioneered the use of endoscopes to decompress the neuroma or entrapped nerve. Hodor (Hodor 1997) and Algan (Algan 2003) describe the use of cryogenic denervation of the intermetatarsal space neuroma. Lastly, Colgrove has evaluated the technique of intermuscular neuroma transposition compared with resection (Colgrove 2000). However, despite these innovations, complete resection of the affected nerve remains the mainstay of surgical intervention for Morton's neuroma.

Steroid injection is often the initial conservative treatment for Morton's neuroma but good evidence is needed about its clinical effectiveness. None of the published studies is a randomised controlled trial (RCT) with adequate blinding procedures. One retrospective study (Bennett 1995) has shown that 47% of patients improved with a steroid injection, and another that most patients were asymptomatic two years after steroid injection (Greenfield 1984). In contrast, a third retrospective study has shown only temporary relief (Rasmussen 1996), and other authors concluded that the outcome was so poor that initial treatment should be surgery (Gaynor 1989). Two case studies have reported adverse events following steroid injection for Morton's neuroma (Basadonna 1999; Reddy 1995).

Other interventions that have been reported in clinical practice include: various physical therapies such as ultrasound, electrical stimulation, whirlpool and massage (Nunan 1997); non-steroidal anti-inflammatory drugs (Nunan 1997); manipulation (Cashley 2000); orthoses (Kilmartin 1994; Gaynor 1989; Hirschberg 2000) and alcohol sclerosing injections (Dockery GL 1999).

The evidence base for the interventions for this common condition is currently weak. The aim of this systematic review was to evaluate the effectiveness of surgical and non-surgical interventions for Morton's neuroma.

OBJECTIVES

To examine the evidence from randomised controlled trials concerning the effectiveness of interventions in adults with Morton's neuroma.

METHODS

Criteria for considering studies for this review

Types of studies

(a) Randomised or quasi-randomised (methods of allocating participants to an intervention which were not strictly random e.g. date of birth, hospital record, number alternation) controlled trials of interventions for Morton's neuroma were selected. Studies where participants were not randomised into intervention groups were excluded from the review.

(b) Trials in which allocation to treatment or control group was not concealed from the outcome assessor were included.

Types of participants

Inclusion in this review was restricted to trials with participants meeting the following criteria:
(a) Adults > 16 years of age.
(b) Pain associated with Morton's neuroma.
(c) No history of significant trauma or systemic inflammatory conditions such as rheumatoid arthritis.

Types of interventions

Any surgical or non-surgical intervention that aimed to reduce pain associated with Morton's neuroma.

Types of outcome measures

Primary outcomes

The primary outcome measure was pain relief defined as proportion of patients reporting at least 50% pain relief after three months (McQuay 1997). This was based on whichever measure of pain was reported (visual analogue scales, McGill Pain Questionnaire etc).

Secondary outcomes

Secondary outcome measures included adverse effects of treatment such as infection, hypoaesthesia, callosities over plantar scars, reflex sympathetic dystrophy (McQuay 1997).

Search methods for identification of studies

Electronic searches

We searched the Cochrane Neuromuscular Disease Group register in January 2003 but no trials on Morton' s neuroma were identified.

We searched MEDLINE (January 1966 to January Week 2 2003), EMBASE (January 1980 to February Week 2 2003), and CINAHL (January 1982 to February Week 1 2003). For MEDLINE strategy see Appendix 1.

Searching other resources

We hand-searched abstracts and proceedings from The Society of Chiropodists and Podiatrists Annual Conference, The British Orthopaedic Foot Surgery Society, The Pain Society of Great Britain and Ireland and The International Association for Study of Pain.

Departments of orthopaedics and schools of podiatry were contacted to request dissertation bibliographies and information on published or unpublished studies. The bibliographies of randomised trials were checked. The authors of these studies were also contacted to identify additional published or unpublished data.

Data collection and analysis

Selection of studies

Following identification of potential trials for inclusion by the previously outlined search strategy (CT), two reviewers (CT and DM) applied the exclusion criteria to each study located and conducted data extraction independently using a customised data extraction form. Disagreements were resolved by discussion of the articles by the third reviewer (JNAG). We wrote to trialists for additional information on trial methodology and results (for example, method of randomisation and standard deviations) when not apparent from the paper.

Assessment of risk of bias in included studies

The methodological quality assessment also took into account: allocation concealment, patient blinding, appropriate randomisation, observer blinding, explicit diagnostic criteria, explicit outcome criteria, how studies deal with baseline differences of the experimental groups, and completeness of follow-up. These were graded using the Cochrane approach: A: adequate, B: moderate risk of bias, C; inadequate, Grade D: not done. The agreement on methodology assessment were reported using kappa statistics. As agreement was poor, we reassessed the studies and reached agreement by consensus.

Measures of treatment effect

Results would have been expressed as relative risks (RR) for dichotomous data and weighted mean differences for continuous data (with 95% confidence intervals).

Data synthesis

If meta-analysis had been possible, for each outcome measure, we would have calculated a pooled estimate of treatment effects across trials using the Cochrane statistical package RevMan. If pooling had been possible and heterogeneity had been detected we would have used a random effects model but if not a fixed effect model.

RESULTS

Description of studies

See: 'Characteristics of included studies'

One hundred and seven references relating to Morton's neuroma were identified from the search strategy. Four RCTs were identified from the search of the literature. One RCT (Quinn 1999) was identified from the hand-search of the podiatric literature. This was an abstract from a conference presentation and did not contain sufficient detail to allow inclusion in the systematic review. We wrote to the principal author requesting details and we were provided with the conference presentation, which still did not contain sufficient details and so the study was excluded.

The other three trials are included (Colgrove 2000; Kilmartin 1994; Nashi 1997). These covered three very different therapeutic approaches to Morton's neuroma. One of the trials considers the conservative approach to the treatment of neuroma and two are concerned with surgical techniques.

The three RCTs included in this review included 121 participants. The mean ages of participants were 47 (no SD), (Colgrove 2000), 43 (1 SD 12) (Kilmartin 1994) and 53 (no SD) (Nashi 1997). The gender profiles were 35 women and 9 men (Colgrove 2000), 21 women and two men (Kilmartin 1994), 44 women and eight men (Nashi 1997). The three trials in question involved patients from the general population rather than specific groups such as athletes.

Details of the diagnostic criteria were lacking from the Colgrove study but in the RCTs by Kilmartin and Nashi, the diagnosis of Morton's neuroma was based on patients' history (such as pain on walking and numbness or pins and needles in the

toes) and clinical examination. The key diagnostic features were presence of a Mulder's click, a painful click thought to be due to the neuroma being expressed from the intermetatarsal space on lateral compression of the metatarsals (Thomson 2001), pain on applying digital pressure to the third/fourth intermetatarsal area and sensory loss in affected toes. No further diagnostic investigations such as ultrasound or histological confirmation were sought in any of the trials reviewed.

Details of individual trials are given in the 'Characteristics of included studies' table and are summarised below.

Transposition of the nerve and resection of the nerve

Description of trial interventions

The pathological plantar digital nerve is divided (transected) and then the cut end of the nerve is implanted into muscle tendon to reduce the risks of symptomatic recurrent neuroma. This compares with the standard technique of resection when the cut end of the nerve is left in situ.

Transposition of the nerve and resection of the nerve (Colgrove 2000): 46 participants were quasi-randomised to receive either the standard resection of the plantar digital nerve or a new technique where the nerve is transposed into the inter-muscular space between the adductor hallucis and the interossei muscles.

Supinatory insoles and pronatory insoles

Description of trial interventions

In-shoe biomechanical orthoses are known to restrict subtalar joint pronation. This is thought to be useful in Morton's neuroma as a restriction of subtalar joint pronation will limit hypermobility of the metatarsal and reduce abduction of the forefoot. Supination is the opposite movement to pronation. This study compares the effect on neuroma pain of insoles designed to pronate the foot and insoles designed to supinate the foot.

Supination insoles versus pronation insoles (Kilmartin 1994): 23 participants were randomised to receive either supination insoles or pronation insoles.

Excision of plantar digital nerve through dorsal and plantar incision

Description of trial interventions

Excision of the pathological plantar digital nerve is possible through either dorsal or plantar incisions. Plantar incision allows ready access to the nerve but results in a scar on the sole of the foot, which may develop painful callosities. The dorsal approach is technically more difficult and requires transection of the transverse plantar ligament, which may cause splaying of the forefoot, but allows early weight bearing following operation and avoids the problem of a painful plantar scar.

Excision of the nerve, plantar approach versus dorsal approach (Nashi 1997): 42 participants. Participants were quasi-randomised to have the plantar digital nerve resected through a plantar incision or a dorsal incision.

Outcome measures

The three RCTs measured different patient outcome measures. Kilmartin used a 100 mm visual analogue scale (VAS) for pain whilst Colgrove used a 100 point scale administered by telephone interview as the primary outcome measure. Kilmartin additionally used the McMaster-Toronto Arthritis patient function preference questionnaire (MACTAR) patient-specific measure of maximal function (Tugwell 1987). Nashi reported pain relief (although the method is very unclear). Nashi also assessed duration of hospital stay, time taken to return to work and activity.

Risk of bias in included studies

The overall quality scores can be found in the 'Characteristics of included studies' table and the 'Quality assessment of included trials' table (Table 1).

Was the randomisation procedure described?

Colgrove allocated participants according to the fourth digit of their eight digit medical record number. Kilmartin used a method of involving the balanced randomisation lists prepared by Peto et al.(Peto 1976). Nashi reported that each participant was allotted alternately to each group but no more details were provided.

Was the allocation schedule concealed?

In the Colgrove study, the allocation schedule was concealed from participants but not clinicians. In Kilmartin and Nashi, there is no indication that the allocation schedule was concealed from patients or clinicians.

Was an intention to treat analysis used?

Intention to treat analysis was not used in any of the RCTs included in this review.

What number of patients were lost to follow up?

Colgrove reported that two patients were lost to follow-up, one from each group. Kilmartin states that two patients were lost to follow-up but does not state from which group. A further six patients requested to exit the trial but again it is not clear from which group or at what stage. Nashi did not report loss to follow-up.

Was the outcome assessment blind?

In the RCT by Colgrove, the outcome assessors were blind to treatment allocation. In the Kilmartin and the Nashi RCTs, there was no apparent blinding of assessors.

Effects of interventions

Because of the diversity of interventions and the difference in the type of patient outcome measures, the type of data collected prevented the pooling of data.

Primary outcome measure

Our primary outcome measure was pain relief defined as proportion of patients reporting at least 50% pain relief after three months (McQuay 1997).

Transposition of the nerve and resection of the nerve

The evaluation of transposition of the nerve compared with resection of the nerve (Colgrove 2000) resulted in 100% of patients in the transposition group and 86% of patients in the resection group with a decrease in pain of greater than 50% (RR 1.79; 95% CI 1.25 to 2.55) at the 36 to 48 months end-point . The authors

state that outcomes were recorded at one month, three months, six months, 12 months and 36-48 months. However, data were not available for the three-month follow-up period.

Supinatory insoles and pronatory insoles

The evaluation of supination insoles versus pronation insoles (Kilmartin 1994) resulted in 50% of participants in the supination group and 45% of participants in the pronation group with a decrease in pain of greater than 50% (RR 1.10; 95% CI 0.45 to 2.70) at the 12 months end-point. Participants were reviewed at one month, two months, three months and 12 months. Data were only presented for the 12 months end-point.

Excision of plantar digital nerve through dorsal and plantar incision

The evaluation of excision of the nerve, plantar approach compared to dorsal approach (Nashi 1997) resulted in 80% of participants in the dorsal incision group and 65% of participants in the plantar incision group with a decrease in pain of greater than 50% (RR 1.26, 95% CI 0.82 to 1.92). Participants were followed up for an average of 3.1 years and the minimum follow-up period was one year. Again, data for the three-month follow-up period were not available.

Secondary outcome measures

Adverse events

Secondary outcome measures included adverse effects of treatment such as infection, hypoaesthesia, callosities over plantar scars, reflex sympathetic dystrophy in terms of numbers needed to harm.

Complications were identified in each of the three studies.

Colgrove (Colgrove 2000) reported that in the transposition group, one patient had a *Staphylococcus* wound infection which subsequently cleared with oral antibiotics. This was asymptomatic after a year. There were no complications in the resection group.

Kilmartin (Kilmartin 1994) reported that in the supination group, one of the 10 patients reported lower limb pain other than that associated with the Morton's neuroma. In the pronation group, two of the 11 participants reported lower limb pain other than that associated with the Morton's neuroma.

Nashi (Nashi 1997) reported that in the dorsal incision group, two of the 26 participants had subsequent infection, two had a painful scar and one had a recurrence of neuroma. In the plantar incision group, two of the 26 participants had infection, five had a painful scar and one had a recurrence of neuroma.

DISCUSSION

This systematic review was conducted in order to evaluate the effectiveness of surgical and non-surgical interventions for Morton's neuroma. We discovered a distinct lack of quality research for this common and troublesome condition. There is a paucity of evidence and only three randomised controlled trials of interventions for Morton's neuroma have been published. However, these studies examined three different aspects of treatment. Because of the heterogeneity of the trials, no pooling of data or meta-analyses was possible. We were aware of poor reporting of the trials, lack of details pertaining to loss to follow-up, inadequate randomisation techniques and a failure to conduct intention to treat analyses.

There is no evidence to support the use of pronatory insoles (RR 1.10; 95% CI 0.45 to 2.70). In clinical practice, it is routine to explore orthotic therapy as part of the conservative regime for Morton's neuroma. However there is very little evidence to substantiate the continuation of this practice and they also have cost implications for patients and health service providers. A variety of insoles are available for this condition and the type reported in this systematic review were designed to prevent foot pronation, but these were shown to be no better than the control group.

In the non-randomised literature, Coughlin (Coughlin 2000) suggests that conservative measures are successful in 50% of cases but Gaynor (Gaynor 1989) suggests that surgical management of Morton's neuroma demonstrates a much higher probability of success when compared to conservative methods. Quirk (Quirk 1987) states that conservative treatment helps occasionally but at least 80% of patients require surgical intervention. Steroid (corticosteroid) injections are standard practice for this condition, yet there were no RCTs reporting the effectiveness of corticosteroids for Morton's neuroma. Three observational studies have provided conflicting results of effectiveness (Gaynor 1989; Greenfield 1984; Rasmussen 1996).

This systematic review has shown that there is, at most, a very limited indication that transposition of the transected plantar digital nerve may yield better results than standard resection of the nerve in the long term (RR 1.79; 95% CI 1.25 to 2.55). This concurs with the findings of (Wolfort 2001) who also concluded that recurrent pain after a dorsal interdigital neurectomy can be treated successfully through a plantar approach with implantation of the proximal end of the nerve into an intrinsic muscle. Clinicians are aware that there is a tendency for an amputation stump to form following resection of the nerve. By attempting to transpose the nerve into muscle, Colgrove (Colgrove 2000) has shown that this may be advantageous compared to the standard excision.

We have also shown that there is, at best, a very limited indication to suggest that dorsal incisions for resection of the plantar digital nerve may result in less symptomatic postoperative scars when compared to plantar excision of the nerve (RR 1.26; 95% CI 0.82 to 1.92). This is consistent with findings from observational studies which carried out resection of the nerve through dorsal incisions (Beech 2000; Keh 1992; Schroven 1995; Wu 1996). In contrast, a retrospective study of 44 participants (81 neuromas) (Wilson 1995) suggests the plantar transverse incision has the advantage of allowing improved exposure and access to the neuroma. The authors of this study also reported no occurrence of amputation neuroma postoperatively. However, it is generally accepted that amputation neuroma will occur in as much as 20% of participants receiving excision surgery regardless of the approach (Mann 1983). Clinically, it is our experience that more and more of these operative procedures for Morton's neuroma are being performed through dorsal incisions to avoid the high risk of painful plantar scars. Although technically more difficult to perform, a dorsal approach has the added benefit of earlier weight bearing following surgery.

Adverse events

Adverse events following excision of the nerve are common. This causes numbness of the affected toes and the most

likely complications include postoperative infection, problematic incisional tenderness or keratosis on the sole of the foot (Richardson 1993). There is also a high incidence of recurrence of pain which is thought to arise from the formation of a 'stump' neuroma (Barret 1994).

Clinical problems such as 'steroid flare' (Greenfield 1984) and anaphylaxis (Tollafield 1996) do occur with corticosteroid injections. In two case reports, skin atrophy and altered pigmentation were noted following corticosteroid injection for Morton's neuroma (Basadonna 1999; Reddy 1995).

Future research

The almost complete lack of investigation in this area can be viewed positively. Since this is not a situation where there are many incompatible papers and conflicting results, there is an opportunity to encourage future work to report outcomes and trial procedures consistently to allow smooth and meaningful pooling of data. Reporting of trials in the future should consider adherence to the CONSORT guidelines (Moher 2001) to allow pooling of data. Careful consideration should be given to the nature of patient outcomes, such as measures for pain and function and healthcare use.

AUTHORS' CONCLUSIONS

Implications for practice

There is insufficient evidence on which to assess the effectiveness of surgical and non-surgical interventions for Morton's neuroma.

Implications for research

Well designed trials are now needed to begin to establish an evidence base for the treatment of Morton's neuroma pain. Unresolved issues are neurolysis in comparison to other forms of surgical procedure such as excision of the plantar digital nerve and the effectiveness of corticosteroid injections.

ACKNOWLEDGEMENTS

We are grateful to the Cochrane Neuromuscular Disease Group Editorial team, Richard Hughes and Kate Jewitt for their guidance and helpful comments. The authors would also like to thank Derek Santos for help with the literature search and for contacting Schools of Podiatry.

REFERENCES

References to studies included in this review

Colgrove 2000 *{published data only}*

Colgrove R, Huang E, Barth A, Greene M. Interdigital neuroma: intermuscular neuroma transposition compared with resection. *Foot & Ankle International* 2000;**21**(3):206-11.

Kilmartin 1994 *{published data only}*

Kilmartin TE, Wallace WA. Effect of pronation and supination orthosis on Morton's neuroma and lower extremity function. *Foot & Ankle International* 1994;**15**(5):256-62.

Nashi 1997 *{published data only}*

Nashi M, Venkatachalam A, Muddu B. Surgery of Morton's neuroma: dorsal or plantar approach?. *Journal of the Royal College of Surgeons (Edinburgh)* 1997;**42**(1):36-7.

References to studies excluded from this review

Guiloff 1979 *{published data only}*

* Guiloff RJ. Carbamazepine in Morton's neuralgia. *British Medical Journal* 1979;**2**(6195):904.

Quinn 1999 *{published data only}*

* Quinn SG, Raja F, Raja D. A study to measure the efficacy of injectable betamethasone (Betnesol) for the treatment of Morton's neuroma. *British Journal of Podiatry* 1999:130-1.

Rasmussen 1996 *{published data only}*

* Rasmussen MR, Kitaoka HB, Patzer GL. Non operative treatment of plantar interdigital neuroma with a single corticosteroid injection. *Clinical Orthopaedics and Related Research* 1996;**326**:188-93.

Wolfort 2001 *{published data only}*

* Wolfort SF, Dellon AL. Treatment of recurrent neuroma of the interdigital nerve by implantation of the proximal nerve into muscle in the arch of the foot. *Journal of Foot and Ankle Surgery* 2001;**40**(6):404-10.

Additional references

Algan 2003

Algan H, Baykan A. Cryoanalgesia relieves neuroma pain. Proceedings of the 4th Congress of EFIC-The European Federation of the International Association for the Study of Pain, Prague. Prague: The European Federation of the International Association for the Study of Pain, 2003.

Barret 1994

Barret SL, Pignetti TT. Endoscopic decompression for intermetatarsal nerve entrapment - the EDIN technique: preliminary study with cadaveric specimens; early clinical results. *The Journal of Foot and Ankle Surgery* 1994;**33**(5):503-8.

Basadonna 1999

Basadonna P, Rucco V, Gasparini D, Onorato A. Plantar fat pad atrophy after corticosteroid injection for an interdigital neuroma: A case report. *American Journal of Physical Medicine and Rehabilitation* 1999;**78**(3):283-5.

Beech 2000

Beech I, Rees S, Tagoe M. Clinical audit of the surgical management of plantar digital neuroma. *The Foot* 2000;**10**:31-5.

Bennett 1995

Bennett GL, Graham CE, Mauldin DM. Morton's interdigital neuroma: a comprehensive treatment protocol. *Foot and Ankle International* 1995;**16**(12):760-3. [MEDLINE: 96352873]

Bourke 1994

Bourke G, Owen J, Machet D. Histological comparison of the third interdigital nerve in patients with Morton's metatarsalgia and control patients. *Australian and New Zealand Journal of Surgery* 1994;**64**(6):421-4. [MEDLINE: 94280343]

Cashley 2000

Cashley D. Manipulative therapy in the treatment of plantar digital neuritis (Morton's neuroma). *British Journal of Podiatry.* 2000;**3**(3):67-9.

Coughlin 2000

Coughlin MJ. Common causes of pain in the forefoot in adults. *Journal of Bone and Joint Surgery* 2000;**82**(6):781-90.

Dellon 1992

Dellon LA. Treatment of Morton's neuroma as a nerve compression. The role for neurolysis. *Journal of the American Podiatric Medicine Association* 1992;**82**(8):399-402.

Dockery GL 1999

Dockery GL. The treatment of intermetatarsal neuromas with 4% alcohol sclerosing injections. *Journal of Foot and Ankle Surgery* 1999;**38**(6):403-8.

Finney 1989

Finney W, Wiener SN, Catanzariti F. Treatment of Morton's neuroma using percutaneous electrocoagulation. *Journal of the American Podiatric Medicine Association* 1989;**79**(12):615-8.

Gauthier 1979

Gauthier G. A nerve entrapment syndrome. A new surgical technique. *Clinical Orthopaedics & Related Research* 1979;**142**:90-3. [MEDLINE: 80045657]

Gaynor 1989

Gaynor R, Hake D, Spinner SM, Tomczak RL. A comparative analysis of conservative versus surgical treatment of Morton's neuroma. *Journal of the American Podiatric Medicine Association* 1989;**79**(1):27-30. [MEDLINE: 89258382]

Greenfield 1984

Greenfield J, Rea J, Ilfield F. Morton's interdigital neuroma: indications for treatment by local injections versus surgery. *Clinical Orthopaedics & Related Research* 1984;**185**:142-4. [MEDLINE: 84157457]

GRO Scotland 1999

General Register Office for Scotland. http://www.gro-scotland.gov.uk/grosweb/grosweb.nsf/pages/home.

Hirschberg 2000

Hirschberg GG. A simple cure for Morton's neuralgia. *Journal of the American Podiatric Medical Association* 2000;**90**(2):100-1.

Hodor 1997

Hodor L, Barkal K, Hatch-Fox LD. Cryogenic denervation of the intermetatarsal space neuroma. *Journal of Foot and Ankle Surgery* 1997;**36**(4):311-4.

Keh 1992

Keh RA, Ballew KK, Higgins KR, Odom R, Harkless LB. Long-term follow-up of Morton's neuroma. *Journal of Foot Surgery* 1992;**31**(1):93-5.

Mann 1983

Mann R, Reynolds J. Interdigital neuroma: A critical analysis. *Foot and Ankle International* 1983;**3**(4):238-43.

McQuay 1997

McQuay HJ, Moore RA, Eccleston C, Morley S, Williams AC. Systematic review of outpatient services for chronic pain control. *Health Technology Assessment* 1997;**1**(6):1-135. [MEDLINE: 98144155]

Moher 2001

Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet* 2001;**357**(9281):585.

Nunan 1997

Nunan PJ, Giesy BD. Management of Morton's neuroma in athletes. *Clinics in Podiatric Medicine and Surgery* 1997;**14**(3):489-501.

Okafor 1997

Okafor B, Shergill G, Angel J. Treatment of Morton's neuroma by neurolysis. *Foot & Ankle International* 1997;**18**(5):284-7. [MEDLINE: 97311029]

Oliver 1998

Oliver TB, Beggs I. Ultrasound in the assessment of Metatarsalgia: a surgical and histological correlation. *Clinical Radiology* 1998;**53**(4):287-9.

Peto 1976

Peto R, Pike MC, Armitage P. Design and analysis of randomised clinical trials requiring prolonged observation of each patient. *British Journal of Cancer* 1976;**34**:585-612.

Price 1992

Price BA, Miller G. Internal neurolysis. *Journal of Foot Surgery* 1992;**31**(3):250-9.

Quirk 1987

Quirk R. Morton's neuroma. *Australian Family Physician* 1987;**16**(8):1117-20.

Reddy 1995

Reddy PD, Zelicof SB, Ruotolo C, Holder J. Interdigital Neuroma: Local cutaneous changes after corticosteroid injection. *Clinical Orthopaedics and Related Research* 1995;**317**:185-7.

Richardson 1993

Richardson EG, Brotzman SB, Graves SC. The plantar incision for procedures involving the forefoot. An evaluation of one hundred and fifty incisions in 115 patients. *Journal of Bone and Joint Surgery* 1993;**75**(5):726-31.

Schroven 1995

Schroven I, Geutjens G. Results of excision of the interdigital nerve in the treatment of Morton's metatarsalgia. *The Foot* 1995;**5**:196-8.

Thomson 2001

Thomson C, Campbell R, Wood A, Rendall G. Disorders of the adult foot. In: Lorimer, et al. editor(s). Neale's Disorders of the Foot. 6th Edition. Edinburgh: Churchill Livingstone, 2001.

Tollafield 1996

Tollafield D, Williams H. The use of two injectable corticosteroid preparations used in the management of foot problems - a clinical report. *Journal of British Podiatric Medicine* 1996;**51**(12):171-4.

Tugwell 1987

Tugwell P, Bombardier C, Buchanan W, Goldsmith C, Grace E, Hanna B. The MACTAR Patient Preference Disability Questionnaire - an individualized functional priority approach for assessing improvement in physical disability in clinical trials in rheumatoid arthritis. *Journal of Rheumatology* 1987;**14**(3):446-51.

Wilson 1995

Wilson S, Kuwada G. Retrospective study of the use of a plantar transverse incision versus dorsal incision for excision of neuroma. *The Journal of Foot & Ankle Surgery* 1995;**34**(6):537-40.

Wu 1996

Wu KK. Morton's interdigital neuroma: a clinical review of its etiology, treatment and results. *Journal of Foot and Ankle Surgery* 1996;**35**(2):112-9.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Colgrove 2000

Methods	Randomisation: Quasi-randomised (based on medical record number) Blinding: both participants and outcome assessors were blinded Loss to follow-up: two participants (4.3%), one from the resection group and one from the transposition group.
Participants	Location: California, USA 44 participants with 45 neuromas Sex: Transposition group: 16 women (73%), Resection group 19 women (86%) Transposition group: mean age 49, Resection group: mean age 46 Inclusion criteria: No cause for foot pain other than interdigital neuroma and should have no interdigital neuroma performed in the same foot
Interventions	Two types of operation were performed; Group 1 (experimental group) an intermuscular transposition of the IDN after release of the IDN distally, Group 2 (Control group) a standard resection of IDN.
Outcomes	Assessments were made at baseline (pre-operatively) 1, 3, 6,12,36, 48 months following surgery (1) Pain rated on a scale from 0-100 by telephone interview (2) Pain interfered with choice of footwear/and or activity Participants with a pain level of 20 or greater at the final interview were requested to return for clinical evaluation.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Kilmartin 1994

Methods	Randomisation: Prepared randomisation list from random numbers list Concealment: inadequate Blinding: (D) Neither participants nor assessors were blind to treatment allocation. Loss to follow-up: two patients (13%) dropped out at one month, a further six requested early discharge from the study so alternative treatment could be tried. It is not clear from which groups the participants were lost.
Participants	Location: UK 23 participants with ? neuromas Sex: 21 Female (91%) Supination group: mean age 40 (SD12), Pronation group: mean age 46 (10.5) Inclusion criteria: Not explicit

Kilmartin 1994 *(Continued)*

	Diagnostic criteria: presence of Mulder's click, pain on applying digital pressure to third/fourth inter-metatarsal area and third/fourth toe sulci, and loss of sharp touch sensation from the adjoining sides of the third and fourth toes.
Interventions	Two types of in-shoe orthoses were provided; Group 1 (experimental group) pronation insole, Group 2 (Control group) supination insole.
Outcomes	Assessments were made at baseline then 1, 2, 3 and 12 months following treatment Outcomes included (1) VAS (100 mm) for pain 2.MACTAR patient specific measure of maximal function
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Nashi 1997

Methods	Quasi-randomised (paticipants allocated alternatively to either group) Blinding: Not blinded Loss to follow-up: No mention of loss to follow-up.
Participants	Location: UK 52 participants with 55 neuromas. Sex: Plantar approach: 26 participants - 24 female (92%), Dorsal approach 26 participants - 20 female (77%). Plantar approach group: mean age 54 Dorsal approach group: mean age 53 Inclusion criteria: None discussed
Interventions	Two types of operation were performed; Group 1: Plantar approach, Group 2: Dorsal approach.
Outcomes	Average follow-up was 3.1 years, minimum was one year. Assessments were based on duration of hospital stay, time taken to full weight bearing, time taken to return to work and activity, participant's subjective assessment and complications.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

IDN - interdigital neuroma

MACTAR - McMaster-Toronto Arthritis patient function preference questionnaire
VAS - visual analogue scale

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Guiloff 1979	A double-blind crossover trial of two patients. Excluded because the treatment was administered for pain occurring at night which we feel is not typical of the symptoms of Morton's neuroma. This report also lacked details and was a crossover trial of only two patients.
Quinn 1999	A published abstract of a conference presentation describes randomisation of participants to betamethasone or placebo. Insufficient details were presented in the published abstract for inclusion in this systematic review. We corresponded with the author requesting further details. We received a copy of the Powerpoint presentation of the trial which was still insufficient information for inclusion in this systematic review.
Rasmussen 1996	Not a randomised controlled trial.
Wolfort 2001	Not a randomised controlled trial.

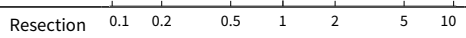
DATA AND ANALYSES

Comparison 1. Transposition versus resection

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of patients reporting 50% pain relief of pain	1	51	Risk Ratio (M-H, Fixed, 95% CI)	1.79 [1.25, 2.55]

Analysis 1.1. Comparison 1 Transposition versus resection, Outcome 1 Proportion of patients reporting 50% pain relief of pain.

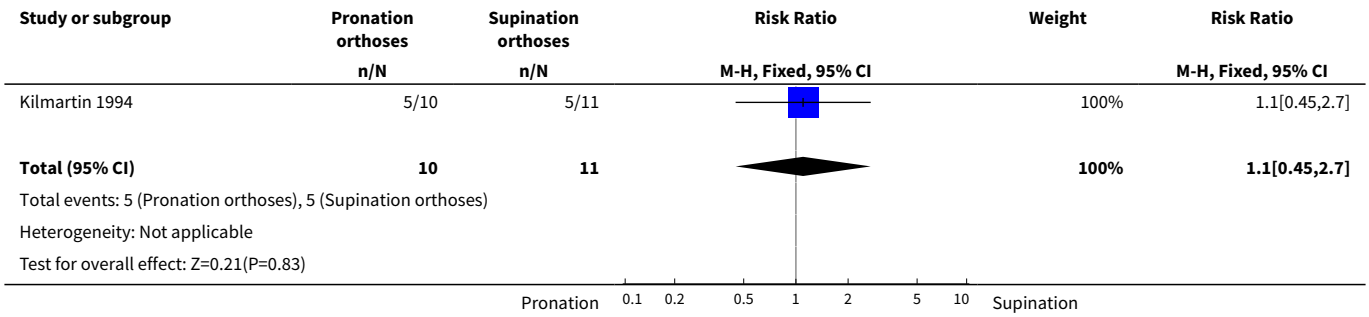
Study or subgroup	Transposition n/N	resection n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Colgrove 2000	22/23	15/28		100%	1.79[1.25,2.55]
Total (95% CI)	**23**	**28**		**100%**	**1.79[1.25,2.55]**
Total events: 22 (Transposition), 15 (resection)					
Heterogeneity: Not applicable					
Test for overall effect: Z=3.19(P=0)					



Comparison 2. Pronation versus supination orthoses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of patients reporting 50% relief of pain	1	21	Risk Ratio (M-H, Fixed, 95% CI)	1.1 [0.45, 2.70]

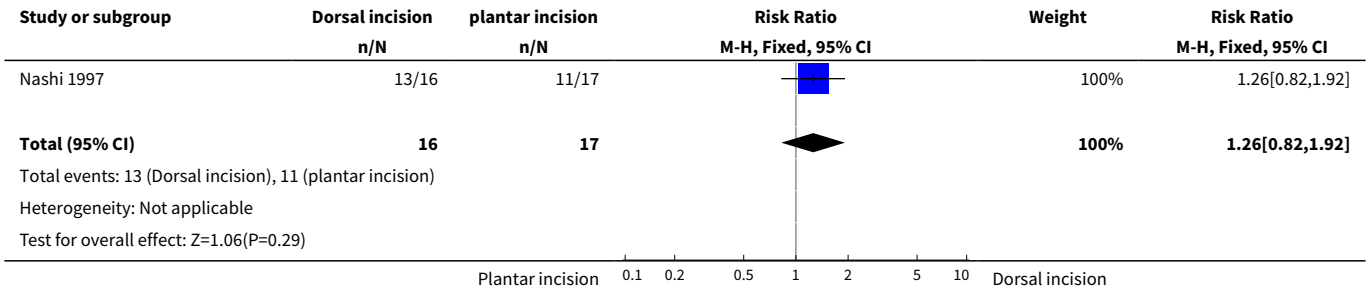
Analysis 2.1. Comparison 2 Pronation versus supination orthoses, Outcome 1 Proportion of patients reporting 50% relief of pain.



Comparison 3. Plantar incision versus dorsal incision

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Proportion of patients reporting 50% relief of pain	1	33	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.82, 1.92]

Analysis 3.1. Comparison 3 Plantar incision versus dorsal incision, Outcome 1 Proportion of patients reporting 50% relief of pain.



ADDITIONAL TABLES

Table 1. Quality assessment of included trials

Study ID	Randomisation method	Allocation con-cealmn	Patient blinding	Assessor blinding	Diagnostic criteria	Outcome criteria	Baseline differ-ences	Completeness of f-up
Colgrove 2000	C	A	A	A	C	A	A	A
Kilmartin 1994	C	D	D	D	B	A	D	A
Nashi 1997	C	D	D	D	A	C	B	D

APPENDICES

Appendix 1. OVID MEDLINE strategy

1 randomized controlled trial.pt
2 randomized controlled trials/
3 controlled clinical trial.pt.
4 controlled clinical trials/
5 random allocation/
6 double blind method/
7 Single-Blind Method/
8 clinical trial.pt.
9 exp Clinical Trials/
10 (clin$ adj25 trial$).tw.
11 ((singl$ or dodubl$ or trebl$ or tripl$) adj25 (blind$ or mask$ or dummy)).tw.
12 placebos/
13 placebo$.tw.
14 random$.tw.
15 research design/
16 (clinical trial phase i or clinical trial phase ii or clinical trial phase iii or clinical trial phase iv).pt.
17 multicenter study.pt.
18 meta analysis.pt.
19 Prospective Studies/
20 Intervention Studies/
21 cross over studies/
22 meta analysis/
23 (meta?analys$ or systematic review$).tw.
24 control.tw.
25 or/1-24
26 animal/
27 human/
28 26 and 27
29 26 not 28
30 25 not 29
31 (morton$1 adj5 (disease$1 or neuroma$1 or neuralgia$1 or metatarsalgia$1)).tw.
32 peripheral nervous system neoplasms/ or exp nerve compression syndromes/ or exp nerve sheath tumors/ or neuralgia/
33 (neurilemmoma$1 or neuroma$1 or neurofibroma$1 neuralgia$1 or entrapment).mp. or (nerve adj compression).tw. [mp=title, abstract, cas registry/ec number word, mesh subject heading]
34 32 or 33
35 exp foot diseases/ or metatarsus/ or exp foot/ or metatarsophalngeal joint/ or metatarsal bones/
36 (foot or forefoot or metatarsal$4 or intermetatarsal$4 or interdigital or metatarsophalangeal or (plantar adj5 digital)).tw.
37 35 or 36
38 34 and 37
39 31 or 38
40 30 and 39
41 from 40 keep 1-51

WHAT'S NEW

Date	Event	Description
1 March 2011	Amended	Contact details updated.

HISTORY

Protocol first published: Issue 2, 2000
Review first published: Issue 3, 2004

Date	Event	Description
2 July 2008	Amended	Converted to new review format.
14 April 2004	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Two reviewers (CT and DM) selected studies for inclusion, assessed methodological quality and extracted data. CT wrote the draft review and all three reviewers agreed the final text.

DECLARATIONS OF INTEREST

None

INDEX TERMS

Medical Subject Headings (MeSH)

Foot Diseases [*therapy]; Metatarsalgia [*therapy]; Neuroma [*therapy]; Randomized Controlled Trials as Topic; Toes [*innervation]

MeSH check words

Humans