Reviewer’s report

Title: The effectiveness of non-surgical interventions for common plantar digital compressive neuropathy (Morton's neuroma): a systematic review and meta-analysis

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Reviewer: Trevor D Prior

Reviewer's report:

This paper has the potential to inform clinician's on the evidence base for the conservative management of intermetatarsal neuroma but not in its current format.

Whilst I understand why the authors have included case series and not just RCTs it is not appropriate to combine the results in a systematic review. In my opinion, the information has been combined and places too much emphasis on treatment options that are not standard practice. Furthermore, case series should not be used in a systematic review to specifically guide treatment recommendations in the manner that has been applied in this paper.

I would recommend the authors separate the RCTs from the case series and report the results as such. They then have two options for recommending how this information can be applied to clinical practice:

Firstly, they could report those interventions that have sufficient evidence and those which show potential but require higher quality studies / more evidence.

Secondly, they can make recommendations on treatments that are non-invasive versus invasive (i.e. stage 1 and stage 2 but I would call them non-invasive / invasive).

For instance, the non-invasive would include wider footwear / metatarsal pads / orthoses (see comments later) and manipulation but state that the evidence to support these is weak but the risks are negligible. In my experience, many patients would be prepared to undertake such treatments on this basis.

For invasive, they should firstly report those that have RCT evidence of efficacy. And secondly report those that show potential but have weak evidence and report the complications with the guidance.

Specific comments
Data collection process pages 6/7
They define RCT and case series but also refer to a pseudo RCT in the paper - this should be defined.

Overview of studies, page 9
Is the country of origin important / need to be reported?
Outcome measures, page 10
Given a number of studies are case series, then the stiffest criteria should be applied. I therefore agree with the comments under the limitations discussed at the end; only satisfied rather than satisfied with limitations should be utilised.

Sclerosing injections, page 11
These studies vary greatly and include up to 9 treatments over 3 months. The data is weak and thus, this needs to be reflected in how this is listed under treatment options as per my general comments.

Radiofrequency / wider footwear / cryoneurolysis / Botox
Weak evidence and same recommendation as per sclerosant

Manipulation, page 12
The treatment protocol / control protocol from the RCT should be reported in the paper as there is no guidance as to what worked. Furthermore, the weakness of the review period should be provided adequate weighting when classified as per my general comments; shown to work in the short term (6 weekly treatments) but no long term results.

ESWT, page 13
This is a good example of how the outcome measures can affect the interpretation. It is not clear exactly what measure recorded a positive treatment effect but, I am assuming from the comments later that this was satisfied / satisfied with reservations. In this instance some common sense is required as, in the clinical environment, patients will be looking for symptoms relief. Furthermore, the study period was just 4 weeks.

As an example, my clinical interpretation of this to a patient would be - ESWT has been used and reviewed at 4 weeks. However, whilst patients felt the treatment was of some benefit, it did not make a significant difference to the pain level and we have no long term evidence of the benefit.

Orthoses, page 12
Some definition of orthoses should be considered to be included as those reported in this study are more simple insoles in a material which will flatten quickly.

In the discussion, the authors recommend that orthoses designed to supinate the subtalar joint should be removed from the treatment algorithm. Since the Kilmartin paper has been published, much has changed in the current thinking of orthoses and foot function. We now appreciate that orthoses rarely change the kinematic angles and certainly not in a consistent manner. Furthermore, the underlying basis of foot function on which this process was based has been demonstrated to be incorrect. Thus orthoses are designed to alter the forces acting on the foot and aim to reduce' for example, supination / pronation forces / moments rather than changing position.
As a result, clinicians will often take an approach of relieving stress to the involved tissues (in this case neuroma) which may include some common options such as a metatarsal pad but other features that may vary depending on the individual circumstances. Thus a decision on the use of orthoses cannot be made from this review and an emphasis on further research should be made. What the authors could say is that insoles with a felt pad to either apply pronation or supination moments to the foot have a minimal effect on pain. It would be of help to reflect on how the evidence and current theory have changed since the paper.

Discussion

Many of my comments are addressed at the beginning of this review and thus, the whole section needs to be re-written. Certainly there are some statements that place undue support for treatments such as cryoneurolysis and sclerosing injections (i.e. lines 377 - 378). However, I do feel they have rationalised the results well; it is more the weighting to treatments with weak evidence and the subsequent recommendations for practice that are the concern.

Line 392 - the evidence around ultrasound guided and non-guided injections has been presented. However, no reference has been made to the potential diagnosis of an intermetatarsal bursa which could cause neuroma symptoms - an US would be required to make this diagnosis and could then be used to directly inject the bursa. As a result, it might be more accurate to state that a clinical injection might be reasonable in the first instance but UG guided if no success, particularly as some papers indicate more than one injection may be required.

Line 429 - do they mean proximal to the metatarsal bases?

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