Brazilian Journal of Physical Therapy 2017;xxx(xx):xxx–xxx

abrapg·ft
Associação Brasileira de Pesquisa e Pós-Graduação em Fisioterapia

Brazilian Journal of Physical Therapy

https://www.journals.elsevier.com/brazilian-journal-of-physical-therapy

SYSTEMATIC REVIEW

Effects of monochromatic infrared phototherapy in patients with diabetic peripheral neuropathy: a systematic review and meta-analysis of randomized controlled trials

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Received 19 June 2016; received in revised form 13 September 2016; accepted 14 September 2016

KEYWORDS
Diabetes;
Foot;
Pain;
Tactile sensitivity;
Physical therapy

Abstract
Background: Monochromatic infrared energy (MIRE) or phototherapy has been used to improve plantar sensitivity and pain in lower limbs of patients with diabetic sensorimotor peripheral neuropathy (DSPN), but the available primary results are inconsistent.
Objective: To review systematically the effects of MIRE on plantar sensitivity and neuropathic pain in patients with DSPN.
Methods: Medline, EMBASE, Cochrane CENTRAL, and Google Scholar were searched up to September 2016. Randomized controlled trials addressing the effects of MIRE on plantar sensitivity and neuropathic pain in patients with DSPN were selected. Study inclusion, risk of bias and quality assessment, and data extraction were completed by two independent reviewers.
Results: Of 2549 records identified, six studies met the selection criteria, with 304 patients (594 feet) randomized. MIRE was not associated with improvement in plantar tactile sensitivity (SMD = 0.22, 95%CI −0.07 to 0.51, low quality of evidence). Subgroups of studies with short-term (up to 2 weeks) follow-up showed significant improvement in plantar sensitivity (SMD = 0.41, 95% CI 0.18–0.64). Neuropathic pain increased significantly in patients who received MIRE (MD = 0.49, 95% CI 0.30–0.68, low quality of evidence).

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http://dx.doi.org/10.1016/j.bjpt.2017.05.008

Please cite this article in press as: Robinson CC, et al. Effects of monochromatic infrared phototherapy in patients with diabetic peripheral neuropathy: a systematic review and meta-analysis of randomized controlled trials. *Braz J Phys Ther.* 2017, http://dx.doi.org/10.1016/j.bjpt.2017.05.008

Conclusions: There was limited evidence that MIRE results in short-term improvement of tactile sensitivity probably not sustained over time. Limited evidence also suggested that MIRE does not provide relief for neuropathic pain. As quality of evidence is low, further studies are likely to change the estimated effect.

Introduction

Diabetic chronic sensorimotor distal symmetrical polyneuropathy (DSPN) is considered one of the most common long-term microvascular complications of diabetes mellitus regardless of type,[1] affecting up to 50% of people with diabetes.[2,3] The onset of DSPN is usually insidious and heralded by sensory symptoms such as numbness and diminished sensation in lower limbs that start in the toes and progress proximally in a symmetrical distribution.[2,3] Symptoms are present in 50% of patients with DSPN, with 10–26% presenting with neuropathic pain.[3] Decreased feet sensitivity associated with DPSN is a significant risk factor for subsequent diabetic ulcers and non-traumatic amputations.[4] These complications lead to impairments in quality of life and high consumption of healthcare resources.[5]

The most effective approach to preventing DSPN and its complications consists in strict control of diabetes.[6,7] Once developed, few specific interventions are available for treatment[8,9] and the management of neuropathic pain is limited due to adverse effects.[3,8,9] Consequently, new adjunctive strategies have been proposed. Monochromatic Infrared Energy (MIRE), delivered through light-emitting diodes (LED), is one of these complimentary therapies. MIRE is approved by the Food and Drug Administration as a complimentary strategy to improve blood perfusion and reduce pain,[10] and it is used in patients with DSPN to improve plantar sensitivity and pain symptoms.[11–13]

The mechanisms by which MIRE produces its biological effects remain unclear. As infrared wavelengths penetrate to a greater depth than visible light,[14] it is suggested that photostimulation of hemoglobin increases nitric oxide release, leading to blood flow improvement.[15–18] Other biological effects of MIRE may be the enhancement of cell metabolism, by stimulating mitochondrial ATP production, accelerating antioxidant mechanisms, and improving cell function.[19–22]

Uncontrolled[11,12,23–26] and controlled[13,27–32] clinical trials assessed the effects of MIRE on plantar sensitivity restoration and pain relief in patients with DSPN, but results are inconsistent and the efficacy of this intervention has not yet been established for this population. Despite controversies about its effects, the use of LED technology is increasing, mostly in home settings, boosted by its low cost and easy access. Therefore, we conducted this systematic review in order to evaluate better the current evidence about the effect of MIRE on plantar sensitivity and neuropathic pain in patients with DSPN.

Methods

Protocol and registration

We performed this systematic review in accordance with the Cochrane Handbook for Systematic Reviews of Interventions[33] and followed the tutorial of the Brazilian Journal of Physical Therapy.[34] The protocol of this systematic review was registered at PROSPERO (CRD42013005068), and it can be assessed online.[35]

Eligibility criteria

We included randomized controlled trials (RCT) evaluating the effect of MIRE on plantar tactile sensitivity and/or neuropathic pain in the lower limbs in patients with DSPN. Trials should have at least one intervention group and one comparison group. MIRE was defined as if delivered through LED with wavelengths in the infrared or near-infrared range (750–1300 nm).[20] The comparison group should not have been exposed to MIRE. Our primary outcome was plantar tactile sensitivity assessed by Semmes–Weinstein monofilament (SWM). Secondary outcome was neuropathic pain in the lower limbs. The exclusion criteria were intervention performed in other regions than feet and follow-up intervention fewer than three days.

Search strategies

We searched in the electronic databases MEDLINE (accessed by PubMed), Cochrane CENTRAL, and Google Scholar and in EMBASE (up to September 30, 2016). The search terms included MeSH and entry terms related to diabetic neuropathy, infrared-ray, and a methodological filter for RCTs.[36] Outcome terms were not included to enhance the search sensitivity. There were no restrictions regarding language or publication date. The terms were adjusted to fit the requirements of each electronic database. We screened the list of references of included studies in order to identify additional RCTs. The complete search strategy applied on PubMed database can be assessed online in the systematic review protocol.[35]

Study selection and data extraction

Two reviewers (CCR, PSK) separately and independently screened the titles and abstracts of studies identified in the initial search. A standard screening checklist based on the

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