THE THERAPEUTIC EFFECTS OF LIGHT-EMITTING DIODE IN WOUND HEALING – SYSTEMATIC REVIEW

EFEITOS TERAPÊUTICOS DO DIODO EMISSOR DE LUZ NA CICATRIZAÇÃO CUTÂNEA – REVISÃO SISTEMÁTICA

Francielle Rodrigues Guimarães¹
Adriana Clemente Mendonça²
Júlia de Paula Tasso³
Regiane Luz Carvalho⁴
Laura Ferreira de Rezende Franco⁵
Elaine Caldeira de Oliveira Guirro⁶

ABSTRACT - The used of phototherapy with Light-Emitting Diode (LED) in clinical treatments as biostimulation methods for tissue repair isn’t established. **Objective**: To assess the therapeutic effects of phototherapy with LED in wound healing. **Methods**: A search and a selection of randomized clinical trials published in the last 10 years in the main data basis were performed. The studies were selected, summarized and evaluated on their methodological quality and level of evidence. **Results**: Most of the studies evaluated the reduction of the wounds through photographs. Some papers also evaluated

¹ Department of Physiotherapy, University Center of Associated Schools of Education (UNIFAE), São João da Boa Vista, São Paulo, Brazil. Department of Dermatology, Faculty of Medicine of Ribeirão Preto, University of São Paulo. Fisioterapeuta e Professora doutora do Centro Universitário das Faculdades Associadas de Ensino - UNIFAE. Endereço: Largo Engenheiro Paulo de Almeida Sandeville, 15 CEP: 13.870-377 São João da Boa Vista - SP- Brazil. FONE/FAX: (19) 3638.0240. E-mail: franfisio@yahoo.com.br or francielle@fae.br;
² Department of Applied Physiotherapy, Federal University of the Triângulo Mineiro;
³ Department of Applied Physiotherapy, Federal University of the Triângulo Mineiro;
⁴ Department of Physiotherapy, University Center of Associated Schools of Education (UNIFAE), São João da Boa Vista, São Paulo, Brazil;
⁵ Department of Physiotherapy, University Center of Associated Schools of Education (UNIFAE), São João da Boa Vista, São Paulo, Brazil;
⁶ Department of Biomechanics, Medicine and Rehabilitation of the Locomotor System, Faculty of Medicine of Ribeirão Preto, University of São Paulo.
THE THERAPEUTIC EFFECTS OF LIGHT-EMITTING DIODE IN WOUND HEALING – SYSTEMATIC REVIEW

ARTIGO

the granulation tissue, erythema, hyperemia, swelling and pain before and after the treatment. Such studies showed a large diversity of parameters: wavelength varied between 400 and 956nm, dose from 3 to 6 J/cm², frequency of application from twice a day to once a week, among others. Control groups received at least the conventional treatment (cleaning of lesions and bandaged) and/or treatment with the equipment turned off. The majority of the studies were classified with a high quality by the PEDro scale and there was a positive evidence for the role of LED in wound healing, by providing a faster and safer repair of the skin. Limitations: The use of the meta-analysis as a quantitative statistic tool was not possible because of some limitations of the selected articles. Conclusion: This first systematic review will help the improvement of the knowledge on the subject, contribute to new research strategies and facilitate evidence based practice.

Keywords: Phototherapy; Laser Therapy; Low-Level; Wound healing; Skin ulcer.
THE THERAPEUTIC EFFECTS OF LIGHT-EMITTING DIODE IN WOUND HEALING – SYSTEMATIC REVIEW

INTRODUCTION

The skin, also known as cutis or integument, is the largest organ of the human body with the role of maintaining body homeostasis (BARBUL, 1990; WERNER, 2003). Such function is damaged after a skin lesion and for its reestablishment a process of healing initiates (BARBUL, 1990). This is a multifactorial, complex process with the involvement of numerous cellular types (WERNER, 2003).

Over the last few years, phototherapy with coherent lights (LASER – Light Amplification by Stimulated Emission of Radiation) and incoherent ones (LED – light emission diodes) has been highlighted as biostimulation methods for tissue repair and have been used in clinical treatments or as a increment of other therapies (CAETANO, 2009; MINATEL, 2009; CHAVES, 2014).

Scientific evidence suggests that both LASER and LED therapy produce similar effects of wound healing, which reinforces the idea that the therapeutic effect of phototherapy depends on photon absorption by cromophores on the target tissue. According to the literature, the use of phototherapy usually increases local circulation, cellular proliferation and the synthesis of collagen (MINATEL, 2009; PRINDEZE, 2012; CHAVES, 2014).

Photobiostimulation activates a mechanism through the mitochondria, which starts producing signaling cells that promote a cascade of intracellular reactions. At cellular level, photobyological responses are the activation of genes of transcription factors, enzymes and pathways related to the increment in metabolism. In a simply manner, cells absorb photons and transform them into adenosine triphosphate (ATP), which will be used in metabolic processes, synthesis of deoxyribonucleic Acid (DNA), ribonucleic Acid (RNA), proteins, enzymes and other products required for tissue repair and to restore homeostasis (KARU, 1988; KARU, 1999).

Despite the use of phototherapy with LED for the treatment of skin wounds is more recent, studies executed in animals and humans have already shown a high healing potential (SMITH, 2005; MINATEL, 2009). It is known so far that such phototherapy...
may induce faster healing because it modulates the inflammatory process and the synthesis of collagen, through photobiostimulation of the cells involved in skin repair (KARU, 1999; PRINDEZE, 2012; CHAVES, 2014).

With such a complicacy for the healing process, its importance for the maintenance of body homeostasis and the recent use of LED in the treatment of wounds, we consider that there is a need to aggregate scientific evidence on its effects in tissue repair, to certify its safety and effective clinical use. The aim of this systematic review is to evaluate the therapeutic effects of phototherapy with LED in wound healing.

METHODS

Two independent review authors performed a search, between January and March, 2015, of papers published in the last ten years on the data basis Cochrane, Lilacs, Medline, SciELO, Pubmed, Scopus, Web of Science and PEDro. The following descriptors from Mesh/Decs were used as strategy for the search: Phototherapy, “wound healing” and “skin ulcer”, and the word “Light emitting diodo”. The Boolean operators “OR” and “AND” were used and the search expressions resulted were: (phototherapy or “Light emitting diodo”) and (“wound healing” or “skin ulcer”).

Studies were selected through the following inclusion criteria: to be published in English or Portuguese over the last ten years, fully available, human clinical trials, presence of a control group, with or without randomization, containing description of the parameters of the equipment used for the treatment, outcomes regarding the healing process characteristics and statistical analysis of the data. Studies including the use of LED associated with other forms of phototherapy (e.g., LASER) were excluded. Discordance between research author for the inclusion was solved by a consensus between them, considering the criteria for inclusion and exclusion.

Data from the studies was summarized in a uniformed descriptive table, based on the following topics: Authors, Characteristics of the sample, Outcomes, Methodological design, Intervention, Results and Conclusions.

Studies were also submitted to an evaluation of their methodological quality according to the PEDro (Physiotherapy Evidence Database) scale. It contains 11 items, each one scores 1 point, except for the first item which does not score. Total score ranges from 0 (zero) to 10 (ten). The PEDro assessment was performed independently by both research authors, since moderate levels of reliability have been observed between
examiners, when assessing the presence or absence of the qualifiers of the scale (MAHER, 2003).

Studies selected were classified as high quality when five or more criteria were positive, according to the PEDro scale, which reliability for the total score is enough for systematic reviews on Physiotherapy clinical trials, according to the Delphi list (MAHER, 2000). For the final classification of the studies, differences were discussed until an agreement was achieved between the authors.

After the quality assessment, papers were evaluated on their levels of scientific evidence for the efficacy of the treatment. Such system, named levels of evidence, classifies the effectiveness of an intervention into four levels (strong, mild, limited or conflicted and no evidence) considering their quality, results and the number of studies that applied the same intervention (Table 1) (VERHAGEN, 2001).

RESULTS

To perform this systematic review was not necessary the approval of the Ethics Committee. An initial number of 1262 articles were found in the electronic data basis, as described in Figure 1. After a filtering by the year of publishing, idiom and clinical trials, 612 remained. From these, titles and abstracts were read, the doubles excluded, such as the trials that applied phototherapy with LASER or the associated use of LED to other forms of phototherapy, and 42 remained. After the reading of these papers, 10 articles were selected according to the inclusion criteria and their information is reunited in Table 2. Article scores in each item of the PEDro scale is shown in Table 3.

DISCUSSION

Because our research was limited to a period of ten years, a few random clinical trials were found, an average of one per year. Size of the samples varied among papers, however none of them presented an n<5. Usually all the studies were concerned about criteria for inclusion and equality between groups, which turns the results more reliable. Only one study has not described the detailed characteristics of the participants (OH, 2015).
When considering the outcomes assessed, most of the studies evaluated wound healing through pictures by verifying their reduction. Some studies also verified the granulation tissue (MINATEL, 2009), erythema (OH, 2015), hyperemia (DE OLIVEIRA, 2014) and swelling (OH, 2015). Three papers assessed the pain before and after treatment through scales and questionnaires (DE OLIVEIRA, 2014; CHAVES, 2012; PARK, 2013). The intensity of the pain reported by the patients in the treated groups reduced significantly after the treatment. One study assessed the inflammatory activity through cytokine dosage (SIQUEIRA, 2015). It is important to remind that more clinical trials that evaluate the role of the LED in the physiopathology of the healing process at a deeper cellular level are required.

The parameters used in the intervention showed variety. The wavelength ranged from 400 to 956nm. The majority of the studies used wavelength around 600nm (visible red light) (CAETANO, 2009; MINATEL, 2009; DEHLIN, 2007; LANDAU, 2011; SCHUBERT, 2011; OH, 2015; DE OLIVEIRA, 2014; SIQUEIRA, 2015), five studies used the wavelength of 800nm (infrared) (CAETANO, 2009; MINATEL, 2009; LANDAU, 2011; CHAVES, 2012; PARK, 2013), two of them used 956nm (infrared) (DEHLIN, 2007; SCHUBERT, 2011) and five studies combined more than one wavelength in the same treatment (DEHLIN, 2007; CAETANO, 2009; MINATEL, 2009; LANDAU, 2011; SCHUBERT, 2011). None of the studies compared the treatment between one wavelength and treatments that used the combination of more than one wavelength.

When comparing the fluence, half of the studies used 3, 4 or 6 J/cm² (CAETANO, 2009; MINATEL, 2009; DE OLIVEIRA, 2014; CHAVES, 2012; SIQUEIRA, 2015) while the rest of them did not inform it. Three articles used the pulsed mode (DEHLIN, 2007; SCHUBERT, 2011; CHAVES, 2012). The time of application ranged from 30 seconds (CAETANO, 2009; MINATEL, 2009), 79 seconds (CHAVES, 2012) 152 seconds (DE OLIVEIRA, 2014), 2 minutes and 40 seconds (SIQUEIRA, 2015), 4 minutes (LANDAU, 2011), 9 minutos (DEHLIN, 2007; SCHUBERT, 2011), 10 minutes (PARK, 2013) to 15 minutes (OH, 2015). Some studies did not inform the accurate distance between the equipment and the wound area during the treatment (CHAVES, 2012; PARK, 2013; OH, 2015). Two studies used a distance of 2 cm (LANDAU, 2011; SIQUEIRA, 2015), other two studies used a distance of 3 cm (DEHLIN, 2007; SCHUBERT, 2011) and three applied the equipment in contact with the skin (CAETANO, 2009; MINATEL, 2009; DE OLIVEIRA, 2014). To use the equipment in direct contact with the skin, a transparent piece of plastic was positioned between them.
THE THERAPEUTIC EFFECTS OF LIGHT-EMITTING DIODE IN WOUND HEALING – SYSTEMATIC REVIEW

Páginas 542 a 556

548
Not only this review will increase the knowledge on this therapeutic, but also it can contribute to generate new research strategies and help the decision making of the therapeutist. It is also important to search for new therapies for wound healing that are well accepted by the patients, easy applied, with minimal side effects and low cost.

CONCLUSION

The results of the articles selected in this systematic review show a positive evidence of LED in wound healing, which can contribute to a faster and safer healing. However, since this is a recent therapy it should be used with caution. This systematic review will help the planning of new research on the topic and can help evidence based practice.

Declaration of interest:

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES


DINNES, J; DEEKS, J; KIRBY, J; RODERICK, P. A methodological review of how heterogeneity has been examined in systematic reviews of diagnostic test accuracy. Health and Technology Mar;9(12):1-113, iii, 2005.


Artigo


Financial funding: CNPq e FUNEPU
FIGURE AND TABLE LEGENDS

Figure 1. Detailed flowchart demonstrating the selection process of the studies

Total records identified (n = 1,262)
COCHRANE: 35; LILACS: 2; MEDLINE: 0; SCIELO: 0
PUBMED: 736; SCOPUS: 379; WEB OF SCIENCE: 106; PEDRO: 4

Filtering publication period, language and clinical trial (n = 612)
COCHRANE: 0; LILACS: 0; MEDLINE: 0; SCIELO: 0
PUBMED: 271; SCOPUS: 234; WEB OF SCIENCE: 104; PEDRO: 3

After removal of repeated trials and exclusion criteria (n = 42)

Reading and selection of trials for inclusion and exclusion criteria (n = 10)
Table 1. Evidence Grade

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Strong: multiples RCTs with high quality and few limitations.</td>
</tr>
<tr>
<td>2</td>
<td>Moderate: one RCT with high quality and one or more RCTs with low quality, or multiples RCTs with consistent results.</td>
</tr>
<tr>
<td>3</td>
<td>Limited: one RCT (with high or few qualities) or multiples RCTs with inconsistent results.</td>
</tr>
<tr>
<td>4</td>
<td>Inadequate: no RCT</td>
</tr>
</tbody>
</table>

* RCT = randomized controlled trials
Table 2. Details of the included studies

<table>
<thead>
<tr>
<th>Authors</th>
<th>Characteristics of the sample</th>
<th>Outcomes</th>
<th>Methodological design</th>
<th>Intervention</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chaves et al</td>
<td>Initial n= 30, final n= 10.</td>
<td>Evaluation of nipple lesions and analysis of photographs.</td>
<td>Randomized, placebo-controlled intervention trial.</td>
<td><strong>Experimental group</strong>: wavelength of 860 nm; frequency of 100 Hz; average power of 50mW; power density of 50mW/cm²; total emission area of 1 cm²; pulsed emission mode with 50% duty cycle; and dose of 4 J/cm². Application time was 79 sec, twice a week for a period of 4 weeks.</td>
<td>A significant difference between experimental and control groups was observed for the healing of nipple lesions. Intensity of pain reduced significantly in the experimental group.</td>
<td>The LED phototherapy successfully accelerated the healing of nipple lesions and reduced the pain intensity in the participants in the experimental group when compared to those in the control group. Advantages: easy to apply, low cost, and acceptance by lactating women.</td>
</tr>
<tr>
<td></td>
<td>Nipple trauma in breastfeeding women.</td>
<td></td>
<td></td>
<td><strong>Control group</strong>: application with the device off. Both groups received general guidelines to prevent trauma during breastfeeding.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No significant differences between the groups.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Landau et al</td>
<td>Initial n= 20, final n= 16 (5 women and 11 men with diabetes and venous ulcers).</td>
<td>Placebo-controlled double-blinded.</td>
<td><strong>Treatment group</strong>: received 180mW/cm² broadband (400–800 nm) visible light, distance of 2 cm, each time for 4 min/treatment, twice a week for a period of 12 weeks.</td>
<td>Wounds reduced in 9 out of 10 patients (90%) from the treatment group, whereas in the placebo group only 2 out of 6 patients exhibited reduced ones (33%). Reduction in wound size in the treatment group versus the placebo group was 89% and 54%, respectively.</td>
<td>Broadband (400–800 nm) visible light was an effective modality for the treatment of leg or foot ulcers. Advantages: light treatments are painless, and no adverse effects have ever been reported.</td>
</tr>
<tr>
<td></td>
<td>No significant differences between the groups.</td>
<td></td>
<td></td>
<td><strong>Placebo group</strong>: received non-healing fluence of light (10mW/cm²).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3. PEDro Scale score.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(item does not score)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Random allocation</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Concealed allocation</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Similar groups at baseline</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Blinding of subjects</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Blinding of therapists</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Blinding of assessors</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Measure of one key outcome obtained for 85% of subjects</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Intention to treat analysis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Between group comparisons of at least one key outcome</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Point and variability measures for at least one key outcome</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Total scores</td>
<td>9/10</td>
<td>8/10</td>
<td>9/10</td>
<td>8/10</td>
<td>7/10</td>
<td>8/10</td>
<td>10/10</td>
<td>3/10</td>
<td>8/10</td>
<td>7/10</td>
</tr>
<tr>
<td>Methodological quality</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>