# Effectiveness of photobiomodulation therapy for nipple pain or nipple trauma in lactating women: a systematic review protocol

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## ABSTRACT

**Objective:** The objective of this protocol is to evaluate the effectiveness of photobiomodulation therapy for the treatment of nipple pain or nipple trauma in women during the breastfeeding period.

**Introduction:** One approach that has been reported on the management of nipple pain or nipple trauma in lactating women is the use photobiomodulation therapy to heal the injury or to decrease pain intensity. However, studies have achieved different results, due to variations in the treatment protocol, such as the source of light used, the application mode, the irradiation, or the light dose parameters, leading to varying outcomes.

**Inclusion criteria:** This review will consider studies that evaluate photobiomodulation therapy for the treatment of nipple pain or nipple trauma in lactating women in the postpartum period that compare the intervention to standard care, placebo, or other type of treatment. The following outcomes will be considered: intensity of nipple pain, healing of nipple trauma, exclusive breastfeeding rate, quality of life, and satisfaction of the women with treatment. There will be no publication time limit, and studies published in any language will be considered for inclusion.

**Methods:** This review will be conducted in accordance with JBI methodology for systematic reviews of effectiveness. The search strategy will search both published and unpublished studies, and the process of study selection, critical appraisal, data extraction, and data synthesis will be performed in accordance to the JBI approach.

**Systematic review registration number:** PROSPERO CRD42019147401

**Keywords:** breast feeding; laser therapy; low-level light therapy; nipples; photobiomodulation therapy

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## Introduction

Breastfeeding is considered by the World Health Organization (WHO) as one of the primary reasons for decreasing child mortality rates related to common diseases in early childhood, like diarrhea and pneumonia. Breast milk provides all the nutrients needed for adequate nutrition and development of the infant until six months of age, so exclusive breastfeeding for six months has been recommended by WHO as the optimal way of feeding infants. Complementary food should be introduced gradually after this time, with mothers continuing breastfeeding for up to two years or more.[1]

Throughout the breastfeeding process, nipple pain or nipple trauma is a very frequent issue that affects lactating women, and which health professionals need to address.[2] Both nipple pain and nipple trauma can impact negatively on breastfeeding practice, due to the mother's intense discomfort caused from breastfeeding the baby, and is associated with an increased risk of early weaning, which means

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*We declare that one of the authors (MVPS) is the founder and chief scientist at Bright Photomedicine, a company that produces phototherapy devices; they will be excluded from the study screening, data extraction, and quality assessment section of the review. The other authors declare no conflict of interest.*

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discontinuing breastfeeding before six months of age.[3] Nipple trauma is defined as a macroscopic cutaneous lesion in the nipple and areola area,[4] or as vascular lesions that can cause a change in color, texture, and shape of the skin.[5]

Best practice recommendations for the management of nipple pain or nipple trauma include assessment by a trained health professional of the infant's positioning and attachment to the breast, as well as breastfeeding support, as incorrect attachment is one of the leading causes of nipple pain or nipple trauma. In cases of persistent nipple pain, other causes should be investigated and managed, which may require clinical judgment.[6]

One approach that has been reported for the management of nipple pain or nipple trauma in lactating women is the use of light therapy at low doses to heal the injury or to decrease pain intensity.[7-11] The terminology involving the therapeutic use of light varies between studies, such as low-level laser therapy, low-level light therapy, low-intensity laser therapy, low-power laser therapy, among others. For this reason, a nomenclature consensus meeting was organized, as these terms may not be accurate because other types of light devices are used with the same purpose, such as light-emitting diode (LED) or broadband light sources. Therefore, in a joint conference with the North American Association for Light Therapy and the World Association for Laser Therapy, the term ''photobiomodulation therapy'' was considered as the most appropriate definition for this kind of intervention.[12]

Photobiomodulation therapy is defined as ''a form of light therapy that utilizes non-ionizing forms of light sources, including lasers, LEDs, and broadband light, in the visible and infrared spectrum. It is a nonthermal process involving endogenous chromophores eliciting photophysical (ie, linear and nonlinear) and photochemical events at various biological scales. This process results in beneficial therapeutic outcomes including but not limited to the alleviation of pain or inflammation, immunomodulation, and promotion of wound healing and tissue regeneration.''[12(p.184)]

Because of the low power of light, the treatment does not cause a temperature rise in the target tissue and has the advantage of being a non-invasive approach, with broad application, including pain relief and wound healing.[13] Although the complete mechanism of action of light therapy is under investigation, it is known that light at low levels (red or near-infrared region) can interact with cells and promote changes at the molecular, cellular, and tissue extent.[13] It is accepted that there is a mitochondrial response to light, involving an increase of electron transport, oxygen consumption, mitochondrial membrane potential, and synthesis of ATP, and that many changes occur in tissues as a response to the absorption of light by the chromophores, leading to short- or long-term beneficial effects, such as increasing blood flow, improved tissue oxygenation, analgesia, reduction of inflammation, and wound healing.[14]

However, studies have achieved different results on the use of photobiomodulation therapy, according to the treatment protocol, as there are some variations on the source of light used, the outcomes assessed, the application mode, the irradiation parameters (wavelength, irradiance, pulse structure), the light dose parameters (energy, irradiation time, treatment interval), and so on.[13,15,16]

Light parameters and the doses applied to the tissue are fundamental for the effectiveness of this kind of therapy. The wavelengths usually applied are in the range of 600 to 700 nanometers (nm) and 780 to 1100 nm (as wavelengths between 700 and 780 nm seem to be ineffective), with an irradiance between 5 mW $cm^{-2}$ to 5 W $cm^{-2}$, using continuous wave or pulsed light with energy density from 0.04 to 50 Joules $cm^{-2}$, and a wide variance of power from 1 mW up to 500 mW.[13] It is known that incorrect parameters on the use of light can lead to ineffective treatment, because there is a biphasic dose response curve, where too low or too high doses (energy density) or irradiance can lead to less benefit, no benefit, or even negative effect, increasing the likelihood of different results if different parameters had been employed by the researchers.[13,14]

With advances in technology, devices used in photobiomodulation therapy have further developed and are being replaced by compact and more economical devices, with a number of different light sources being used to deliver treatment, such as gallium-aluminum-arsenide, aluminium gallium indium phosphide, and indium gallium arsenide, among others.[13,16]

All these aspects can be observed in some studies regarding the treatment of nipple pain or nipple trauma in lactating women, in which both LED[7,8] and low-level laser[9,10,11] therapies have been used by

researchers, encompassing different treatment protocols, and consequently, different results.

Therefore, the objective of this systematic review is to evaluate the effectiveness of photobiomodulation therapy on the treatment of nipple pain or nipple trauma for breastfeeding women.

A preliminary search of PROSPERO, MEDLINE, the Cochrane Database of Systematic Reviews, and the *JBI Database of Systematic Reviews and Implementation Reports* was conducted and no current or in-progress systematic reviews on the topic were identified. One study[16] conducted a literature review of the evidence on the therapeutic application of photobiomodulation for wound healing in PubMed, but did not include any primary studies regarding nipple pain or nipple trauma treatment.

## Review question

What is the effectiveness of photobiomodulation therapy for nipple pain or nipple trauma in lactating women?

## Inclusion criteria

### *Participants*

This review will consider studies that include lactating women with any type of nipple trauma (fissures, cracks, excoriation, blisters, redness, etc.) or nipple pain due to breastfeeding, in any postpartum period, regardless of age, nationality, setting, number of children, type of birth, or term or preterm birth.

### *Interventions*

This review will consider studies that evaluate the therapeutic use of low-dose light for the treatment of nipple pain or nipple trauma in lactating women. The different types of low-dose light therapy, and its wavelength variations, potency, application mode, and frequency will be considered for inclusion. The different forms of light sources to be included will follow the definition of photobiomodulation therapy by Anders *et al.*[12]: ''A form of light therapy that utilizes non-ionizing forms of light sources, including lasers, LEDs, and broadband light, in the visible and infrared spectrum.''(p.184)

### *Comparators*

This review will consider studies that compare the intervention to standard care, placebo, or other type of treatment for nipple pain or nipple trauma.

### *Outcomes*

This review will consider studies that include the following outcomes.

The primary outcomes that will be focused on include: intensity of nipple pain (measured by validated scales, such as numeric scale, Visual Analogue Scale, etc.), and healing of nipple trauma (assessed by clinical observation, measurement of the extension of the lesion, photographs, or other type of assessment; the length of time for injury healing will also be considered).

Secondary outcomes include: exclusive breastfeeding rate (in percentage, in any follow-up time period or maintenance of exclusive breastfeeding [in any time period]; the period of time of interrupted breastfeeding during the treatment will also be considered), Quality of Life (assessed by validated tools, such as The Quality of Life Scale [QOLS], The World Health Organization Quality of Life [WHOQOL], etc.), satisfaction of the women with treatment (maternal satisfaction measured by scales or descriptive self-report), and adverse effects/side effects of the treatment (any adverse or side effects reported by the mother or observed by the researcher).

### *Types of studies*

This review will consider both experimental and quasi-experimental study designs including randomized controlled trials, non-randomized controlled trials, controlled before and after studies, and interrupted time-series studies.

Studies published in any language will be included in this review and translations will be sought where necessary. There will be no publication date restrictions.

## Methods

The proposed systematic review will be conducted in accordance with JBI methodology for systematic reviews of effectiveness evidence.[17] This protocol is registered in PROSPERO (CRD42019147401).

### *Search strategy*

The search strategy will aim to locate both published and unpublished studies. An initial limited search of MEDLINE and CINAHL was undertaken to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles, and the index

terms used to describe the articles were used to develop a full search strategy for MEDLINE (PubMed; see Appendix I). The search strategy, including all identified keywords and index terms, will be adapted for each included information source. The reference list of all studies selected for critical appraisal will be screened for additional studies.

The following databases will be searched from inception to present: MEDLINE (PubMed), CINAHL (Embase), The Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, ScienceDirect, and LILACS. Sources of unpublished studies and gray literature to be searched will include ClinicalTrials.gov, Google Scholar, OpenGrey, ProQuest Dissertations and Theses, Coordination for the Improvement of Higher Education Personnel (CAPES), and MedNar.

### Study selection

Following the search, all identified citations will be collated and uploaded into EndNote X9 (Clarivate Analytics, PA, USA) and duplicates removed. Titles and abstracts will then be screened by two independent reviewers for assessment against the inclusion criteria for the review. Potentially relevant studies will be retrieved in full and their citation details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia).[18] The full text of selected citations will be assessed in detail against the inclusion criteria by two independent reviewers. Reasons for exclusion of full text studies that do not meet the inclusion criteria will be recorded and reported in the systematic review. Any disagreements that arise between the reviewers at each stage of the study selection process will be resolved through discussion or with a third reviewer. The results of the search will be reported in full in the final systematic review and presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.[19]

### Assessment of methodological quality

Eligible studies will be critically appraised by two independent reviewers at the study level for methodological quality in the review using standardized critical appraisal instruments from JBI for experimental and quasi-experimental studies.[17] Authors of papers will be contacted to request missing or additional data for clarification, where required. Any disagreements that arise will be resolved through discussion or with a third reviewer. The results of critical appraisal will be reported in narrative form and in a table.

All studies, regardless of the results of their methodological quality, will undergo data extraction and synthesis (where possible).

### Data extraction

Data will be extracted from studies included in the review by two independent reviewers using a modified version of the JBI SUMARI standardized data extraction tool (see Appendix II), including specific data regarding the characteristics of the intervention.

The data extracted will include specific details about author(s); year of publication; study design; setting; characteristics of participants; characteristics of the intervention (including type of light, wavelength, doses, frequency, and locality of the application); description of the intervention and control group and its respective sample size; the outcomes of relevance to the review objective assessed; time of follow-up; the main results related to the review question; and study limitations or comments of the reviewer. Any disagreements that arise between the reviewers will be resolved through discussion or with a third reviewer. Authors of papers will be contacted to request missing or additional data, where required.

### Data synthesis

Studies will, where possible, be pooled in statistical meta-analysis using JBI SUMARI, considering the different sources of light used (laser, LED, or broadband light). Effect sizes will be expressed as both risk ratio (for dichotomous data) and weighted (or standardized) final post-intervention mean differences (for continuous data) and their 95% confidence intervals will be calculated for analysis. The $I^2$ test will be used to quantify the amount of heterogeneity, and statistical analyses will be performed using a random effects model.[20] To investigate potential sources of heterogeneity, subgroup analyses will be performed based on wavelength variation, irradiance, energy density, pulse structure (continuous wave or pulsed light), irradiation time, and treatment interval. Also, sensitivity analysis

will be performed, excluding studies with high risk of bias for selection bias (randomization and allocation concealment) and blinding (use of placebo). Where statistical pooling is not possible due to clinical or methodological heterogeneity, the findings will be presented in narrative form including tables and figures to aid in data presentation where appropriate. A funnel plot will be generated using RevMan V5 (Copenhagen: The Nordic Cochrane Centre, Cochrane) to assess publication bias if there are 10 or more studies included in a meta-analysis. Statistical tests for funnel plot asymmetry (Egger test, Begg test, Harbord test) will be performed where appropriate.

### *Assessing certainty in the findings*

The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach for grading the certainty of evidence will be followed[21] and a Summary of Findings will be created using GRADEPro GDT V5 (McMaster University, ON, Canada). The Summary of Findings will present the following information where appropriate: absolute risks for the treatment and control, estimates of relative risk, and a ranking of the quality of the evidence based on the risk of bias, directness, heterogeneity, precision, and risk of publication bias of the review results. The outcomes reported in the Summary of Findings will be: pain intensity, nipple trauma healing, exclusive breastfeeding rate, quality of life, and the women's satisfaction.

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## Appendix I: Search strategy

**MEDLINE (PubMed)**

| Date | Search strategy | Results retrieved | Studies selected |
|---|---|---|---|
| 13/09/2019 | (((((((("Breast Feeding"[Mesh]) OR breast feeding) OR breastfeeding) OR "Nipples"[Mesh]) OR nipple)) AND ((((((((("Wounds and Injuries"[Mesh])) OR wound) OR injury) OR injuries) OR trauma) OR "Pain"[Mesh]) OR pain) OR lesions) OR fissure))) AND ((((((((((((((((((((((((("Lasers"[Mesh]) OR "Laser Therapy"[Mesh]) OR "Low-Level Light Therapy"[Mesh]) OR laser) OR "pulsed laser") OR "continuous wave laser") OR "low level light therapy") OR "low-level light therapy") OR "low-level laser therapy") OR "low level laser therapy") OR "low power laser therapy") OR "low-power laser therapy") OR "low-power laser irradiation") OR "low power laser irradiation") OR photobiomodulation) OR "photobiomodulation therapy") OR "laser biostimulation") OR "laser bio stimulation") OR "laser bio-stimulation") OR "laser phototherapy") OR "biolaser") OR "laser treatment") OR "light-emitting diode") OR LLLT) OR LED) | 114 | 8 |

## Appendix II: Data extraction instrument

| | Study 1 | Study 2 | Study 3 | Study 4 | Study 5 | Study 6 | Study 7 |
|---|---|---|---|---|---|---|---|
| Study reference (author, year) | | | | | | | |
| Study design | | | | | | | |
| Setting | | | | | | | |
| Characteristics of participants (including postpartum period, age, nationality, setting, number of children, type of birth, term or preterm birth, etc.) | | | | | | | |
| Type of Intervention (type of light) | | | | | | | |
| Characteristics of the Intervention: wavelength, pulse structure, irradiance, energy density, irradiation time, frequency, and area of the application | | | | | | | |
| Group description (intervention and control) | | | | | | | |
| Sample size (intervention and control) | | | | | | | |
| Outcomes of interest assessed | | | | | | | |
| Follow-up time | | | | | | | |
| Main results | | | | | | | |
| Study limitations or reviewer comments | | | | | | | |