

Effects of phototherapy on tissues with dermal fillers: systematic review protocol

Efeitos da fototerapia em tecidos com preenchedores dérmicos: protocolo de revisão sistemática

Efectos de la fototerapia en tejidos con rellenos dérmicos: protocolo de revisión sistemática

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Liliane Akemi Kawano Shibasaki

ORCID: <https://orcid.org/0000-0002-2894-3778>

Bahiana School of Medicine and Public Health, Brazil

E-mail: lilianeshibasaki.pos@bahiana.edu.br

Nathalia Alves Pereira Sá

ORCID: <https://orcid.org/0000-0001-8772-6442>

Bahiana School of Medicine and Public Health, Brazil

E-mail: nathaliasa21.1@bahiana.edu.br

Maria Paula Vidal Grisi

ORCID: <https://orcid.org/0000-0002-9902-7486>

Bahiana School of Medicine and Public Health, Brazil

E-mail: mariagrisi19.2@bahiana.edu.br

Silvia Regina de Almeida Reis

ORCID: <https://orcid.org/0000-0003-1195-0485>

Bahiana School of Medicine and Public Health, Brazil

E-mail: srareis@bahiana.edu.br

Abstract

This systematic review protocol aims to verify the existence of synergistic effect of phototherapy in tissues that received dermal fillers. The review will be carried out through the stages of preparation of the research question, search for primary studies, selection of studies according to eligibility criteria, data extraction, analysis, and synthesis of evidence. The question will be based on the PICOS strategy: “Does the combined use of dermal fillers and phototherapy have a synergistic effect on facial rejuvenation?” The search in the literature will be carried out in seven databases and in sources of gray literature. The results will be exported to the Rayyan application for the purpose of deleting duplicate studies. The reading of the titles and abstracts will be carried out by two independent and blind reviewers. Randomized clinical studies that associated phototherapy in tissues that received dermal fillers will be selected for full reading. The data will be extracted and submitted to a narrative synthesis, and if possible, the meta-analysis. In the methodological quality analysis, the RoB2 tool will be used for the risk of bias and the GRADE tool for the quality of evidence.

Keywords: Dermal fillers; Phototherapy; Low-level light therapy; Intense pulsed light therapy; Lasers.

Resumo

Este protocolo de revisão sistemática objetiva verificar a existência de efeito sinérgico da fototerapia em tecidos que receberam preenchedores dérmicos. A revisão será realizada através das etapas de elaboração da pergunta da pesquisa, busca dos estudos primários, seleção dos estudos de acordo com os critérios de elegibilidade, extração de dados, análise e síntese das evidências. A pergunta será baseada na estratégia PICOS: “A associação de preenchedores dérmicos e fototerapia tem efeito sinérgico no rejuvenescimento facial?” A busca na literatura será realizada em sete bases de dados e em fontes de literatura cinzenta. Os resultados serão exportados para o aplicativo Rayyan com a finalidade de excluir os estudos duplicados. A leitura dos títulos e resumos será realizada por dois revisores independentes e cegos. Estudos clínicos randomizados que associaram a fototerapia em tecidos que receberam preenchedores dérmicos serão selecionados para a leitura na íntegra. Os dados serão extraídos e submetidos à uma síntese narrativa, e se possível, a realização de metanálise. Na análise da qualidade metodológica, será utilizado para o risco de viés a ferramenta RoB2 e para a qualidade da evidência o GRADE.

Palavras-chave: Preenchedores dérmicos; Fototerapia; Terapia com luz de baixa intensidade; Terapia de luz pulsada intensa; Lasers.

Resumen

Este protocolo de revisión sistemática tiene como objetivo verificar la existencia de efecto sinérgico sobre la fototerapia en tejidos que recibieron rellenos dérmicos. La revisión se llevará a cabo a través de las etapas de preparación de la pregunta de investigación, búsqueda de estudios primarios, selección de estudios según criterios de elegibilidad, extracción de datos, análisis y síntesis de evidencia. La pregunta se basará en la estrategia PICOS: “¿El uso combinado de rellenos dérmicos y fototerapia tiene un efecto sinérgico en el rejuvenecimiento facial?” La búsqueda en la literatura se realizará en siete bases de datos y en fuentes de literatura gris. Los resultados se

exportarán a la aplicación Rayyan con el fin de eliminar estudios duplicados. La lectura de los títulos y resúmenes será realizada por dos revisores independientes y ciegos. Se seleccionarán estudios clínicos aleatorizados que asociaron fototerapia en tejidos que recibieron rellenos dérmicos para una lectura completa. Los datos serán extraídos y sometidos a una síntesis narrativa, y si es posible al metaanálisis. En el análisis de la calidad metodológica se utilizará la herramienta RoB2 para el riesgo de sesgo y la herramienta GRADE para la calidad de la evidencia.

Palabras clave: Rellenos dérmico; Fototerapia; Terapia por luz de baja intensidad; Tratamiento de luz pulsada intensa; Rayos láser.

1. Introduction

Facial aging is a complex process that occurs in all layers of the face (Cotofana et al., 2016; Fedok, 1996). In aesthetic treatments it is necessary to perform procedures that act in different tissue depths to reduce facial damage (Ramos-e-Silva et al., 2007; Shah & Kennedy, 2018). With only one treatment it is not always possible to solve the needs of patients and it becomes necessary to association of techniques. As a result, aesthetic medicine has evolved a lot in recent decades with the development of materials, appliances, and different methodologies to try to achieve facial rejuvenation. Among the materials are facial fillers, which are injectable substances, also called implants, which vary in composition, mechanisms of action, tissue interactions and duration in the body (Loghem et al., 2015).

According to the International Society of Plastic Surgery (ISAPS), non-surgical facial rejuvenation procedures increased by 13.9% in 2020 alone. The ease of postoperative recovery and versatility in correcting minor changes allows new facial treatments minimally invasive approaches, which make them increasingly popular and already exceed surgical procedures (International Society of Aesthetic Plastic Surgery, 2021). The injectable materials considered safe by the U.S. Food and Drug Administration (FDA) are hyaluronic acid, calcium hydroxyapatite, poly-L-lactic acid and polymethylmethacrylate (U.S. Food & Drug Administration, 2020).

Photobiomodulation is a therapy that uses previously calculated and controlled light to provide energy to regulate cellular metabolism. In phototherapy, ablative, non-ablative, fractionated, LED and pulsed light lasers are used (Escudero et al., 2019). Studies with photobiomodulating therapies have shown effectiveness in accelerating tissue repair and increasing collagen production during the healing process. It has been demonstrated that low energy density laser therapy promotes synergism by being associated with biomaterials, such as hydroxyapatite in bone tissue, promoting collagen growth and improvement in the repair process (Hanna et al., 2021; Magri et al., 2021). However, the association of photobiomodulation with dermal fillers in facial soft tissues is still poorly understood, especially regarding its aesthetic and biological effects (Carruthers et al., 2016; Fabi et al., 2016; Urdiales-Galvez et al., 2019).

The aim of this systematic review is to verify, through a question based on the PICOS strategy in randomized clinical trials, whether the association of phototherapy in the tissues that received the dermal fillers has a synergistic effect. Thus, the benefits of the association of the two treatments in improving facial aesthetic treatment will be evaluated. Based on this strategy, a preliminary search was conducted in the International Prospective Register of Systematic Reviews (PROSPERO) whose similar search record was not found. Following, the protocol of the systematic review entitled “Combined use of facial fillers and phototherapy: a systematic review”, was then recorded as CRD42021258048.

2. Methodology

This systematic review protocol was developed in accordance with the recommendations of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) (Moher et al., 2015; Shamseer et al., 2015) and follows the guidelines of the Cochrane Collaboration (Higgins et al., 2019) to describe the steps in which the systematic review will be conducted. The study design chosen was a systematic review that aims to assess the quality of existing data in the

literature individually to support clinical decision and knowledge construction in relation to the structured question. (Donato & Donato, 2019).

The research question “Does the combined use of dermal fillers and phototherapy have a synergistic effect on facial rejuvenation?” was elaborated based on the acronym PICOS with the following definitions: Population (P) adults who received dermal fillers for aesthetic reasons. Includes only fillers that are currently FDA approved (hyaluronic acid, calcium hydroxyapatite, poly-L-lactic acid, polymethyl methacrylate) (U.S. Food & Drug Administration, 2020). Intervention (I) treatment with phototherapy of any wavelength. Comparison (C) split-face type control (intra-individual comparison) or control group. Outcome (O) effects of phototherapy interaction of different wavelengths on tissues with dermal fillers. Study design (S) randomized controlled trials.

Eligible articles as primary studies of the systematic review will be based on the following inclusion criteria: randomized clinical studies evaluating the association of phototherapy of any wavelength in tissues that received dermal fillers. Only studies with dermal fillers of cosmetic use approved by the FDA will be considered (U.S. Food & Drug Administration, 2020). Studies should have as results clinical and/or histological parameters for evaluation of the effects of phototherapy. There will be no restriction on location, time, or language. Research with patients with systemic diseases or on medication will not be included. Narrative studies, systematic reviews, cases and case series, in vitro and animal studies, comments, interviews and abstracts will not be accepted as primary studies.

The search will be performed in the Databases PubMed/MEDLINE (Chart 1), The Cochrane Central Register of Controlled Trials, LILACS, BVS, Web of Science, Scopus and EMBASE. Google Scholar will be included as a source of gray literature. The search strategies will use the combination of keywords and terms MeSH (Medical Subjective Headings) and DeCS (Health Sciences Descriptors) with Boolean operators OR and AND will be adapted to the parameters of each base.

Chart 1: Article search strategy that will be used in one of the systematic review databases:

Database	Vocabulary
PubMed	(“skin filler*”[All Fields] OR “cosmetic filler*”[All Fields] OR “durapatite”[MeSH Terms] OR “durapatite”[All Fields] OR “calcitite”[All Fields] OR “calcium hydroxyapatite”[All Fields] OR “calcium hydroxylapatite”[All Fields] OR “hydroxyapatite compound”[All Fields] OR “hydroxylapatite”[All Fields] OR “poly l lactic acid”[All Fields] OR “plla”[All Fields] OR “sculptra”[All Fields] OR “polylactic acid”[All Fields] OR “polylactide”[All Fields] OR “polymethyl methacrylate”[MeSH Terms] OR “polymethyl methacrylate”[All Fields] OR “poly methyl methacrylate”[All Fields] OR “polymethylmethacrylate”[All Fields] OR “pmma”[All Fields] OR “hyaluronic acid/therapeutic use”[MeSH Terms] OR “hyaluronic acid”[All Fields] OR “hyaluronate sodium”[All Fields] OR “restylane”[All Fields] OR “biostimulat*”[All Fields]) AND (“phototherapy”[MeSH Terms] OR “phototherapy”[All Fields] OR “phototherapies”[All Fields]) OR “laser therapy”[MeSH Terms] OR “laser biostimulation”[All Fields] OR “laser phototherapy”[All Fields] OR “photobiomodulation therap*”[All Fields] OR “non ablative devices”[All Fields] OR “lasers, semiconductor”[MeSH Terms] OR “laser ablative”[All Fields] OR (“laser s”[All Fields] OR “lasers”[MeSH Terms] OR “lasers”[All Fields] OR “laser”[All Fields] OR “lasered”[All Fields] OR “lasering”[All Fields]) OR “fractional laser*”[All Fields] OR “pulsed light”[All Fields] OR “phototherap*”[All Fields] OR “photoradiation therapy”[All Fields] OR “light therapy”[All Fields] OR “wavelength light”[All Fields] OR “polarized light”[All Fields] OR “non-polarized light”[All Fields] OR (“low level light therapy”[MeSH Terms] OR (“low level”[All Fields] “light”[All Fields] “therapy”[All Fields]) OR “low level light therapy”[All Fields] OR “llt”[All Fields]) OR “LPLT”[All Fields] OR “LILT”[All Fields] OR “cold laser*”[All Fields] OR “therapeutic laser*”[All Fields] OR “light emitting diode*”[All Fields] OR “LED”[All Fields] OR “low reactive level laser”[All Fields] OR “diode laser”[All Fields]) AND (“randomised controlled trial”[All Fields] OR “randomized controlled trial”[All Fields] OR “controlled clinical trial”[All Fields] OR (“random allocation”[MeSH Terms] OR (“random”[All Fields] AND “allocation”[All Fields]) OR “random allocation”[All Fields] OR “random”[All Fields] OR “randomization”[All Fields] OR “randomized”[All Fields] OR “randomisation”[All Fields] OR “randomisations”[All Fields] OR “randomise”[All Fields] OR “randomised”[All Fields] OR “randomising”[All Fields] OR “randomizations”[All Fields] OR “randomize”[All Fields] OR “randomizes”[All Fields] OR “randomizing”[All Fields] OR “randomness”[All Fields] OR “randoms”[All Fields]) OR (“placebos”[All Fields] OR “placebos”[MeSH Terms] OR “placebos”[All Fields] OR “placebo”[All Fields]) OR “clinical trials as topic”[MeSH Major Topic] OR “randomly”[All Fields] OR (“clinical trials as topic”[MeSH Terms] OR (“clinical”[All Fields] AND “trials”[All Fields] AND “topic”[All Fields]) OR “clinical trials as topic”[All Fields] OR “trial”[All Fields] OR “trial s”[All Fields] OR “trialed”[All Fields] OR “trialing”[All Fields] OR “trials”[All Fields]) OR (“groups”[All Fields] OR “grouped”[All Fields] OR “grouping”[All Fields] OR “groupings”[All Fields] OR “groups”[All Fields] OR “population groups”[MeSH Terms] OR (“population”[All Fields] AND “groups”[All Fields]) OR “population groups”[All Fields] OR “group”[All Fields]) OR “clinical trial”[All Fields] OR “random allocation”[All Fields] OR “double-blind method”[All Fields] OR “comparative study”[All Fields] OR “evaluation study”[All Fields] OR “follow-up studies”[All Fields] OR “cross-over studies”[All Fields] OR “research design”[All Fields])

Source: Authors.

The citations found in the databases will be exported to the Rayyan software of the Qatar Computing Research Institute (Ouzzani et al., 2016) and will be independently and double-blindly evaluated by two LAKS and SRAR examiners. If there is disagreement between reviewers, a third reviewer is consulted. Duplicate titles and abstracts will be removed initially and then the studies will be verified by the examiners according to the eligibility criteria. The selected studies will be read in full and will have their information extracted and analyzed. The Endnote 20 application distributed by Clarivate Analytics (EndNote 2013) will be used as a reference manager.

The following information will be extracted from the studies by the LAKS examiner and provided by SRAR and will be arranged in a table: author, country, year, sample size, gender, age, dermal filler, phototherapy, energy density, site of irradiation, method of analysis, evaluation period and outcome. The outcomes of interest in primary studies are the clinical and histological parameters of the combined use of phototherapy in tissues with fillers, as well as identifying the wavelength with better performance in synergism. All outcomes found will be described in results. The measures of evaluation of the improvement of treatments will be compared and synthesized. If possible, a quantitative analysis will be carried out through meta-analysis.

The methodological quality will be performed through the Tool RoB 2 (revised tool for Risk of Bias in randomized trials) (Sterne et al., 2019), provided by the Cochrane Collaboration to assess the risk of bias in randomized clinical studies and performed by two reviewers. The studies will be individually evaluated for selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias, with the criteria “low”, “high” and “some concerns” (Higgins et al., 2011).

Finally, the analysis of the certainty of the evidence recommendation to use phototherapy in tissues that received dermal fillers will be evaluated with the GRADE (Grades of Recommendation, Assessment, Development and Evaluation Working Group) (Guyatt et al., 2011).

3. Expected Results

It is expected that this systematic review will identify randomized clinical studies with methodological quality and certainty of reproducible evidence in aesthetic treatments with association of phototherapy and dermal implants, which can support the clinical decision in choosing treatments with better results for patients.

4. Partial Final Considerations

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