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REVIEW

Photodynamic Therapy Interventions in Facial Photodamage: A Systematic Review

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KEYWORDS
Photodamage;
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Abstract
Introduction: Photodynamic therapy (PDT) involves the combination of a light source and a photosensitizing agent to induce tissue damage via the generation of singlet oxygen. Although topical PDT has been approved for other indications, its use in facial photodamage is uncertain.
Aims: To assess the efficacy and safety of PDT in facial skin photoaging.
Methods: All randomized clinical trials (RCTs) evaluating the efficacy and safety of any form of topical PDT for the treatment of facial photodamage (dermatoheliosis) or photoaging in patients older than 18 years, were included. Photodynamic-therapy using any topical photosensitizing agent at any dose, and with any light-source, were considered. Comparators were chemical exfoliation, intense pulsed light (IPL), light emitting diodes (LED), dermabrasion or microdermabrasion, ablative or non-ablative lasers, injectables, surgery, placebo and/or no treatment.

A systematic search in PubMed, Embase, Lilacs, Google Scholar and RCT's registry databases, was performed.
Results: Search was conducted up to May 4th 2016. Four authors independently selected and assessed methodological quality of each RCT. According to inclusion criteria, twelve studies were included (6 aminolevulinate (ALA) trials and 6 methyl aminolevulinate (MAL) trials), but the majority of them had methodological constraints particularly in randomization description and patients/outcome assessors blindness.
Discussion and conclusions: Overall results indicated that PDT either with ALA or with MAL was effective and safe for facial photodamage treatment, but high quality of evidence was found mainly for MAL studies.

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PALABRAS CLAVE
Fotodaño;
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Fotoenvejecimiento;
Terapia fotodinámica

Terapia fotodinámica en el fotodaño facial: revisión sistemática

Resumen

Introducción: La terapia fotodinámica (TF) incluye una combinación de una fuente de luz y un agente fotosensibilizante para inducir daño tisular a través de la generación de oxígeno singlete. Aunque la TF se ha aprobado para otras indicaciones, su uso en el fotodaño facial resulta incierto.

Objetivo: Valorar la eficacia y seguridad de la TF en el fotoenvejecimiento de la piel del rostro.

Métodos: Se incluyeron todos los ensayos clínicos aleatorizados (ECA) que evalúan la eficacia y seguridad de cualquier forma de TF tópica para el tratamiento del fotodaño facial (dermatoheliosis) o fotoenvejecimiento en pacientes mayores de 18 años. Se consideró la TF que utiliza cualquier dosis de agente fotosensibilizante, así como cualquier fuente lumínica. Los comparadores fueron: exfoliación química, luz pulsada intensa (IPL), diodo emisor de luz (LED), dermoabrasión o microdermoabrasión, láseres ablativos o no ablativos, inyectables, cirugía, placebo y/o ausencia de tratamiento.

Se llevó a cabo una búsqueda sistemática en las bases de datos de los registros de PubMed, Embase, Lilacs, Google Scholar y ECA.

Resultados: La búsqueda se realizó hasta el mes de mayo de 2016. Cuatro autores seleccionaron y valoraron de manera independiente la calidad metodológica de cada ECA. Con arreglo a los criterios de inclusión, se incluyeron 12 estudios (6 ensayos sobre aminolevulinato [ALA] y 6 sobre metiloaminolevulinato [MAL]), aunque la mayoría de ellos contenían limitaciones metodológicas, particularmente en cuanto a la descripción de la aleatorización y la valoración a ciegas de los asesores de los pacientes/resultados.

Discusión y conclusiones: Los resultados generales indicaron que la TF, tanto con ALA como con MAL, era una terapia efectiva y segura para el tratamiento del fotodaño facial, aunque se encontró evidencia de alta calidad principalmente en los estudios realizados sobre MAL.

Introduction

The interplay of intrinsic (age-related decline of cutaneous cellular functions and/or genetic predisposition) and extrinsic factors (exposure to ultraviolet (UV) radiation, smoking or environmental changes) all lead to visible skin changes that result from an abnormal water distribution in tissue, (or a lack of hygroscopic substances), from an increase in skin pH, and from a prevailed oxidative cell metabolism that overwhelms local antioxidant activity. Those changes as a whole are usually referred as photodamage or actinic damage.[1,2] Such disturbances result in a dry appearance of the skin, in an increase in skin surface pH and in a continuous production of reactive oxygen species (ROS) in mitochondria due to an oxidative cell metabolism and a decrease in antioxidant activity.[3,4] Keratinocyte functional disturbances also occur due to a decreased mitotic activity and a 50%-increase in keratinocyte-migration time from the basal cell layer to the stratum corneum and an increase in cell-cycle duration.[5,6] Skin aging is also accompanied by spinous cell layer atrophy and dermo-epidermal junction flattening which both contribute to skin fragility.[6]

Aged skin is also characterized by an overall collagen synthesis reduction via the diminution of procollagen production, a down regulation of the transforming growth factor-b (TGF-b) type II receptor (a major regulator of dermal extracellular matrix (ECM) synthesis), and by a disturbed TGF-b activity that also stimulates fibroblast proliferation.[7–10] Skin collagen is also affected by UV-induced matrix metalloproteinases (MMP)[11] such as MMP-1 (fibroblast collagenase), MMP-9 (gelatinase) and MMP-3 (stromelysin),[10,12] and solar elastosis seems to be a consequence of an increased production of elastic fibers and elastin degradation by MMP-12 (human macrophage metalloelastase).[10,13–15]

Photodynamic therapy (PDT) is a selective therapeutic modality that combines an oxygen rich environment and a light source that stimulates a photosensitizing agent to produce singlet oxygen which is highly toxic to the cells.[16,17] Porphyrins and particularly hematoporphyrins (e.g.: photofrin) were the first intravenous substances used for PDT, characterized by their long-term accumulation in target tissue that required rigorous photoprotection for several weeks after administration.[17]

In 1990 new topical porphyrins such as 5-aminolevulinic acid (ALA) or its methyl ester (MAL) emerged, which could both easily penetrate the epidermis and produce short-term circumscribed photosensitivity.[18] More recently, hexylester 5-aminolevulinate (HAL) has been proposed to induce formation of high concentrations of PpIX in neoplastic tissue, but its use is still experimental.[19]

These molecules intervene in heme biosynthesis intracellular pathway, by inducing the formation of a photoactive porphyrin known as protoporphyrin IX (PpIX), which is an efficient photosensitizer that accumulates particularly in photodamaged skin.[17]

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