ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 10, Issue, 02, pp. 34023-34027, February, 2020

RESEARCH ARTICLE OPEN ACCESS

MAJOR CONSIDERATIONS ON THE USE OF PLASMA IN EYE AESTHETICS AND THE POTENTIAL ASSOCIATION WITH PLATELET RICH PLASMA AND COENZYME Q10

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ARTICLE INFO

Article History:
Received 17th November, 2019
Received in revised form
06th December, 2019
Accepted 17th January, 2020
Published online 29th February, 2020

Key Words:

Aesthetics. Eye aesthetics. Skin.
PRP. Plasma. Coenzyme Q10.

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ABSTRACT

The anatomy of the human face is complex. Particularly thin skin, elasticity and tone of the ligaments are also key. In this sense, Platelet Rich Plasma (PRP) contains numerous growth factors responsible for its effectiveness. Plasma is more uniform than ablative resurfacing lasers, including carbon dioxide (CO2) resurfacing lasers, as it does not depend on interaction with a particular target. In addition, as a potentiating and catalyzing effect, coenzyme Q10 (CoQ10) is a natural constituent of food and is also often used in foods and functional supplements. **Objective:** To present, through a systematic review, the main considerations of aesthetic ocular treatment using PRP, Plasma and Coenzyme Q10. Methods: Reviews, systematic reviews, prospective studies, retrospective studies, randomized, double-blind, placebo-controlled trials in humans with a recent publication were selected and analyzed. After criteria of literary search using the MeSH Terms that were cited in the item below under "Search Strategies", a total of 25 articles were collated and submitted for eligibility analysis and, after that, 18 studies were selected to compose the textual part of the manuscript and 12 to make the Systematic Review, following the rules - PRISMA. **Major findings and conclusion:** The use of Plasma can promote regeneration, lifting, wrinkling, improved sagging, collagen, elastin production, anti-inflammatory drugs, antibacterials, TDDS (transdermal delivery system), sterilization, skin remodeling. PRP has the potential to improve infraorbital dark circles in terms of color homogeneity in the region. PRP has been shown to promote wound healing and aid in facial lifting, volumetric skin, rejuvenation, skin regeneration and reconstruction, improved wrinkling. Ingestion of CoQ10 has limited seasonal viscoelastic deterioration and reduced some visible signs of aging. In addition, the results showed that stressed skin benefits from topical Q10 treatment, reducing free radicals and increasing antioxidant capacity.

Citation: ***Gabriella Carolina Vilerá, Malú Inês Peres Moura, Isabella Souza Magalhães, Igor Soubhia Liedtke, Fernanda Soubhia Liedtke Kaiser and Idiberto José Zotarelli Filho.*** **2020.** "Major considerations on the use of plasma in eye aesthetics and the potential association with platelet rich plasma and coenzyme Q10", *International Journal of Development Research*, 10, (02), 34023-34027.

INTRODUCTION

The anatomy of the human face is complex. A particular feature of the lower eyelid region is that there is no superficial fat layer to support the skin. On the other hand, this is an important factor behind the early visibility of aging processes (Sotirios, 2018). Particularly thin skin, elasticity, and tone of the ligaments are also key (Zoumalan, 2016).Regarding the described chronological aging process that affects the skin, actinic elastosis is another important aspect (Zoumalan, 2016). Ultraviolet (UV) radiation results in the formation of reactive oxygen species, increased production of matrix metalloproteinases and induction of transcription factor AP-1, which inhibits collagen production and causes accelerated collapse of collagen fibers. In addition, UV radiation inhibits the expression of TGF-β2, which promotes collagen production. Although this UV-related skin damage is not initially visible over time and subjected to harmful UV exposure, it results in wrinkles and actinic elastosis

(Zoumalan, 2016). In this sense, Platelet Rich Plasma (PRP) contains numerous growth factors responsible for its effectiveness (Cantisani, 2019). Growth factors are released after endogenous or exogenous platelet activation and then have a chemotactic effect and act directly and indirectly to regenerate tissue. Some platelets are activated by mechanical influences during centrifugation. Collagen activates platelets in vivo endogenously, while injection-induced needle bleeding may further contribute to coagulation. Exogenous activation by calcium addition has become less popular in recent years (Mehryan, 2014). Thus, aesthetic results in patients' demand for cosmetic treatments were influenced by some parameters such as clinical improvement after procedures, risk and potential complications and periods of inactivity. These parameters could validate plasma technology as a new regenerative modality. A basic understanding of plasma physical and histopathological aspects of plasma is needed to understand the impact of aesthetic medicine technology (Elghblawi, 2017). The mechanism of action of plasma on the skin involves two steps, immediate tissue contraction, and thermal rupture. Denaturation of collagen and other proteins in the dermis after the thermal effect of plasma induces an immediate and clinically observed tissue contraction (Sotirios, 2018). Neo-collagenization cascade was stimulated by thermal disruption of dermal solar elastosis, fibroblast activation, and deeper dermal migration and cytokine release (Sotirios, 2018).Plasma is more uniform than ablative resurfacing lasers, including carbon dioxide (CO2) resurfacing lasers, as it does not depend on interaction with a particular target (Sotirios, 2018). Regarding the energy level of plasma and tissue, high energy plasma shedding induces shedding in the epidermis and upper dermis, while low energy plasma induces shedding only in the upper part (Sotirios, 2018).

In addition, as a potentiating and catalyzing effect, coenzyme Q10 (CoQ10) is a natural constituent of food and is also often used in foods and functional supplements (Žmitek, 2016). In addition, it is a common ingredient in cosmetics, where it is believed to reduce the signs of skin aging (Knott, 2015). In addition, CoQ10 represents an endogenously synthesized fat-soluble antioxidant that is crucial for cellular energy production but is decreased with age and under the influence of external stressors on human skin (Herndon, 2015).Therefore, the present study aimed to present, through a systematic review, the main considerations of aesthetic ocular treatment using PRP, Plasma and Coenzyme Q10.

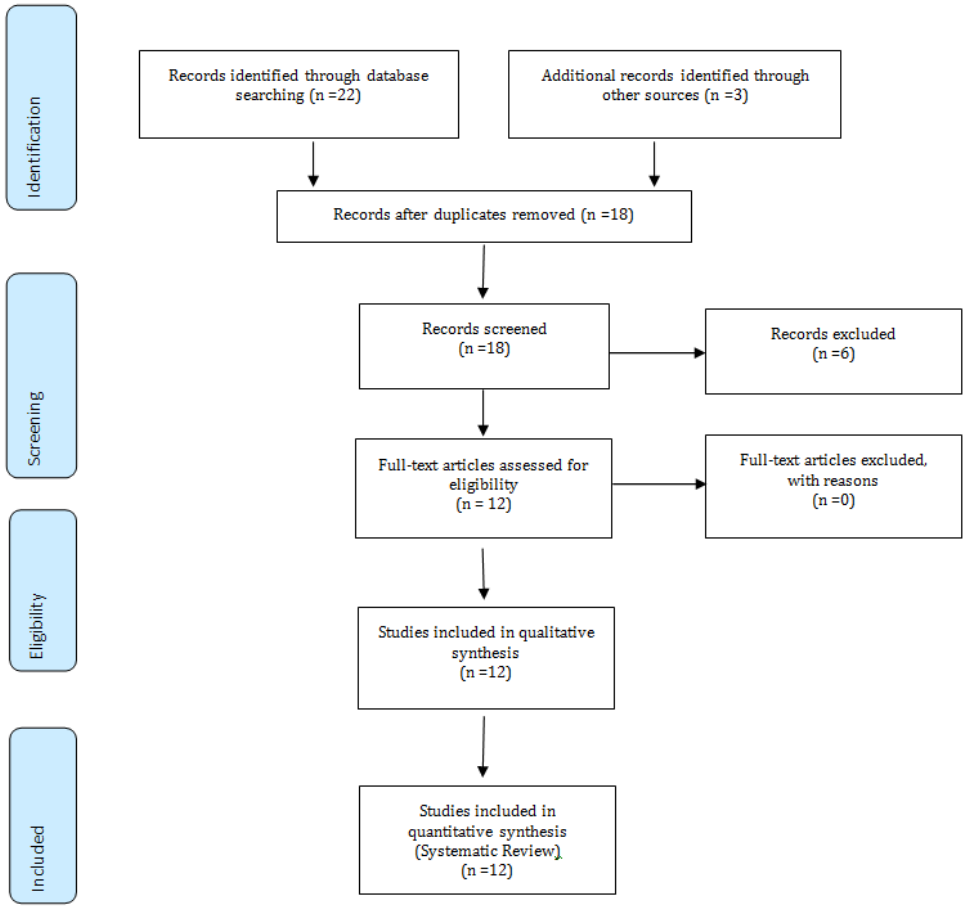
METHODS

Eligibility criteria and study selection

Selection criteria: Were selected reviews, systematic reviews, prospective studies, retrospective studies, randomized, double-blind, placebo-controlled trials in humans with a publication time of recent years were selected and analyzed.

Study selection and risk of bias in each study: Two independent reviewers (1 and 2) performed research and study selection. The data extraction was performed by reviewer 1 and fully reviewed by reviewer 2. A third investigator decided some conflicting points and made the final decision to choose the articles. Only studies reported in Portuguese and English were evaluated. The Cochrane instrument was adopted to assess the quality of included studies.

Flow Chart



Search Strategy and Information Sources: After criteria of literary search using the MeSH Terms that were cited in the item below under "Search Strategies", a total of 25 articles were collated and submitted to the eligibility analysis and, after that, 18 studies were selected to compose the textual part of the manuscript and 12 to make the Systematic Review, following the rules – PRISMA (Transparent reporting of systematic reviews and meta-analysis-Http: //www.prisma-statement.org/), according flow chart bellow. In general, as an example, the search strategy in MEDLINE / Pubmed, Web of Science, ScienceDirect Journals (Elsevier), Scopus (Elsevier), OneFile (Gale) followed the following steps: - search for M*eSH Terms (Aesthetics. Eye aesthetics. Skin. PRP. Plasma. Coenzyme Q10)*, - use of the booleans "and" between mesh terms and "or" among historical findings.

Risk of bias: Considering the Cochrane tool for risk of bias, the overall evaluation resulted in 4 studies with high risk of bias and 3 studies with uncertain risk. Also, absence of the source of financing of pharmaceutical companies responsible for the marketing of medicines. One study mentioned the source of funding, while 2 did not disclose this information in the conflict of interest statement.

RESEARCH AND DEVELOPMENT RESULTS

Using a high breaking voltage of about 5 kV, which is between the tip of the device and a patient's skin and maintaining the 2 mm distance between the tip and the skin (this constant distance is provided by a specific applicator).), the spark discharge is generated. To be able to generate the discharge of spark, the air, which contains free electrons, absorbs a large amount of energy, collapsing, that is, it is no longer an insulator and starts to conduct electric current, generating the discharge. With this, the air is ionized, becomes plasma (Sotirios, 2018).Plasma use can promote regeneration, lifting, wrinkling, improved sagging, collagen, elastin production, anti-inflammatory drugs, antibacterials, TDDS (transdermal delivery system), sterilization, skin remodeling. The number of Plasma treatment sessions varies according to the treatment goal, and usually, 1 to 3 sessions are required. This amount should be evaluated and indicated by the physician prior to the initiation of treatment (Sotirios, 2018). For patient comfort, a topical or injectable anesthetic may be applied prior to the procedure. During the session, the doctor or his assistant performs a series of impacts with the equipment, which forms sublimation crusts on the skin, which induces instantaneous retraction of the treated area. These crusts remain in the area for an average of 5 days and should not be manipulated to be naturally eliminated (Sotirios, 2018).

Effect on cells: Each cell has potential in its membrane (the difference in electrical potential between the two sides of the membrane). The inner side of membrane has a negative charge, the outer side has a positive charge. As the skin is aging, the electrical charge is unevenly distributed throughout the membrane, and the electrical voltage of the membrane is altered. The membrane potential is created and influenced by potassium and sodium cations. It is difficult for sodium cations to pass through the cell membrane, whereas potassium cations can pass through it easily (Sotirios, 2014).

Main Effects

- Significant increase in type I collagen;
- Reduction of keloid fibroblasts in scar areas;
- Intr Increased intracellular Ca;
- Extra Extracellular K increase;
- Unto Increased Chemotaxis;
- Increased growth factors as well as increased concentration ofnitrogen oxide.
- Increased fibroblast migration and its proteosynthesis;
- Increases skin permeability, decreased permeation of positively charged ions and soluble compounds;
- The new orientation of newly created collagen fibers or formed in the direction of direct current.
- Reduction of pain at the application site and increased healing speed (Sotirios, 2018).

Table 1. Below presents the main applications in relation to each Plasma type

Table 1. Main Applications of Plasma [1].

Surgical Plasma	Plasma Shower
• Scar, stretch marks, Acne Removal	• Skin Regeneration, Lifting
• blepharoplasty, Eye/Eyelid Correction	• Wrinkle, sagging improvement
• Acne Care	• Anti-inflammatory, anti-bacteria
• Epidermalpigmentation, Tatoo Removal	• TDDS (Transdermal Drug Deliverysystem)
• Skin Regeneration, Lifting	• Acne care, sterilization

In this context, the eyes are an important component of facial aesthetics. They are at the center of an anatomical area of the face, very important for rejuvenation procedures, the so-called "periorbital region". Therefore, the appearance of the eyes decisively influences the aesthetic perception and aging of the entire face. At a young age, the skin of the periocular area is elastic and tonic, with no sun damage; the eyebrow is full, well defined and does not come down, there is a clear and visible fold of the upper eyelid, with minimal dermatochalasis, the lower eyelid is tense and well-positioned (Cantisani, 2019).Thus, a study aimed to define a protocol for the use of plasma technology in the treatment of signs of aging in the periorbital region. As a result, immediately after treatment, all patients had redness and swelling of the treated area and small punctual carbon deposits where the handpiece of the device was applied. These small deposits disappear after post-treatment cleaning. A more open aspect of the eye and a flattening of wrinkles on the crow's feet were observed. Twenty-four hours after treatment, the eyelids appear to be very swollen due to edema. After three weeks of treatment, a significant improvement in eyelid appearance is appreciated, dermatochalasis is considerably reduced, periocular wrinkles are smoothed, and the eyes look younger. Finally, about two months after treatment, the result becomes stable (Cantisani, 2019).

Major Results – PRP

Infraorbital skin hyperpigmentation, commonly called dark circles, and crow's feet wrinkles are common cosmetic concerns. Thus, a study was conducted to evaluate the effectiveness of PRP injection in the treatment of periorbital dark circles and crow's feet. Ten participants with a mean age of 41.2 years were treated in a single session with intradermal injections of 1.5 mL of PRP in the lacrimal area and wrinkles of the crow's feet on each side. The effects on melanin content, color homogeneity of the treated area, hydration of the

epidermal stratum of the cornea and the volume and visibility index of the wrinkles were compared three months after baseline treatment. The physician's overall assessment, participant satisfaction and any potential side effects were also assessed. The improvement in infraorbital color homogeneity was statistically significant ($p = 0.010$), but no statistically significant changes were observed in melanin content, stratum corneum hydration, wrinkle volume and visibility index. The participant's satisfaction score and the physician's overall assessment score were 2.2 and 1.7, respectively, on a scale from 0 to 3. Therefore, PRP had the potential to improve infra-orbital dark circles in terms of homogeneity. region colors (Mehryan, 2014). In this context, the clinical application of PRP is based on the increase in the concentration of growth factors released by the concentrated platelet alpha granule and on the secretion of proteins capable of capitalizing the healing process at the site. Also, PRP can start the natural process of skin rejuvenation and aiming to make it function as a younger and keep the skin young and maintain it. Thus youth is in their blood, for it has a magical power imposed on platelet factors. However, there is no standardization of the techniques, besides the insufficient description of the adopted procedures (Gennai, 2017). Not long ago, PRP has appeared strongly in a variety of medical specialties, including plastics, wound healing and diabetic ulcers, orthopedics, trauma, eye surgery, dry eyelid injection, urinary incontinence urology, sexual well-being, skin surgery, medicine. sports, dentistry and dermatology and aesthetic applications. PRP has been proven to promote wound healing and aid in facial lifting, volumetric skin, rejuvenation, skin regeneration and reconstruction, improved wrinkles, stimulated hair growth, increased hair follicle viability and survival rate; prevent apoptosis, increase and prolong the anagen hair growth stage, and delay progression to the hair density and hair transplantation stage of the hair cycle (Elghblawi, 2017).

Also, treating the lower eyelid region to rejuvenate the skin or treat actinic elastosis is often a difficult test. Established treatment options, such as hyaluronic acid injections, botulinum toxin injections, micro-pitting, skin resurfacing (microdermabrasion, chemical peeling (exfoliation), laser treatment) as well as blepharoplasty may be associated with significant risks and increased patient burden. . In addition, they may not be effective in treating signs of skin aging or actinic elastosis, including dark rings under the eyes, lack of volume and cutis laxa. A minimally invasive treatment approach using PRP may improve the above conditions and involve minimal risk and patient burden would be a desirable alternative (Aust, 2009).A striking feature of the modern era of facial plastic surgery is the growing demand for superior facial rejuvenation for both sexes and the growing variety of options, including surgical and non-surgical modalities. So now more than ever, differentiating these aesthetic ideals between the sexes and understanding their nuances has become a necessity for the facial cosmetics community. In this paper, a detailed comparison of the relevant anatomical and topographic differences is presented, followed by a review of the historical evolution of these aesthetic trends (Sedgh, 2018).

In addition, PRP is traditionally used as an injectable material to improve healing, hair growth and facial rejuvenation. This research examined the new use of topical autologous PRP added to a preservative cosmetic base and applied twice daily to the face after electroporation for 8 weeks. We included 20 healthy female and male subjects, aged 30 to 60 years, in this vehicle-controlled, vehicle-blinded, investigator-controlled, single-sided study to evaluate the effect of a PRP-containing serum versus the isolated serum. in facial photoaging. Immunohistochemical analysis showed positive regulation for type I collagen with qPCR data demonstrating concomitant positive regulation of collagen mRNA after 8 weeks of topical PRP use. These pilot study findings may indicate value for topical PRP in facial rejuvenation (Draelos, 2019).

Ubiquinone (Coenzyme Q10) and Aesthetic

Coenzyme Q10 (CoQ10) is a natural constituent of food and is also often used in foods and functional supplements. It is also a common ingredient in cosmetics, where it is believed to reduce the signs of skin aging. However, existing data on the effect of dietary CoQ10 intake on skin parameters and conditions are scarce. To gain insight into this problem, a double-blind, placebo-controlled experiment was conducted with 33 healthy subjects. The objective was to investigate the effects of 12 weeks of daily supplementation with 50 and 150 mg CoQ10 on skin parameters and conditions. The study was conducted with a water-soluble form of higher bioavailability CoQ10 (Q10Vital®). CoQ10 intake limited seasonal deterioration of viscoelasticity and reduced some visible signs of aging. We determine significantly reduced wrinkles and micro-relief lines and improve skin smoothness. CoQ10 supplementation did not significantly affect skin hydration and dermis thickness (Žmitek, 2016).In addition, CoQ10 represents an endogenously synthesized fat-soluble antioxidant that is crucial for cellular energy production but is decreased with age and under the influence of external stressors on human skin. Here it is shown that topical treatment with Q10 is beneficial with regard to effective Q10 replenishment, increased cellular energy metabolism, and antioxidant effects. Applying formulas containing Q10 significantly increased the levels of this quinone on the skin surface. In the deeper layers of the epidermis, the ubiquinone level was significantly increased, indicating effective supplementation. Simultaneous elevation of ubiquinol levels suggested metabolic transformation of ubiquinone resulting from increased energy metabolism. Incubation of cultured human keratinocytes with Q10 concentrations equivalent to the treated skin showed a significant increase in energy metabolism. In addition, results have shown that stressed skin benefits from topical Q10 treatment, reducing free radicals and increasing antioxidant capacity (Knott, 2015).

In addition, a clinical trial was conducted to determine the effectiveness of a multi-ingredient anti-aging moisturizer designed to improve the appearance of facial skin (Herndon, 2015). The parameters studied included fine lines and wrinkles, clarity/brightness, visual roughness, tactile roughness, skin tone uniformity (redness), skin tone uniformity (hyperpigmentation), and overall appearance. Thirty-seven women, aged 35 to 60, completed the study. Effective ingredients incorporated into the anti-aging facial moisturizer include:Astragalusmembranaceus root extract, a mixture of peptides including palmitoyl tripeptide-38, standardized rosemary leaf extract (ursolic acid), tetrahexyldecilascorbate (THD ascorbate) and ubiquinone. (coenzyme Q10). Subjects were instructed to apply the moisturizer twice a day, once in the morning and once in the evening. Subjects were assessed at baseline and after 4, 8, and 12 weeks of product use. Therefore, the results of the clinical evaluation show that the multi-ingredient anti-aging moisturizer produced a statistically

significant improvement in the scores of all evaluated clinical classification parameters compared to baseline. Statistically significantly greater improvement was observed at 12 weeks. At week 12, there was a statistically significant percentage of favorable versus unfavorable outcomes in all results of the self-efficacy and aesthetic self-assessment questionnaire. In addition, the multi-ingredient anti-aging moisturizer is considered light and well-tolerated (Herndon, 2015).

Conclusion and limitations

Plasma application has great potential in ocular aesthetics, however, further clinical and histopathological studies are needed to support previous findings and address some safety and efficacy questions and questions.

Conflict of interests: There is no conflict of interest between authors.

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