A REJUVENATION THERAPY OF MEDICAL NEEDLING AND 3D-MATRIXLIFT® IS SAFE AND IMPROVES THE ELASTICITY OF THE SKIN

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ABSTRACT

The use of platelet-rich plasma and growth factors is emerging as an anti-ageing regimen for the skin. We tested the safety and efficacy of 3D-MatrixLift®, a new treatment regimen for skin rejuvenation that combines medical needling and the application of a stem cell and growth factor-rich solution with irradiation by LED light. A total of 15 participants were enrolled in a single-centre, prospective pilot study. The elasticity parameters of the skin increased significantly after five rounds of treatment, with no signs of adverse effects. 3D-MatrixLift improves the elasticity of the skin and can be used safely in combination with medical needling for skin rejuvenation.

Keywords: 3D-MatrixLift, medical needling, rejuvenation.

INTRODUCTION

Measuring approximately 2 m^2, the skin is the largest organ of the human body. The outer skin layer, the epidermis, is a dynamic system that is constantly proliferating and differentiating. The most important function of the skin, besides many others such as temperature regulation, sensory perception, and protection against harmful substances and mechanical impacts, is as a hydration barrier that prevents the dehydration of the skin and the organism and maintains the osmotic balance of the inner tissues. During ageing, the physiological regeneration process slows down and the ability to bind water is reduced. As a result, the skin loses its elasticity, becomes increasingly cracked, and barrier damage and wrinkles occur (intrinsic ageing). Furthermore, the skin is damaged by environmental factors such as smoking and UV radiation (external ageing).

Several studies have shown that physiological growth factors improve the signs of skin ageing.[1-5] One source of growth factors is platelet-rich plasma (PRP), an autologous concentration of human platelets suspended in a small volume of plasma. PRP contains constituents including platelet-derived growth factor, transforming growth factor, vascular endothelial growth factor, epidermal growth factor, and fibroblast growth factor.[6,7] In recent years, PRP has become increasingly attractive for skin rejuvenation as it has been shown that PRP promotes tissue remodelling in aged skin.[8-10]

3D-MatrixLift® is a new treatment regimen for skin rejuvenation that combines a new cell separation technique using human blood with irradiation by LED light and medical needling. Differential centrifugation separates platelets, leukocytes, and mesenchymal stem cells from erythrocytes. The concentrated cell suspension contains growth factors and is enriched with trace elements such as copper, zinc, magnesium, and amino acids including glycine and arginine which influence epigenetic factors.

Mesenchymal stem cells are undifferentiated adult stem cells that self-renew and differentiate into cell types of their cell linage (multipotency). Age-associated accumulation of mutations in the mitochondrial DNA of adult stem cells has been

proposed to be responsible for the age-associated defects found in elderly humans. Hashizume and colleagues[11] found that ageing is controlled not only by mutations but also by epigenetic regulation. They showed that reprogramming of aged fibroblasts restored age-associated mitochondrial respiration defects, indicating that ageing is reversible and is controlled by epigenetic factors. Treatment of aged fibroblasts with glycine modified epigenetic regulation and effectively prevented these ageing phenotypes.[11] There are a number of clinical case reports that describe stem cell use in dermatology, including a report by Rigotti and colleagues[12] that describes the successful use of adult stem cells for treating severe radiodermatitis.

Irradiation of the 3D-MatrixLift solution by LED light in the blue spectrum (440 nm) stimulates the synthesis of nitric oxide (NO). Gaseous NO has recently emerged as a key player in the mediation of epigenetic changes associated with cell cycle arrest and differentiation. Many other nuclear factors involved in proliferation and differentiation of skin cells are directly regulated by NO.[13] Blue light irradiation photolytically generates NO from nitrosated proteins, which are known to initiate differentiation and vasorelaxation in skin cells and in smooth muscles. Nitrosated proteins and amino acids such as arginine are light receptors and signal transducers. NO inhibits neutrophil migration, rolling, and adhesion in inflammation and induces apoptosis in keratinocytes. NO protects against cellular damage by reactive oxygen species and stimulates regeneration of the skin.[14-21]

Medical needling is performed with an automated device that penetrates the skin with fine needles, thereby creating channels for improved absorption of topically applied compounds through the top layer of the skin. This is important as large (>20 kDa) and hydrophilic (>500 Da) molecules penetrate poorly into the hydrophobic stratum corneum.[22,23] Therefore, medical needling is necessary to improve absorption and subsequent pharmacological effect. Furthermore, medical needling in itself improves the appearance of the skin through a process called percutaneous collagen induction.[24-32] Percutaneous collagen induction is based on the natural inflammation reaction of the skin after an injury. This reaction induces the release of growth factors, epigenetic factors, and cytokines that stimulate the synthesis and deposition of new collagen and elastin in the upper dermis. This leads to remodelling of the skin structure and an improved appearance.[25-30,32-35]

The 3D-MatrixLift regimen also includes an irradiation step of the treated skin area by LED light in the blue and red/infrared spectra. It has recently been shown that red/infrared irradiation is a safe and effective method to increase intradermal collagen and to rejuvenate the skin.[32] At the same time, the anti-inflammatory effects of LED energy at 633 nm and 830 nm have been well documented in the treatment of psoriasis and in acceleration of wound healing.[33] Furthermore, Papageorgiou and colleagues[35] successfully used phototherapy with blue and red LED light for the treatment of acne vulgaris.

As a large number of human populations grow older, an increasing number of individuals want to be treated for signs of ageing with a safe and effective procedure. Therefore, the aim of this study was to evaluate the efficacy and safety of 3D-MatrixLift in the treatment of ageing skin.

MATERIAL AND METHODS

Study Design and Participants

The study was conducted at the Private Practice for Functional Medicine in Lindenthal, Cologne, Germany. A total of 15 healthy adult participants were recruited for this single-centre, prospective pilot study (14 women, 1 man). Participants were 38–69 years of age (mean: 55 years). Written informed consent was obtained from each patient. Exclusion criteria were: open skin infections and wounds, florid acne, neurodermatitis, and psoriasis. Medical and cosmetic histories were documented and a photo of the facial skin was taken.

3D-MatrixLift

A total of 8 mL of autologous whole blood was collected from each patient into a sterile CPT™ Cell Preparation Tube (BD Becton Dickinson) and centrifuged according to the manufacturer's instructions. A density gradient is formed in the CPT tubes during differential centrifugation. After centrifugation, the mononuclear cells, adult stem cells, and platelets were re-suspended in a small volume of plasma, mixed with 0.5 mL of a trace elements/amino acid solution, and transferred to a sterile syringe via a closed transfer system. The 3D-MatrixLift solution was subsequently irradiated with LED light (Kernel, China) for 5 minutes at 440 nm to stimulate NO synthesis. Half of the

solution was used immediately after preparation, while the other half of the solution was stored at 4°C for 1 week in closed sterile syringes and used for the next treatment.

Non-Invasive, Objective Skin Elasticity Measurements

The measurement of skin elasticity was performed with the CUTOMETER® Dual MPA 580 (Courage + Khazaka Electronic GmbH, Cologne, Germany). In accordance with the manufacturer's instructions, the measurement was taken from the right temple and the right cheek before the start of the treatment and 10 days after the last treatment. The parameters R0 and R2 were determined; R0 represents the passive behaviour of the skin force and R2 represents the gross elasticity.

Treatment

Participants received five treatments at 1-week intervals. First, the face was cleaned and disinfected. A topical anaesthetic cream (lidocaine 23% and tetracaine 10%) was then applied for 15 minutes. Any excessive anaesthetic was then removed and physiological saline solution was applied to smooth the medical needling treatment. Medical needling was carried out using Revive MN (MT.Derm GmbH, Berlin, Germany), which is an automated medical needling device. The needle length of the 6 point needle plate cartridge was adjusted to 0.5 mm and the skin was perforated through circular movements at a speed of 150 per minute. After medical needling treatment, the 3D-MatrixLift solution was applied to the treated areas for 5 minutes. The treated area was subsequently irradiated with LED light (Kernel, China) for 3 minutes at 440 nm and then for an additional 3 minutes at 640/830 nm to photostimulate the skin. CUTANOVA - Cream Nanorepair (Dr. Rimpler GmbH, Wedemark, Germany) was applied to the treated areas to regenerate the skin barrier.

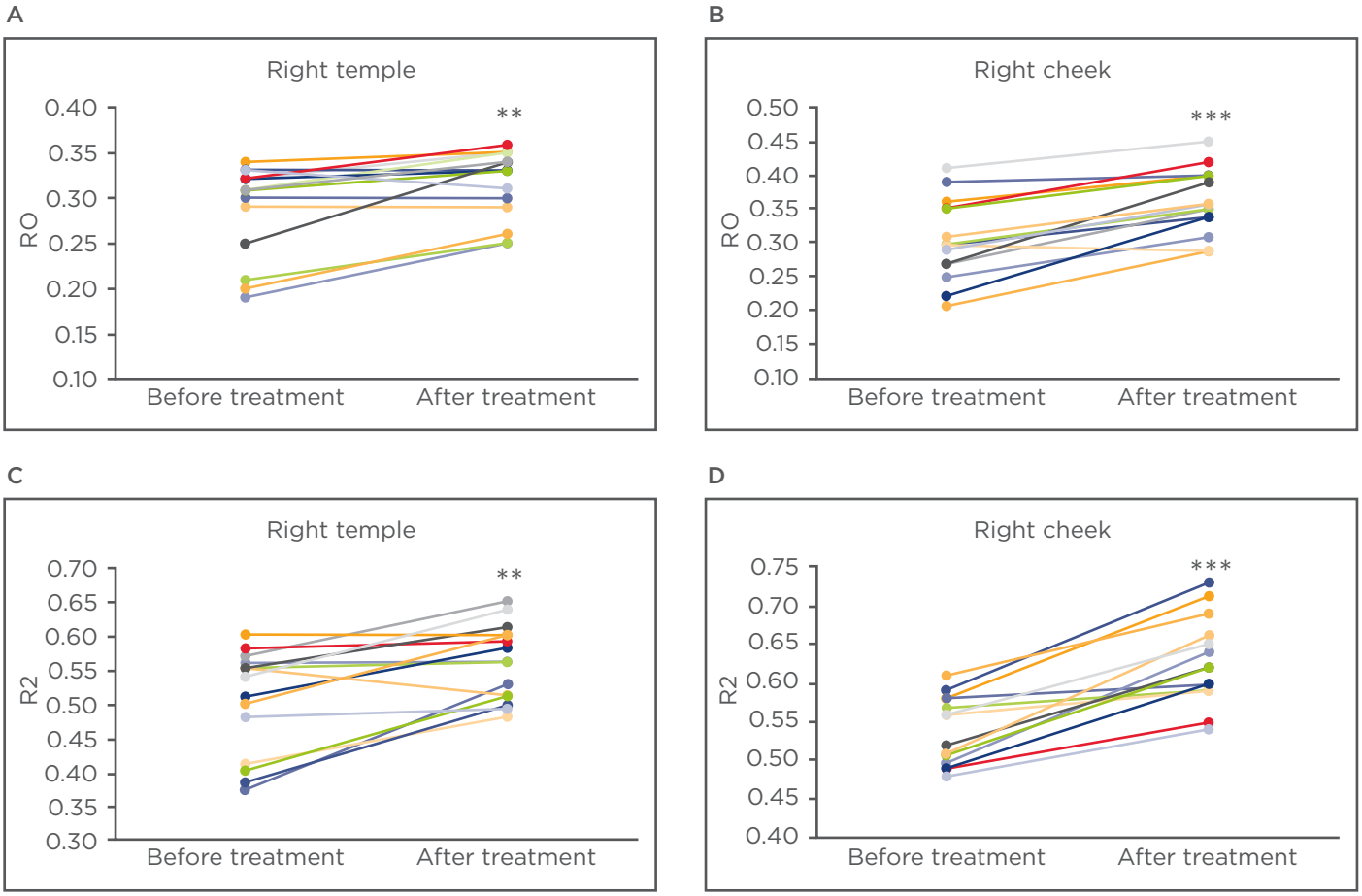

Figure 1: The two parameters of skin elasticity, R0 and R2, both increased significantly after treatment. A) R0 before and after treatment on the right temple; **p<0.01; B) R0 before and after treatment on the right cheek; ***p<0.001; C) R2 before and after treatment on the right temple; **p<0.01; D) R2 before and after treatment on the right cheek; ***p<0.001.

Statistical Analysis

The data was analysed using Excel. A paired t-test was performed to determine significant changes.

RESULTS

3D-MatrixLift is a new treatment regimen for skin rejuvenation that combines medical needling and the application of a stem cell and growth factor-rich solution with irradiation by LED light. To test the efficacy of this new treatment, 15 participants were enrolled in a single-centre, prospective pilot study. The 3D-MatrixLift was performed five times with 1-week intervals. Skin elasticity was measured prior to treatment and 10 days after the last treatment on the right temple and the right cheek with a CUTOMETER Dual MPA 580. The skin elasticity parameters R0 (passive behaviour of the skin to force) and R2 (gross elasticity) were determined.

All participants completed the study and no adverse effects were observed. Small dot-like bleedings were observed, although these were mainly limited to the forehead region and could be stopped rapidly with a swab drained in saline solution. A reddening of the facial skin similar to sunburn appeared after the treatment but faded after 3–6 hours.

Skin Elasticity Measurements

The passive behaviour of the skin to force (R0) and the gross elasticity (R2) increased significantly on the right temple as well as on the right cheek after the treatment regimen (Figure 1). Some participants, however, responded more strongly to the treatment regimen than others.

DISCUSSION

The present study confirms that 3D-MatrixLift, a combination of medical needling and application of a stem cell and growth factor-rich solution with LED light, is a safe and effective procedure to treat signs of ageing.

The passive behaviour of the skin in relation to force, represented by the value R0, increased significantly after treatment indicating that the skin was softened by the treatment regimen. This might be due to a reduction in stress between the stratum corneum and the underlying epidermis and dermis through remodelling of the collagen structures.

Gross elasticity, represented by the value R2, also increased significantly after treatment indicating that the ability of the skin to return to its original position after deformation increased. This effect is probably due to improved function of the elastic fibres of the skin and confirms the skin remodelling effect of the treatment.

However, a response to the treatment was not observed in all participants. It was noted that the participants who showed an observable response mainly included those with skin damage, for example due to chemotherapy. Participants who had seen a beautician at least once per month for longer than a year showed no improvement in elasticity parameters. These results confirm that regular skin care can reduce the signs of ageing.

In comparison with previous PRP preparations, the 3D-MatrixLift regimen includes a novel cell separation technique through differential centrifugation that allows the enrichment of the solution with mononuclear cells, mesenchymal stem cells, and platelets, which release growth factors and epigenetic factors for modulation of gene expression and cell cycle modification. NO, for example, is involved in the epigenetic regulation of proliferation and differentiation of skin cells. The production of NO in the skin is activated via nitrosated amino acid metabolism induced by LED light stimulation and promotes regeneration and wound healing of the skin. Following this pilot study, another study focussing on sun-damaged skin and inflammatory skin diseases is planned. This study will feature a higher number of participants.

In conclusion, this is the first study to demonstrate that 3D-MatrixLift, a combination of medical needling and the application of a stem cell and growth factor-rich solution with LED light, improves skin elasticity with no significant adverse effects.

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