Microneedling and transepidermal distribution of drugs

Microagulhamento e distribuição transepidérmica de drogas

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ABSTRACT

Microneedling or Percutaneous Collagen Induction is a minimally invasive dermatological procedure that utilizes needles to create orifices or in the skin. Its aim is to induce collagen formation, neovascularization and production of growth factors. There is increased demand because it is a relatively simple procedure, cost-effective, safe and that yields satisfactory results. It treats localized areas and studies are being done to evaluate its role in inflammation, dyspigmentation, and photodamage. The therapeutic use includes the treatment of acne scars, stretch marks, wrinkles, melasma, hyperhidrosis, alopecia. Lately, it has been used for the transepidermal distribution of active compounds and vaccines.

Keywords: Acne vulgaris; Alopecia; Collagen rejuvenation; Dermatologic surgical procedures; Percutaneous collagen induction; Treatment outcome; Wound healing

RESUMO

Microagulhamento ou indução percutânea de colágeno é procedimento dermatológico minimamente invasivo que usa agulhas para criar orifícios ou microcanais na pele. Tem como objetivo induzir formação de colágeno, neovascularização e produção de fatores de crescimento. Há aumento da procura por ser procedimento relativamente simples, com bom custo/benefício, seguro e com resultados satisfatórios. Trata áreas localizadas, e estudos estão se desenvolvendo para avaliar seu potencial em inflamações, discromias e fotodano. O uso terapêutico inclui tratamento de cicatrizes de acne, estrias, rítides, melasma, hiperidrose, alopecia. Atualmente tem sido usado para distribuição transepidérmica de ativos e vacinas.

Palavras-Chave: *Acne vulgar; Alopecia; Cicatrização; Cicatriz; Colágeno; Indução percutânea de colágeno; Procedimentos cirúrgicos dermatológicos; Rejuvenescimento; Resultado de tratamento*

INTRODUCTION

Microneedling (MN), also known as Percutaneous Collagen Induction Therapy (PCIT), involves performing repeated punctures on the skin using sterilized microneedles.[1,2] Its original conception dates from 1995, when Orentreich *et al.* developed the concept of subincision with the use of hypodermic needles for the breaking of fibrotic bands in the treatment of depressed scars.[3] Three years later, Camirand and Doucet reported significant improvement in the clinical appearance and texture of surgical scars through dermabrasion with needles by using a tattoo machine.[4] In 2000, the first MN device was used to treat facial rhytids and cutaneous flaccidity. In 2006, Desmond Fernandes developed the first MN device called Dermaroller® 5 (Environ, South Africa).

Review Articles

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MATERIALS AND METHODS

The studies in this review were selected by searching on PubMed database. The following key words were used on the search: *microneedling, review, percutaneous collagen induction therapy, microagulhamento*. Articles published in English and Portuguese were included in the review. *In vivo* studies were considered, and priority was given to controlled, prospective and retrospective clinical studies as well as review articles.

DEVICE SPECIFICITY

There is a wide variety of cylindrical mechanical devices available, what differentiates them are the length, amount, diameter and material of the needles. They act by rolling perpendicularly over the skin's surface up until the emergence of superficial bleeding.[1,3]

The standard MN device, Dermaroller®, has 192 needles that are 2mm long and 0.07mm in diameter, and when applied 15 times on the skin inflicts approximately 250 punctures per cm^2 towards the papillary dermis depending on the applied pressure, without causing injury to the epidermis.[6,7]

Other devices available:[6,8,9]

- Dermaroller® for home use: it has needles measuring less than 0.15mm in length and are used to reduce pore size, fine lines and sebum production. They can be used from two to three times per week.

- Derma-stamp: miniature version of the Dermaroller. Application is carried out pressuring the device against the skin. It is available in different sizes and its needles measure 0.2 to 3 mm in length. Used for treatment of localized scars, such as those of varicella.

- Dermapen®: pen-like instrument with needle adjustment capability. Used for mechanical resurfacing, with disposable needles.

- DermaFrac®: A technique that combines MN with microdermabrasion, LED therapy and infusion of active ingredients.

- Delivery systems with microneedles: minimally invasive and painless method of transepidermal drug administration, used for vaccines.

- Fractional radiofrequency: needles that penetrate the skin and release – or not – electric current, producing thermal damage to the epidermis or dermis and consequent neocollagenesis.

MECHANISMS OF ACTION

Micropunctures caused by MN result in controlled mechanical trauma and stimulate the production of collagen by activation of the post inflammatory cascade and release of growth factors, without causing damage to the epidermis. With the recruitment of neutrophils and platelets, the normal cascade of repair and healing begins with the release of growth factors such as TGF-α, TGF-β, as well as platelet derivatives (PDGF), resulting in fibroblast deposition of collagen.[2,10]

In a study conducted by Lima *et al.* (2013),[11] whose objective was to establish the correlation between needle length and damage depth, a classification based on the histological analysis of fragments of pig skin was proposed:

- Mild injury (0.5mm long needles): mainly used for transepidermal drug delivery (DD) and fine wrinkles (RHYTIDS);

- Moderate injury (1 and 1.5mm long needles): used for medium-sized wrinkles (RHYTIDS);

- Deep injury (2 and 2.5mm long needles): used for depressed scars and stretch marks.[11]

There are three phases in the healing process that, predictably, follow the sequence described by Falabella and Falanga:[12]

1. Release of connective tissue growth factors, TGF-beta, PDGF, and connective tissue activating protein, by platelets and neutrophils. These factors increase the production of intracellular matrix.

2. Monocytes also release growth factors that increase the production of collagen, elastin and glycosaminoglycan (GAGs). After five days, fibronectin matrix formation occurs, with aligned fibroblasts, which determines the deposition of collagen.

3. Increased expression of the gene(s) and protein(s) linked to the production of collagen, glycosaminoglycans and growth factors (endothelial and epidermal fibroblasts), crucial for improving clinical aspects of aging. It is possible to observe a quantitative and qualitative increase of the collagen fibers in the papillary and reticular dermis that are distributed in interlaced pattern – which is diverse from the parallel pattern found in cicatricial tissues. Neovascularization and neocollagenesis result in improvement of the scars and their appearance.

Studies show that fibronectin matrix formation occurs within five days, followed by the deposition of type III collagen, which persists for a period ranging from five to seven years.[1] Six months after four MN sessions with 30-day intervals, there was a 400% increase in collagen and elastin deposition, with increased thickness of the spinous layer.[6,13]

MICRONEEDLING AND DRUG DELIVERY

Microneedling (MN) combined with Drug Delivery (DD) is a method for administering substances by transepidermal route in which each needle penetrates the skin, with the ensuing application of topical active ingredients.[2,14]

Promising results have been shown in the treatment of atrophic scars, alopecia, actinic keratoses and pigmentation disorders such as melasma.[14] Evidence of efficacy in the treatment of vitiligo remains limited.

Among the numerous studies, stands out the one by Aust *et al.* (2008), which showed a 140% increase in the thickness of the epidermis after eight weeks with the use of MN followed by the application of a product containing vitamins A and C.[1,13] When compared to the use of the isolated antioxidant, the increase in thickness of the epidermis was of 22%.

Bal *et al.* (2008) used laser scanning microscopy to analyze the dynamics of passive absorption of fluorescein in the

depth of microchannels created after MN. The absorption peak of the substance occurred after five minutes, declining within the following ten minutes, and returning to baseline after 15 minutes.[15,16]

The study carried out by Gordon *et al*. showed that the time interval of 5 to 30 minutes seems to be the best to apply and massage substances or platelet rich plasma (PRP) into the microchannels created by MN.[17] These findings have influence on the time and maximum absorption that the topical agent will exert if applied immediately after MN.

The use of Laser Assisted Drug Delivery (LADD) was first described in 1987, with ablative lasers.[18,19] The fractional ablative laser (FAL) produces small ablation channels, with density of the channels and the depth of the microscopic ablation zones (MAZ) serving as the main control parameters.[20,21] Density corresponds to the area of surface that underwent ablation, and is determined by the laser device tip's diameter (spot size) and the number of channels inflicted per unit of skin. The depth of the channels is controlled by the laser's fluence (pulse energy) and corresponds to the extent of the MAZ.[20,21] Modifications in the parameters can influence the amount and biodistribution of the active substance, thus favoring the increase of the clinical efficacy and treatment objectives.[18]

Haedersdal *et al*. evaluated 16 preclinical studies and evidenced an increase in the absorption of substances after treatment with FAL.[18] In the literature, the use of aminolevulinic acid (ALA) for the treatment of actinic keratoses seems to offer the best level of evidence.[22] Although no adverse effects have been observed in these studies, DD following FAL carries the risk of systemic absorption of the drugs, in special when performed in large areas.

CLINICAL APPLICATION AND RESULTS

Microneedling leads to a significant improvement in scarring, stretch marks and rhytids, with a short recovery period and limited adverse effects.[6] The clinical results obtained are a consequence of the stimulation of the tissular repair cascade, with an increase in collagen production.[2] A number of published studies have demonstrated the histological changes induced by this treatment and its clinical effectiveness. Its best indications include acne scars, periorbital and perioral rhytids, sagging, hypertrophic scars, melasma and alopecias.[1]

ACNE SCARS

Histological changes resulting from the use of MN for the treatment of acne scars were studied by El-Domyati *et al*. (2018) in 10 patients with atrophic acne scars on the face using before and after biopsies.[23] They showed a significant increase in the production of collagens type I, III and VII, as well as a decrease of elastin at the end of the treatment ($p < 0.05$). Patients reported pain of moderate intensity and edema that subsided within 24 hours, with absence of other adverse symptoms.[2,23] Patients also reported improvements in scar appearance (51-60% of patients) and skin texture (40-50%) 90 days (six sessions) after, describing satisfaction with the procedure (80-85%).[7] Box-type scars showed improvement (50-70%) after three to five sessions at intervals of two to four weeks. Likewise, stretch marks, atrophic scars and contractures due to burns also showed good results with MN (Table 1).[1,23]

Although still with few and inconclusive studies, the use of platelet-rich plasma (PRP) associated with MN for acne scars has been described. It is believed that activated platelets, applied after the procedure, stimulate the release of growth factors such as VEGF, PDGF and IGF. Promising results with this association were observed in a study by El-Domyati *et al*. in 2018, when compared to the treatment of acne scars with MN isolatedly ($p = 0.015$).[23] Fabrocini *et al*. (2011) proposed that PRP could improve the response to wound healing due to the presence of autologous growth factors.[24] These authors demonstrated that their use in association with MN was more effective than that of isolated MN.

Some studies compared results between laser and MN. Cachafeiro *et al*. compared the use of non-ablative erbium laser (1,340nm) with MN in atrophic acne scars.[25] Patients ($n = 46$) were randomized into two groups that received three monthly sessions. Both groups experienced improvement, without significant difference between them.[25] Nevertheless, the group treated with laser reported prolonged erythema (averaging three days) and post inflammatory hyperpigmentation (PIH), effects that had not been seen in the MN group, who reported erythema for only one day, with absence of PIH.[25]

Table 1: Studies on the treatment of acne scars

Type of scar	Author	Treatment	Needle length	Sample (n)	Number of Sessions	Results	Study design
Atrophic acne scars	El-Domyati *et al.* 2015[26]	Dermaroller®	1.5 mm	10	6 (2-week interval)	Increase in collagen types I, III, VII, as well as new collagen synthesized at the end of the treatment ($p < 0.05$). Patients reported satisfaction of 80-85% with the treatment ($p <= 0.01$)	Prospective Clinical Study
Atrophic acne scars	Cachafeiro *et al.*, 2016[25]	Non-ablative Erbium Laser 1,340 nm + Dermaroller®	2mm	46	3 (4-week interval)	Both groups had improvement in the degree of acne scars, with no significant difference between groups ($p = 0.264$)	

HYPERTROPHIC SCARS

The treatment of hypertrophic scars has been associating MN to DD in deep layers of the skin. A significant improvement of post-burn hypertrophic scars was demonstrated by Aust *et al.* in patients (n = 16) who used vitamins A and C for 30 days prior to treatment in order to increase collagen production.[2,13]

The pre-treatment average VAS score (Visual Analog Scale) was 4.5. This scale has values that range from 1 to 10, where 10 corresponds to the highest degree of satisfaction regarding the appearance of the scar. After the treatment with one to four MN sessions followed by topical application of vitamins A and C twice a day yielded an improvement of 3.5 points in the VAS scale, which corresponds to an average VAS score of 8.5. Histological analysis (employing 3mm punches and Van-Gieson's and Hematoxylin-eosin Staining) after one year showed a quantitative increase in the deposition of collagen and elastin as well as qualitative improvement of the fibers.

RHYTIDS

The use of MN for the treatment of facial rhytids has been demonstrated in some studies. Fabbrocini *et al.* obtained a two-point improvement in the Rhytids Intensity Scale after MN.[27] El-Domyati *et al.* reported a significant increase in type I, III and VII collagen, and tropoelastin levels after six MN sessions.[23] Improvement in sagging, resulting in skin tightening caused by MN, possibly occurs due to the reorganization of existing collagen fibers and the simultaneous increase in the production of new structural components of the dermis.[23] The increase in dermal collagen and elastic fibers explains the mechanism that leads to the decrease and smoothing of rhytids after the MN.

ALOPECIAS

The treatment consists in the use of a cylindrical device with needles varying in length from 0.5 to 1.5 mm, repeatedly applied over the area to be treated in several directions (vertical, horizontal and diagonal), for approximately 15 to 20 times, producing in average 250 channels per one square centimeter.[2,17] The treatment's goal is to achieve pin-point bleeding or moderate erythema (Table 2).

More recently, the use of MN in the treatment of hair diseases has become frequent, with a number of published studies. Microneedling is believed to stimulate dermal papillae's stem cells, increase the blood flow to the hair follicles inducing the recruitment of growth factors, and intensify the signaling of pathways that induce hair restoration.[3] Studies show that after the procedure, there is release of PDGF, EGF and bulge activation, in addition to increased expression of Wnt3a and Wnt10b,[28,29] gene-encoding proteins involved in signaling pathways. All these factors stimulate the stem cells of the dermal papilla and induce hair growth.

In the first controlled, randomized, clinical trial, in which the evaluator had no information on the groups (blind evaluator) and that was performed in patients with mild to moderate androgenic alopecia (AGA) (n = 100), aged 20-35 years, Dhuran *et al.* randomly distributed the sample into two groups of 50 individuals.[30] One group was treated with weekly MN sessions associated with 5% minoxidil solution twice daily, starting 24 hours after of the procedure, while the other group made use of minoxidil exclusively. Twelve weeks after, the MN group showed a significant increase in strand count (91.4 strands per cm^2) as compared to the control group (22.2 strands per cm^2) (P = 0.039). There was agreement between evaluator and participants regarding the superiority of the treatment with MN and minoxidil when compared to the control group, a result maintained for eight months after the last MN session. Strand growth was evidenced 6 weeks after the MN procedure, as compared to the 10 weeks in the group where minoxidil was used as the sole treatment.

This same author followed up four male patients with AGA (ages 28, 30, 35, 40) who were resistant to finasteride and Minoxidil. In the six months of treatment, they underwent MN sessions associated with the use of Minoxidil and finasteride, receiving four weekly sessions, followed by two sessions every 15 days (15 sessions in total). The evaluation of results showed that approximately 50% of the patients reported improvement in comparison to the maximum grade of the score system that was used.

The study by Kim *et al.* of MN in hairless mice resulted in better strand growth as compared to the control group.[28,29] There was increase in the regulation of Wnt-3, Beta-catenin, endothelial growth factors, Wnt10b and mRNA, in addition to protein expression. Wnt/β-catenin encourages morphogenesis and hair growth.

Farid *et al.* (2016) followed up 40 female patients with AGA and comparing the use of MN associated to mesotherapy with PRP and the use of 5% minoxidil as monotherapy. In the first group, the use of PRP in the scalp was aimed at stimulating the release of growth factors such as VEGF, PDGF, IGF, leading to increased vascularization and growth of cells of the dermal papillae, hair follicle and production of new hair strands. After the application of a device with needles of 0.5 mm long up until obtaining moderate erythema, PRP solution (1 ml) was instilled followed by re-application of the device. The control group used 5% Minoxidil twice daily for six months. Strand growth was observed within 12 to 28 weeks after the beginning of the treatment. Both groups showed increased strand count. The authors concluded that Minoxidil monotherapy was effective and should remain the first treatment option based on improved strand count and faster growth time. These findings led the authors to recommend MN with PRP as the second treatment option in patients with absence of response to topical Minoxidil.[33]

A pilot study by Lee *et al.* (2013) evaluated women (n = 11) with a mean age of 41.4, bearing female pattern alopecia (FAGA).[34] Half of the scalp was treated with five weekly sessions of topical application of a product (composed of fibroblast, endothelium, insulin-like, keratinocyte, stem cell and superoxide dismutase growth factors) followed by MN with a 0.5mm long needle. The other half of the scalp was used as a control (ap-

Table 2: Studies on the treatment of alopecias

Type of Alopecia	Author	Year	Sample (n)	Treatment group	Control group	Results	Study design
Androgenetic Alopecia	Dhurat *et al.*[30]	2013	100	MN 1x/week + 1ml 5% Minoxidil 2x/day	1ml 5% Minoxidil 2x/day	MN Group - strand count 91.4 versus 22.2 (p = 0.039)	Controlled, randomized study, blind evaluator, 12-week duration
Androgenetic Alopecia	Dhurat *et al.*[31]	2015	4	15 MN sessions in 6 months (in addition to maintenance of use of oral Finasteride and topical 5% Minoxidil)	N/A	MN stimulated the growth of new strands by >75% in 3 patients and >50% in 1 patient	Case series, four patients, 6-month duration
Androgenetic Alopecia	Farid *et al.*[32]	2016	40	PRP + MN 1x/month for 6 months	1ml 5% Minoxidil 2x/day	Both treatments stimulated hair growth, and patients were equally satisfied. However, the use of 5% Minoxidil achieved results more rapidly	Controlled, randomized study, blind evaluator
Androgenetic Alopecia	Lee *et al.*[34]	2013	11	Application of growth factors followed by MN in half of the scalp of each patient	Application of saline solution followed by MN in half of the scalp of each patient	The average strand count was 52.91 +/- 10.85 on the treated side versus 45.91 +/- 9.98 on the control side of the scalp	Placebo, controlled, blind, split- scalp study, 5-week duration
Alopecia Areata	Chandrashekar *et al.*[35]	2014	2	Topical triamcinolone applied before and after MN, 3 sessions with 3-week intervals between them	N/A	Excellent restoration of hair growth	2-patient case series, 9-week follow-up

plication of saline solution followed by MN). The half treated with the combination of MN associated and the topical product showed more than a 10% increase in capillary growth starting from the fifth week as compared to the control group.

Chandrashekar *et al.* (2014) described successful treatments in patients with alopecia areata using MN and topical application of triamcinolone.[35] These patients had not responded to previous treatments with triamcinolone injection in the scalp, steroids and topical 5% minoxidil. The topical triamcinolone solution (0.1ml) was applied to the affected areas, followed by MN with 1.5mm long needles and a new application of triamcinolone – three applications with three-week intervals. Patients had improvement in hair strand growth after each session.

MELASMA

Microneedling seems to lead to good results in the whitening of recalcitrant melasma, however the mechanism of action has not yet been clarified.

Lima *et al.* (2017) studied patients bearers of melasma who had undergone two sessions of MN, with 1.5 mm long needles and a 0-day interval between sessions.[36] Twenty-four hours after the MN session, there was an application of Kligman's Triple Formula (Triluma®) and broad spectrum sunscreen. There was a perceptible improvement of melasma in all participants and a subjective description of improvement in softness, texture and brightness of the skin, in addition to the maintenance of the results in the six-month follow-up. All patients showed increased epithelial thickness, decreased melanin in the epidermis and increased collagen density in the superficial dermis (p = 0.03) (Table 3).

In a previous histological study on the use of the triple combination in melasma, it was not possible to observe thickening of the epidermis or changes in the upper dermis after six months of treatment.[36,37] These data corroborate the results described above, indicating that dermal thickening was induced by MN. Furthermore, there was an increase in transepidermal DD for at least 72 hours after the procedure, which can also increase the effect of the triple combination on melanogenesis.[38]

In addition to the classic treatment (triple combination and broad spectrum sunscreen), MN promoted clinical and histological improvement of recalcitrant facial melasma. Additional randomized and controlled trials are needed to investigate MN treatment schemes in order to maximize their effectiveness and maintain long-term outcomes.[36]

Regarding the use of whitening agents, MN with DD showed better results than the topical treatment alone. Budamakuntla *et al.* (2013) observed better results in patients with moderate to severe melasma (n = 60) with the use of MN associated with tranexamic acid as compared to microinjections of tranexamic acid. Patients were observed after three months (three sessions) with a 35% MASI improvement in the microinjection group (p <0.01) compared to 44% in the MN group (p <0.001). Notably, only 26% of the patients who underwent microinjections had a 50% improvement, as compared to 41%

in the MN group. None of the two groups reported severe side effects, however some patients reported moderate discomfort, burning sensation, and erythema.

The combination of therapies with MN led to more favorable results in the treatment of melasma when associated with daily use of sunscreen.[2]

In a retrospective study of patients with recalcitrant melasma (n = 22) who did not respond to whitening and sunscreen, MN was applied followed by a depigmentation formula (0.05% tretinoin + 4% hydroquinone + 1% fluocinolone acetonide), with daily use of SPF 60 sunscreen.[40] The procedure was repeated after 30 days. All 22 patients reported satisfactory results after two months of follow-up, with the 24-month photograph follow-up demonstrating maintenance of skin whitening – already observed in the second month of treatment – in 11 patients.[40]

WARTS

One study showed good results in the association of MN with topical bleomycin (0.2 -0.5 ml) in the treatment of plantar warts.[41] There was good tolerance to pain and absence of reports of tissue necrosis, which is observed when intralesional bleomycin is used.

ACTINIC KERATOSES (TABLE 4)

The use of MN in the treatment of field cancerization and actinic keratoses was evaluated by Torezan *et al.* (2013) in a split-face study (n = 10).[22] Microneedling was applied in one of the hemifaces after photodynamic therapy combined with Methylamino levulinate (MAL-PDT) and compared with the use of isolated MAL-PDT in the other hemiface. Methylamino levulinate-PDT combined with MN led to superior results in all parameters studied[22] (including facial erythema and photoaging) when compared to the isolated use of MAL-PDT (p = 0.01).

Spencer and Freeman (2016) performed a split-face randomized study (n = 20) in two groups.[42] One of the groups used MN followed by the application of delta-aminolevulinic acid (ALA-PDT), and the other group underwent application of ALA-PDT as monotherapy. There was a significant difference (p

Table 3: Studies on melasma treatments

Pigmentation disorder	Author	Treatment	Needle's length	Sample (n)	Number of sessions	Results	Study design
Melasma	Lima *et al.*, 2015[40]	Depigmenting formula (0.05% tretinoin + 4% hydroquinone + 1% fluocinolone acetonide) associated to SPF +/- application of MN	2mm	22	2 (4-week intervals)	Results varied from "good" to "very good" in 100% of the patients, who reported being satisfied with the treatment. 50% of patients maintained the whitening of the spots at the 1-year follow-up	Retrospective analysis
Melasma moderado a grave	Bundamakuntla *et al.*, 2013[39]	MN + application of topical tranexamic acid (TA)	1.5mm	60	3 (4-week intervals)	44% of the MASI improvement in the TA + MN group, compared to a 36% improvement in the group that used TA isolatedly	Controlled and randomized clinical trial

Table 4: Studies in the treatment of actinic keratoses

Author	Treatment	Needle's length	Sample (n)	Number of sessions	Results	Study design	Study design
Torezan *et al.*, 2013[22]	MAL-PDT +/- MN	1.5mm	10	1	The average reduction in AKs was 88.3%, however there was no significant statistical difference between groups. The MN group showed improvement in rhytids and erythema, and improvement in all parameters (p = 0.01)	Controlled and randomized, prospective, split-face clinical trial	Retrospective analysis
Spencer e Freeman, 2016[42]	ALA-PDT +/- MN	0.5mm	19	1	The average reduction in AKs was 89.3% in the MN group versus 69.5% in the isolated PDT group (p <0.05). 87% of the patients in the MN group showed improvement in rhytids compared to 11% from the other group	Controlled and randomized, double-blind, prospective, split-face clinical trial	Controlled and randomized clinical trial

<0.05) between the groups, with improvement of 89% of actinic keratoses in the ALA-PDT and MN group, as compared to 69% in the monotherapy group.

CONTRAINDICATIONS

Contraindications to MN are limited and include inflammatory acne, active labial herpes or another infection in the area being treated, predisposition to keloid formation and immunosuppression. In addition, care must be taken with the concomitant application of MN near the areas of botulinum toxin injection with a view to preventing its undesired diffusion.

SIDE EFFECTS AND COMPLICATIONS

Microneedling is deemed as a minimally invasive procedure with few associated adverse effects, with moderate erythema and localized edema that usually resolve within 48 to 72 hours being the most common and expected. Pin-point-type bleeding is limited to the minutes after the procedure, and should be treated with the application of gentle manual pressure and gauze with cold saline solution. Transient erythema is the most common adverse event.

Depigmentation events used to be a worrying complication in higher phototypes. However, it is rarely observed when there is no exposure to the sun after the treatment. In addition, histological analysis of melanocytes 24 hours after MN evidenced absence of changes in the epidermis or in the number of melanocytes, suggesting that the risk of undesirable depigmentation is possibly minimal.

In a series of cases (2014) three patients developed granulomatous reaction caused by the topical use of vitamin C serum after MN.[43] Drug delivery (DD) during or immediately after MN should be carried out with caution since the formation of channels in the epidermis and dermis are a gateway for microorganisms to occur and may also increase the incidence of adverse effects, thus enabling the development of an immune response to potentially immunogenic particles. Nonetheless, adverse reactions are rare and systemic toxicity reactions have not been reported. Patients should be instructed not to use products that have not been prescribed by physicians within the first week after MN, as they may potentially induce a local or systemic hypersensitivity reaction. It is recommended that DD associated with MN be performed with caution, as non-sterile substances may contain particles that penetrate the layers of the skin possibly leading to future complications. In addition, the application of topical agents to the skin immediately after MN should be performed with extreme caution aimed at avoiding the above described complications. Further studies are necessary on transepidermal substances and vehicles for DD, aimed at minimizing the risks of unwanted absorption, allergic reactions, infections and others.

CONCLUSION

In recent years there has been a significant increase in the demand for minimally invasive procedures, which suggests that MN will be of special interest for patients who wish clinical results without a prolonged recovery time. In general, the procedure is efficacious, cost effective, has few adverse effects and stands as a viable option in the rejuvenation of patients with higher phototypes.[44] It is generally well tolerated with only the application of topical anesthetics when using needles of up to 1 mm in length. Greater needle lengths demand that the extent of the area to be treated be evaluated, meaning that block and/or infiltration anesthesia are often required.[11]

Since the introduction of the subincision concept by Orentreich *et al.*, which evolved with the help of Camirand et Doucet and Desmond Fernandez, MN quickly became a dynamic procedure with the use of electrical and manual equipment.[1,4,5] Microneedling is safe, minimally invasive and effective in the treatment of many dermatological conditions such as acne, scars, rhytids and stretch marks. With rapid postoperative recovery, limited side effects and significant clinical outcomes, MN is an alternative to more invasive procedures such as laser resurfacing and deep chemical peels.

This review article highlights scientific evidence related to the use of MN in various dermatological conditions. In addition to its cosmetic use (e.g. in pigmentation disorders), it also has excellent indication for the treatment of premalignant lesions (actinic keratoses), acne scars and scalp disorders.

The advantages of this procedure include good patient tolerability, the possibility of increasing transepidermal drug delivery (DD), and practicality and safety of use in higher phototypes.

Further controlled clinical trials are required in order to verify the use of MN as a scientific evidence-based procedure in the treatment of various dermatological diseases, as well as for aesthetic purposes. Moreover, the required number of sessions, the ideal devices, including needle length and depth to be reached, should be better studied. Finally, studies elucidating the details of the mechanism of action of MN, especially in the treatment of alopecia and pigmentation disorders, are required. ●

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