TRANSEPIDERMAL DELIVERY OF TRIAMCINOLONE ACETONIDE OR PLATELET RICH PLASMA USING EITHER FRACTIONAL CARBON DIOXIDE LASER OR MICRONEEDLING IN TREATMENT OF ALOPECIA AREATA

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INTRODUCTION

Alopecia areata (AA) is one of the most common forms of non-scarring alopecia involving the scalp and/or body. (1) Estimated incidence of alopecia areata is 20.9 per 100,000 person-years with a cumulative lifetime incidence of 2.1%. (2)

The exact pathophysiology of alopecia areata remains unknown. The most widely accepted hypothesis is that alopecia areata is a T cell-mediated autoimmune condition that is most likely to occur in genetically predisposed individuals. (3)

Alopecia areata can be classified according to its pattern, as follows: patchy, reticular, ophiasis, alopecia totalis and alopecia universalis. (4)

Although, alopecia areata is a benign condition and most patients are asymptomatic, it can cause emotional and psychosocial distress in affected individuals. (5)

First-line therapies include intralesional corticosteroids, topical corticosteroids, minoxidil, anthralin, topical immunotherapy, prostaglandin analogues, topical retinoids bexarotene, and capsaicin. (6) Second- and third-line treatments include topical and systemic immunomodulatory therapies such as oral and topical psoralen plus UVA radiation and photodynamic therapy. (7) No treatment is either curative or preventive. (8) Since no single treatment option is certain to treat alopecia areata, the need for new therapies is mounting.

Intralesional corticosteroids, most commonly triamcinolone acetonide are considered a first-line treatment method for limited disease and can be used as adjunctive therapy in extensive disease. (9) Because triamcinolone is only
emulsified temporally to the water, usually it is delivered by the painful intralesional injection.\(^{(10)}\)

Platelet-rich plasma (PRP) has emerged as a new treatment modality in dermatology, and preliminary evidence has suggested that it might have a beneficial role in hair growth.\(^{(8)}\)

Drugs applied topically have the advantage of fewer side effects and bypassing the first-pass effect.\(^{(11)}\) However, transepidermal dermal drug delivery has limitations, including decreased penetration of larger and water-soluble molecules.\(^{(12)}\) Only lipophilic and smaller than 500Da molecules are capable of penetrating an intact stratum corneum. Furthermore, only 1% to 5% of the product applied to the skin is absorbed and becomes bioavailable to exert its therapeutic effect.\(^{(13)}\) In addition, the stratum corneum acts as a barrier that limits the penetration of substances through the skin.\(^{(14)}\)

Several strategies have been used to improve many drug penetrations into the skin: microneedling, ultrasound, and more recently transepidermal drug delivery (TED). TED is a technique based on applying a medication following an ablative method (CO2 laser, erbium lasers or ablative radiofrequency), which create vertical channels to assist the delivery of topically applied drugs into the skin. The use of nonablative lasers as well as microneedling technique has been reported with the same purpose.\(^{(14)}\)

Fractional laser–assisted drug delivery of corticosteroids for resistant alopecia areata is a new concept in dermatological therapy.\(^{(15)}\) Lasers stimulate drug delivery by the means of three processes: tissue ablation, which removes the stratum corneum and the most superficial layers of the epidermis; photomechanical waves, resulting from the conversion of light into mechanical energy; and non-ablative resurfacing, where thermal and physical injuries rupture the skin barrier, promoting the delivery of medications.\(^{(16)}\)
Microneedle devices, such as Dermaroller and Dermapen, are minimally invasive devices that bypass the stratum corneum barrier, thus accessing the skin microcirculation and achieving systemic delivery by the transepidermal route.\(^{(17)}\) They create transient aqueous microchannels in the stratum corneum, that vary from 0.5 to 2.5 mm. Subsequently, a conventional, topically applied drug formulation can permeate through these microchannels via passive diffusion.\(^{(18)}\)

Trichoscopy, hair and scalp dermoscopy, is a fast, non-invasive method useful in the diagnosis and therapeutic monitoring of scalp and hair diseases.\(^{(19)}\) The trichoscopic features of alopecia areata were first described in 2004.\(^{(20)}\) The reported features of alopecia areata are: yellow dots (6–100% patients), short vellus hairs (34–100%), black dots (0–84%), broken hairs (0–71%) and exclamation mark hairs (12–71%). The diagnosis should be based on the coexistence of several trichoscopic findings, not on the presence of a single feature.\(^{(19)}\)
AIM OF THE WORK

The aim of this study is to evaluate the use of fractional carbon dioxide laser versus microneedling in the transepidermal delivery of triamcinolone acetonide and platelet rich plasma in treatment of alopecia areata.
PATIENTS

This study will be carried out on sixty patients, of either sex, presenting with alopecia areata to the outpatient clinic of Dermatology, Venereology and Andrology, Alexandria University Hospitals, after approval of the local Ethical Committee and having an informed written consent from every patient included in the study, or his/her legal guardian in case of children.

Inclusion criteria:

1. Patients with alopecia areata of either gender, diagnosed both clinically and by trichoscopy

2. Patients not responding to treatment (topical and/or systemic), used properly and regularly, for at least 3 months duration

Exclusion criteria: (8, 21-23)

1. Alopecia areata with evidence of spontaneous hair regrowth
2. Patients having active scalp inflammation or other scalp or hair diseases
3. Pregnant and lactating women
4. Patients with any bleeding disorder or receiving anti-coagulant therapy
5. Immunocompromised patients
METHODS

History will be obtained at baseline according to the guidelines of the National Alopecia Areata Foundation including: (8, 15, 21, 24)

- Patient demographics (name, age, sex, address, contact number,...)
- Hair loss: age of onset, total duration of disease, number of relapses, family history
- Onset and duration of hair loss of the present episode, and number of aa patches
- Associated symptoms,
- Any history of previously received treatment for the hair loss,
- History of bleeding tendencies, or intake of any anticoagulant drugs
- History of any medical or autoimmune disease

Clinical evaluation: (15, 21, 24)

The clinical evaluation of alopecia areata will be made in accordance with the guidelines of the National Alopecia Areata Foundation. (24) Under adequate illumination, patient will be examined for:

- The pattern of hair loss
- Number of patches
- Skin changes over the affected area
- Baseline SALT score (24-26)
- Any associated nail changes
- Also the patient will be thoroughly assessed for any associated autoimmune and endocrine disorders with relevant history, physical examination, and investigations wherever indicated.
Trichoscopic/Dermoscopic evaluation: (25, 27, 28)

Trichoscopic evaluation will be performed using a DermLite® IV (3 Gen, San Juan Capistrano, CA, USA), which can be used without immersion gels because of the presence of polarizing filters. The dermoscopic/trichoscopic features of the alopecic patch(es) will be noted.

**Patients will be randomly allocated, by closed envelope method, into one of four equal groups, fifteen patients each:**

Group I: Fractional Carbon dioxide laser (CO₂ Laser) and triamcinolone acetonide (TrA; 10 mg/ mL).

Group II: Microneedling with Dermapen and triamcinolone acetonide (TrA; 10 mg/ ml).

Group III: Fractional Carbon dioxide laser (CO₂ Laser) and Platelet-rich plasma (PRP)

Group IV: Microneedling with Dermapen and Platelet-rich plasma (PRP)

Each patient will receive four treatments, with an interval of three weeks between the treatment sessions, for a total of 12 weeks. (14, 21, 29) This will be followed by a follow up period of another 4 weeks. The patients will be given no topical treatments for the alopecia areata in between the sessions. Topical post-procedure care in the form of topical antibiotics, emollient or sunscreen may be used.

**Group I:** Fractional Carbon dioxide laser (CO₂ Laser) and triamcinolone acetonide (TrA; 10 mg/ ml) (14, 15)

The ablative fractional CO2 laser is delivered to the patients’ scalp.

The fractional ablative method is applied immediately before the topical medication.

Laser treatment will be given to the affected area, and immediately after the treatment, triamcinolone solution (10 mg/ml) will be dropped on the treated area and spread evenly.

**Group II:** Microneedling with Dermapen and triamcinolone acetonide (TrA; 10 mg/ ml) (29-32)
Microneedling is performed using Dermapen.

This creates pin point bleeding or mild erythema which will be considered as the end point.

Triamcinolone acetonide in concentration of 10 mg/ml (0.1 ml containing 1 mg of triamcinolone) will be applied on each lesion twice, before and after performing microneedling.

**Group III: Fractional Carbon dioxide laser (CO\(_2\) Laser) and Platelet-rich plasma (PRP)**\(^{(33)}\)

The same laser parameters as group I will be used, followed by application of freshly prepared PRP. The applied PRP will be spread over the whole affected area.

**Group IV: Microneedling with Dermapen and Platelet-rich plasma (PRP)**\(^{(21, 29-32)}\)

Microneedling using dermapen is performed as Group II.

Microneedling is preceeded and followed by intermittent application of freshly prepared PRP. The applied PRP will be spread over the whole affected area and again rolled till pinpoint bleeding points are noticed.

**Assessment criteria:**\(^{(21, 24)}\)

Each patch will be digitally macrophotographed, and evaluated clinically and by dermoscopy at baseline and at the end of the study, for signs of hair regrowth.

**Other criteria that will be evaluated:**

- Patient's satisfaction
- Any complications, side effects clinically and using a dermoscope
- Ease of the technique
- Cost
ETHICS OF RESEARCH

Research on human or human products:

✓ Prospective study: Informed consent will be taken from patients. In case of incompetent patients the informed consent will be taken from the guardians.

☐ Retrospective study: Confidentiality of records will be considered

☐ DNA / genomic material: Informed consent for DNA / genomic test and for research will be taken from patients. No further tests will be carried out except with further approval of committee and patients. If the samples will travel outside Egypt the researcher will be responsible for transportation and security approval.

✓ All drugs used in the research are approved by the Egyptian Ministry of Health

Research on animal:

☐ The animal species are appropriate for the test.

☐ After test, if the animal will suffer, it will be euthanized and properly disposed.

☐ After operation, it will have a proper postoperative care.
RESULTS

The results obtained from this study will be tabulated and statistically analyzed using the standard statistical methods.
DISCUSSION

The results obtained from this study will be discussed in view of achievement of the aim and compared with any available published data in the same field of the research.
REFERENCES


33. Brownell N, Panchaprateep R, Glinhom R. Combination of a non-ablative 1,927 nm thulium fiber fractional laser and autologous platelet-rich plasma in