



Intradermal Therapy (mesotherapy) in Dermatology

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Abstract

Mesotherapy consists of a series of micro injections in the superficial layer of the skin of active ingredients that slowly diffuse into the underlying tissues. This technique is applied in different clinical conditions and also in dermatology it could play a useful role in the treatment path of many patients. However, further clinical studies are needed to standardize its application in various dermatological pathologies. The recommendations of the Italian Mesotherapy Society aim at personalized therapy based on evidence, efficacy and safety.

Intradermal therapy, also known as mesotherapy, is an injection technique which, if well applied alone or in combination with other therapies, is useful in various clinical conditions¹. It has rapidly spread in the field of pain medicine for the management of painful syndromes², in chronic veno-lymphatic insufficiency^{3,4}. It is also used in the cosmetic field but little scientific evidence supports this application⁵. The scientific rationale for this technique is based on the fact that a drug injected in small doses into the surface layer of the skin slowly spreads to the underlying tissues and remains longer than systemic administration, as confirmed in preclinical studies¹. In fact, higher concentrations of intradermally injected drug have been detected in the skin, muscles and joints underlying the infiltration site compared to intramuscular administration. Furthermore, a higher immune response, both primary and secondary, has been reported after intradermal injection compared to intramuscular administration^{1,6}. Furthermore, it has also been hypothesized that the micro trauma induced by the needle and the chemical-physical reactions induced by the liquid infiltrated into the dermis could induce dermal reactions capable of increasing the effect of the drug injected into the dermis⁷. The set of these intradermal mechanisms, called meso-dermal modulation, constitute hypotheses that must be experimentally verified⁸.

Many advantages of this technique have been described: minimally invasive, lower dose of drug compared to systemic treatment, lower risk of systemic adverse events, simple application^{1,6,8}. Mesotherapy consists of one or more micro intradermal injections in the area to be treated or along the edges of the dermatological lesion. 13 mm needles (30 or 32 gauge) or 4 mm needles (27 gauge) are

used¹. Infiltration should be performed after adequate disinfection of the skin to be treated. The needle should be introduced quickly and the drug should be injected gently to avoid pain. To date, the clinical data available do not allow to standardize the technique in dermatological indications. However, the various authors agree on the depth of infiltration and recommend tilting the needle between 30° and 45° to deposit the drug in the dermis to a depth of about 2 millimeters^{1,6,8}. The number of treatment sessions and the frequency (weekly or with greater or lesser frequency) depend on the pathology treated, but there are no standard dermatological protocols and therefore the response of the individual patient represents the driver for the treatment^{1,6,8,9}.

In the dermatological field, mesotherapy has been applied in many skin conditions¹⁰⁻²³ (Table 1) and several drugs have been used¹⁰⁻³² (Table 2). However, in addition to pain medicine and dermatology, mesotherapy has also been applied in the field of aesthetics.

Table 1: Dermatological pathologies that have been treated with intradermal drugs

Alopecia ¹⁰
Cystic acne ¹¹
Keloid ¹²
Suppurative hidradenitis ¹³
Psoriasis ¹⁴
Warts ¹⁵
Cutaneous leishmaniasis ¹⁶
Vitiligo ¹⁷
Melasma ¹⁸
Pretibial myxedema ¹⁹
Necrobiosis lipoidica ²⁰
Cutaneous neoplasms ^{21,22,23}

Table 2: Drugs used intradermally for the treatment of certain dermatological diseases

triamcinolone acetonide ^{10-15, 18,24,26}
bleomycin ¹⁵
meglumine antimoniate ¹⁶
5-fluorouracil ¹⁷
glucocorticoid ^{19,20}
interferon alpha-2b ²¹
interleukin-2 ²³
lincomycin ²⁴
botulinum toxin ²⁵
methotrexate ²⁶
cyclosporine ²⁶
platelet rich plasma ²⁷
minoxidil ²⁷
tranexamic acid ²⁸
ixekizumab ²⁹
secukinumab ³⁰
brodalumab ³¹
verapamil ³²

For over a century pharmacologically active substances have been injected intradermally, for example in 1910 Mantoux³³ wondered about the clinical interpretation of intradermal reaction to tuberculin.

Since 1952 Michel Pistor popularized this technique suggesting its usefulness in various clinical conditions³⁴ but, following the French suggestions, the trend spread of applying mesotherapy with products (or mixtures of substances) without scientific support in favor of efficacy and tolerability in the pathology treated^{5,35}. For this reason the Italian Society of Mesotherapy has conducted national and international consensus to limit indications, suggesting that the choice of the drug must be based on clinical tolerability and efficacy data and that mesotherapy should only be conducted by qualified doctors^{1,6} (general recommendations are shown in Table 3). For example, even if some authors report a consolidated efficacy of steroids both in monotherapy and in combination¹⁰⁻¹⁴ we have doubts about the use of corticosteroid intradermally for erythema, pain, sterile abscess, hypopigmentation and skin atrophy caused by this drug and we suggest diluting the dose and injecting minimum quantities only if necessary. In fact, one of the main advantages of mesotherapy is the drug sparing effect with respect to the deeper route of administration. Moreover, the dose-saving effect is also well reported in the field of immunoprophylaxis practiced with the intradermal routes³⁶⁻³⁷. These studies show that the dermis has a microcirculation capable of interacting with the immune system and the intradermal inoculation of vaccines offers

Table 3: General recommendations for correct application of mesotherapy in dermatology^{1,6}

Mesotherapy is a technique based on the administration of pharmaceutical substances in the upper layers of the skin
Mesotherapy should be applied by skilled doctors
If it is used for indications without evidence of efficacy and tolerability, it should be conducted in accordance with the rules of good clinical practice
Mesotherapy must be integrated with standard treatments according to the needs of the individual patient
Before applying mesotherapy, a diagnosis must be made
When the intradermal route is useful, mesotherapy can be considered to reduce the systemic impact of drugs
Collect all clinical data in the patient's medical record
Doctors should report the pros and cons of this technique to allow the patient to make a valid decision (informed consent)
A single drug is recommended in the syringe (the use of mixtures is allowed only if there is data to support efficacy tolerability and chemical stability)
The doctor must avoid any contamination to avoid the risk of infections. Disposable gloves and materials are mandatory
The drugs are used according to the authorized indications. When used off label are the current rules must be respected in individual countries

numerous advantages over the intramuscular route of administration, including a reduction in the necessary dose of antigen, a reduced need for adjuvant, a greater immune response and a simpler method of administration. Furthermore, the intradermal route could have enormous potential in anticancer therapy, as demonstrated by dendritic cell vaccines³⁸⁻³⁹. Even some biological drugs are now injected intradermally in the treatment of psoriasis and obtain prolonged clinical remission and a reduction in the severity index of the psoriasis area^{40,41}.

Although the intradermal route has many applications in clinical practice, we do not know how the drugs spread through the various thicknesses of the skin and how it affects the pressure with which the substances are injected⁴² or what role the cytochromes play on the metabolism of the drugs injected locally⁴³.

In conclusion, mesotherapy applied in dermatology needs more clinical confirmation. Studies are needed to identify the ideal drug concentration, the short depth of infiltration and the patients who benefit most from this technique. The dermis appears to be a target organ for many pathologies and clinical dermatologists will play a crucial role in the development of mesotherapy. Preclinical and clinical dermatological research could help other professionals to understand the mechanism of action of mesotherapy. While ad hoc studies are being conducted, mesotherapy must be considered a medical act and must be applied by qualified doctors⁴⁵. Evidence-based recommendations are needed to standardize this technique also for the management of dermatological conditions. Pending new guidelines, we recommend following the recommendations available today^{1,6}.

Author Disclosure Statement

The Authors declare that no conflicts of interest exist in relation to the contents of this article. Compliance with ethics guidelines. This article is based on previously conducted studies. The Authors does not involve any new studies (on human or animal subjects).

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