

Mesotherapy – The french connection

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ABSTRACT

Mesotherapy involves the use of multiple intradermal or subcutaneous injections of a mixture of compounds in minute doses, by means of very fine needles, directly over/near the affected sites. Originally invented in France to manage painful medical conditions, it is presently the buzz word in the field of cosmetic dermatology, chiefly to get rid of disfiguring fat. Depending upon the condition treated, the drugs injected, the techniques followed and the number of sessions involved vary. The wider reception of mesotherapy by its stakeholders are probably due to factors like inexpensive equipments, relatively minimal training for providers, much reduced dosage need of the drugs with resultant minimal untoward effects, quicker realization of benefits, minimal invasiveness/pain involved and not the least it is an outpatient procedure. Despite so many plus points, it has to be noted that currently there is a dearth of rigorous scientific studies to prove its efficacy and safety. Further, the average cost per session alone ranges from 200 USD to 600 USD.

Key words: Body sculpting, cellulite, injection lipolysis, intradermotherapy, nappage

INTRODUCTION

This mini-review is about one of the rapidly developing field of therapeutics called ‘mesotherapy’ which involves multiple intradermal or subcutaneous injections of a mixture of compounds (plant extracts, homeopathic agents, pharmaceuticals, vitamins, and other bioactive substances) in minute doses, using very fine gauge needles, to treat medical (mainly local) and cosmetic conditions. The term ‘*meso*’ also means ‘*middle*’ and ‘*mean*’, hence variably explained with reference to the injection route (into the *middle* layer of skin or ‘intradermotherapy’) and the *mean* dose of the medication used (dose in between allopathy and homeopathy).^[1]

Mesotherapy does not denote a treatment of any condition in particular; it simply describes a method of drug delivery.^[2] Mesotherapy is performed in those structures that were derived from mesoderm rather than itself since the latter ceases to exist beyond the embryonic stage of human development.

It has been suggested that the skin acts as a natural time-release system when drugs are injected by mesotherapy.^[3] Other advantages claimed for mesotherapy include inexpensive

equipments, relatively minimal training needed for providers, prompt and undiluted reach of drugs to the target area, much reduced dosage need of the drugs, quicker accomplishment of benefits, minimal invasiveness hence attendant pain and no necessity for hospitalization.

HISTORY

Insertion of needle(s) for alleviation of diseases has a long history, starting from Hippocrates (400 B.C.) who used a local application of cactus for shoulder pain, the Chinese using acupuncture (since 2000 years) and then, injection of substances following the invention of the hollow needle since nineteenth century.

Mesotherapy is a medical technique developed in 1952 by the renowned French physician, Dr Michel Pistor for the management of pain and vascular disorders.^[4,5] Pistor was bestowed the Legion of Honor (“*Legion d’Honneur*”), the highest award to persons considered as national heroes with significant accomplishments in France.

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It all started when Pistor injected procaine intravenously to treat an asthmatic, and discovered that though the original condition did not improve, the patient's impaired hearing did. With an intent to strengthen the effect, Pistor injected small doses of procaine 3 to 5 mm deep around the target area i.e. the ear itself. From then on scores of deaf patients paraded themselves to Pistor. However, it was noted that other associated conditions like eczema of the auditory canal, temporomandibular joint pain, and tinnitus were to benefit.^[1]

Pistor coined the term '*mesotherapy*' in his first publication of the technique, in a local medical journal in 1958. He defined it as treatment of the mesoderm (the primary germ layer that develops into connective tissue, muscle and circulatory system) referring to the effects of local procaine on such wide number of tissues.^[6] Thus, '*mesotherapy*' may be considered as an off shoot of pharmacotherapy, consequent to the serendipitous manipulation of the intradermal route, hitherto less well explored, to treat medical conditions.

Pistor founded the French Society of Mesotherapy in 1964 and extended the technique to treat general medical, veterinary, and cosmetic conditions. In 1987, The French National Academy of Medicine officially acknowledged mesotherapy as a medical specialty. In the meantime, mesotherapy became popular in most parts of Europe, South America, and more recently in the United States and Asian countries. Pistor died in the year 2003. It would be a fitting tribute if the mesotherapists worldwide pronounce Dr Pistor as the '*The Father of Mesotherapy*'.

MESOTHERAPY: INDICATIONS AND MEDICATIONS USED

Mesotherapists routinely employ FDA approved drugs for uses not reviewed by the FDA.^[7] Such off-label use by physicians is not claimed to violate FDA rules and even the courts have held that off-label use by itself does not constitute negligence or medical malpractice, unless otherwise it is contraindicated or used experimentally in the given condition.^[8] On the contrary, it is also argued that the mixture of drugs and other ingredients in mesotherapy formulations produce a new drug that is not FDA approved for any purpose, and hence would not be considered "off-label" use.^[9] All said, the practice of mesotherapy not only endures but also grows.

Like corticosteroids, mesotherapy too is claimed to have a wide array of applications, with proof of 'before-and-after-treatment' photographs especially in the field of cosmetic dermatology. Only the current and widely practiced indications along with the drugs used in them are discussed below.

Pain

Evidence for mesotherapy in the treatment of pain are currently available in French, mainly as case reports. Mesotherapy

was traditionally employed for pain relief, in conditions like fibromyalgia, gout, headache, neuralgia,^[10] low back ache, sports injuries (i.e., sprains, strains, bursitis, tendinitis),^[11] and dental procedures.^[12] The procedure involves multiple small volume injections of an analgesic i.e. NSAID (commonly piroxicam or ketorolac), surrounding the painful area e.g. inflamed tendon. Skeletal muscle relaxants like baclofen or diazepam are also commonly co-administered. Another widely employed drug in France, for chronic pain disorders, is salmon calcitonin (sCT) which is already used in conventional medicine as an analgesic in painful bone disorders ranging from osteoporosis to cancer.^[13]

In the vast majority of mesotherapy protocols, either lidocaine 1% (for acute conditions) or procaine 1% (for chronic conditions) without epinephrine is used to minimize the pain of the procedure. In France, drugs like buflomédil (vasodilator) and pentoxifylline are also commonly used which are believed to increase local tissue microcirculation, and facilitate metabolic waste elimination.^[14] In animal studies, pentoxifylline has also been shown to possess antihyperalgesic effect.^[15] Herbs like artichoke, ginko biloba, melilotus are also used to improve local circulation.

Unwanted fat removal

Mesotherapy is the buzz word in the cosmetic world of "melting fat" for weight loss and cellulite treatment. It is also a form of "injection lipolysis". Presently, mesotherapy is gaining lure *mainly for non-surgical cosmetic applications*, like removal of disfiguring fat (cellulite)^[16] in thighs, buttocks, hips, legs, arms, and facial areas^[17] including eye pads,^[18] skin rejuvenation, to minimize wrinkles and tighten loose skin, body contouring,^[5] striae,^[18] vitiligo, hyperpigmentation, acne,^[19] and alopecia.

The drugs found to be very effective in the elimination of unwanted fat deposits and skin rejuvenation include phosphatidylcholine (PC), L-carnitine, aminophylline, hyaluronidase, collagenase, glycolic acid, retinoic acid, multivitamins (A, D, E, K), trace elements [minute quantities of zinc, copper, selenium, chromium and manganese], an acetylcholine analog dimethylaminoethanol (DMAE), lidocaine etc.

The proposed mechanisms for the various compounds in removal of unwanted fat are as follows. PC has lipolytic activity by affecting the permeability of the adipocyte membrane and subsequent fat mobilization. Some add small quantities of sodium deoxycholate^[17] to increase the fat-dissolution effectiveness of PC through disintegration of adipocytes. Thyroid preparations, aminophylline and isoproterenol are supposed to stimulate insulin release which help in breaking down of fat cells.^[8]

Hyaluronidase and collagenase disintegrate the bands of fibrous tissue formed between fat lobules in cellulite. Glycolic acid exfoliates the skin (peels). Vitamin A regulates cell turnover of skin and keratinization; Vitamin C enhances the synthesis of collagen and reduces hyperpigmentation as it inhibits melanin production; Vitamin E, an antioxidant, aids in anti-aging of the skin; Vitamin K affects clotting mechanisms and thus regulates the microcirculation of the skin; DMAE cause myofibril contraction and smoothen the lax skin; while trace elements are important for regulating turnover and repair of skin cells.^[20]

Body contouring or sculpting is a sort of ‘image overhauling’, assists the body to reduce fat while moderately increases the muscles, thereby re-shaping the figure for a lean and toned look. Mesotherapy is considered as a non-surgical alternative to liposuction, though removal of large volumes of fat is not possible. Further, the individual must also care about fat intake and exercise. Upto ten or more sessions may be needed. As of 2004 the average cost range is 200 USD to 600 USD per session.^[21]

Cellulite is a condition where collections of fat push against the connective tissue causing cosmetically unacceptable lumpy, dimpled appearance of skin resembling cottage cheese.

The drugs used to reduce cellulite include pentoxiphylline, carnitine, coumarin, hyaluronidase/collagenase, calcium pyruvate, aminophylline/caffeine, artichoke, melilotus or ginkgo biloba.

OTHER CONDITIONS

Biorejuvenation

In a preliminary study in a small population of subjects ($n=20$), mesotherapy with multiple microinjections of hyaluronic acid has been found to be effective for skin photoaging, as confirmed by ultrasound, though not all patients responded uniformly.^[22]

Alopecia

Injections of minoxidil, finasteride, lidocaine, multivitamins, T3/T4 are used in treatment of alopecia.

The concept of mesotherapy has been extended to other fields, e.g. an intermittent vaginal injection of rhFSH every 3 days has successfully been applied in women receiving *in vitro* fertilization (IVF) treatment, mainly in an attempt to reduce the number of hospital visits.^[23]

As mentioned in the previous paragraphs, the medications used are a wide array of pharmaceutical substances, plant extracts, vitamins, and other ingredients. There is no standardized formulation for mesotherapy and ingredients vary depending

on indications. The components and combination of injected material is based on anecdotal reports or the physician’s experience. The purported mechanism of action of the components is yet to be substantiated. For exhaustive details of indications, drugs, doses and techniques one can refer to the text book.^[24]

MODE OF ACTION

Other than the mechanism(s) of certain components discussed under the heading ‘Indications and medications,’ a general mode of action for mesotherapy has been proposed.

“The dermis is a common denominator of three units i.e. circulatory, neuro-vegetative and immunological functions. It is proposed that by an action at each of these units, mesotherapy corrects the functional disorder that causes the suspected pathology”.^[24]

MESOTHERAPY INJECTION TECHNIQUES

Each session of mesotherapy involves superficial injections of medications using specialized short needles and specific techniques directly over the sites of the affected structures. Several hundred injections are given, though the number may vary depending upon the indication. In general, 1–3 sessions in acute cases, such as sports injuries, and 10-15 with maintenance sessions every 6 months or a year for chronic conditions such as “cellulite” may be required.^[25]

Commonly three different techniques are used.^[14]

Point by point

First described by Dr. Pistor, involves injection of 0.02 ml to 0.05 ml of drug solution perpendicular to the skin (4 mm deep), given 1 cm to 2 cm apart.

Nappage (French for “covering”)

Involves more superficial (2 mm deep) injections with a 4-mm needle, covering a large area. Injections are given at a 45 degree angle from the skin while applying light, constant positive pressure on the plunger, the practitioner rapidly flicks the wrist (mimics shaking a salt shaker or the action of a sewing machine). At each site, a drop of solution is introduced. Relatively, this is a more discomforting procedure to the patient.

Epidermic

The most superficial (1 mm deep) of all the techniques in which the basal layer of skin is not penetrated. Needle size of 27 to 31 gauges is used with the bevel oriented away from the skin and dragged along with light, positive pressure applied to the plunger. It is done in a grid pattern at 1-cm intervals over the entire affected area.

Multiple injections of small doses of medications, in precise locations, in a single sitting are highly demanding to the therapist. To overcome this difficult task, many practitioners in Europe and South America use a device called ‘mesogun’. The benefits of mesogun include faster injections, precise dose delivery, consistent depth of penetration and more comfort for the physician and patient.^[16] Some experts use a special technique called ‘mesoperfusion’ wherein same volume is injected over 10 minutes instead of 30 seconds as in a normal session.^[24]

ADVERSE EFFECTS^[26,27]

It is claimed that side effects following mesotherapy are extremely rare in experienced hands and if they occur they are mild. Despite the involvement of multiple injections in mesotherapy, the main reason cited for less frequent untoward effects is the much less dosage than one large dose used in modern medicine.

Non-specific common adverse effects include nausea, vomiting, diarrhea, mild pain, skin hyperesthesia, edema, itching, erythema and tender subcutaneous nodules at injection site.

Pigmentation problems include post-inflammatory hyperpigmentation and urticaria pigmentosa which may remain for many months, and can be very distressing, though not serious. Rarely full-thickness skin and fatty tissue necrosis have also occurred.

Hypersensitivity reactions like immediate or delayed (especially to hyaluronidase, collagenase), pruritic, maculopapular rash distant from the treated area (phosphatidylcholine allergy) have also been reported.

Specific adverse effects due to individual components like isoproterenol, yohimbine, aminophylline, anxiety, tremor, palpitations, muscle cramps due to potassium wasting, phosphatidylcholine-induced mild, transient elevations in LFT's are known to occur.

Adverse effects due to faulty techniques include localized infections, scars and subcutaneous nodules. Very recently, several cases of nontuberculous mycobacterial skin infections manifesting as nodules and draining abscesses owing to poor aseptic measures were reported to occur within 1 and 12 weeks of the procedure.^[28] One has to keep in mind the risk of transmission of infections (AIDS, HBV, HBC etc) which is applicable to any procedure that invades the intact skin, apart from the hitherto unknown long-term local and systemic effects.

CONTRAINDICATIONS^[29]

The contraindications to mesotherapy include a body mass

index greater than 30, known hypersensitivity to any of the components, less than 18 years of age, pregnancy, lactation, patients on anticoagulants, cardiac drugs (like amiodarone, hydralazine, calcium channel blocker, beta blocker), disease conditions like insulin dependent diabetes, liver and kidney disorders, AIDS, seizure disorders and lupus.

FLIPSIDE

Any new technique/therapy or for that matter drug will be accepted (depending upon the indication), if it is more effective or more safe or preferably both and not the least, cost-effective. The crux of mesotherapy is that there are no rigorous scientific studies comparing it to existing modes of gold standard therapy in a given condition. Until today, there is paucity of knowledge about the efficacy, mechanism of action and long-term consequences of mesotherapy.^[5,30]

Even the few available evidence are of low validity^[9] or even not encouraging.^[31] We may have to wait for such studies to accept mesotherapy as a standard mode of therapy.

About 16,000 US physicians use mesotherapy in their daily medical practice, the growth of number of mesotherapy-trained physicians by 300 per month,^[32] publication of a dedicated journal (*American Journal of Mesotherapy*), established clinics in reputed hospitals, mushrooming of mesotherapy centers across the globe and the conduct of numerous international congresses, all speak of its status. *American Academy of Aesthetic Medicine*^[33] is one among the leading organizations advocating quality physician training and conducting professional assessment for certification in mesotherapy. Thus it may not be an understatement to say that mesotherapy is gaining popularity as a specialty discipline among both the therapists and public at a swift pace.

The needle of evidence oscillates between safety and efficacy on the one end and popularity on the other, while hovering through uncertain and controversial zones. The optimists would be content with the oft repeated quote ‘Just as absence of proof is not proof of absence, lack of scientific validation is not proof that it does not work’.^[34]

Note

Attempts toward obtaining permission for reproduction of images of ‘before and after mesotherapy treatment’ of clinical conditions did not elicit any response from the concerned. However, the readers may find such photographs in Google images by entering appropriate keywords.

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