

Novel technology affords safe, efficient iontophoretic transdermal drug delivery

Pilot study documents penetration of hyaluronic acid to improve facial rhytids

BY CHERYL GUTTMAN
STAFF CORRESPONDENT

New Orleans — Transdermal delivery of hyaluronic acid is possible using a technology combining microdermabrasion with a novel electrophoretic system (Ultrapeel with Transderm Ionto, Mattioli Engineering), and this procedure appears to be a safe and effective method for improving facial rhytids, says Jaggi Rao, M.D.

Dr. Rao, an associate clinical professor in the division of dermatology, University of Alberta, Edmonton, Canada, discussed the principles of the electroporation-like transdermal drug delivery technology (termed "dermelectroporation") and the results from a preliminary study in which it was used to deliver hyaluronic acid to treat periorbital rhytids in a series of 10 women. Participants had symmetrical periorbital rhytids at rest, but were treated only on one randomly selected side of the face in two sessions spaced two weeks apart. Clinical and histological results were evaluated at four weeks with comparisons to baseline and the untreated contralateral side.

Effective, assessors say

Overall, the procedures were well-tolerated, resulting in only transient local side effects, and were effective based on patient assessments and reviewer ratings of changes noted clinically and photographically. Histological evaluation of tissue obtained in 2 mm punch biopsies also demonstrated safety and efficacy by demonstrating unaltered stratum corneum integrity, absence of epidermal damage and retention of

hyaluronic acid in the papillary and mid-dermis.

"This technology seems to have promise as a breakthrough alternative to parenteral administration for effective delivery of medications and other substances into the skin," Dr. Rao tells *DermatologyTimes*. "Additional studies are now in progress to further examine its use for enhancing the efficiency of various topical therapies."

Dr. Rao was introduced to the transdermal delivery system while completing a dermatologic surgery fellowship at the Dermatology/Cosmetic Laser Associates of La Jolla, Calif., under the direction of Mitchel P. Goldman, M.D. The study of hyaluronic acid transdermal delivery was performed in collaboration with Dr. Goldman at his center in California.

Dr. Rao explains that transdermal drug delivery aims to overcome the barrier function of the stratum corneum to improve cutaneous penetration of medications and other macromolecules that have structural and chemical properties limiting their bioavailability when applied topically. Electroporation as a method for achieving transdermal drug delivery has been around for more than a decade. It uses electricity to create ionic-based channels within the lipidic component of cellular membranes (eg, the stratum corneum). However, the utility of previous systems was limited because they employed unidirectional pulses that caused too much tissue damage when applied at the higher currents or lengthy treatment durations necessary for efficacy. In addition to tissue damage, the possibility of drug alteration was very likely.



A patient before (left) and four weeks after (right) two treatments with the Ultra-peel with Transderm Ionto, each separated by two weeks.

Photo: Jaggi Rao, M.D.

Pulses inverted

The new "dermelectroporation" system uses a patented, modified iontophoretic approach in which the electric pulses are stopped intermittently and inverted in terms of their polarity. As a result, the treatment is less traumatic but also more efficient.

"With this design, higher currents can be safely used without causing degradation of delivered molecules or alterations to the stratum corneum or epidermis," Dr. Rao says. The hyaluronic acid used in the pilot study is a product obtained from a Texas-based company (Apotheure). The initial study was performed using a low-viscosity, 15 mg/ml product that was diluted in normal saline. The concentration was selected arbitrarily, and both lower and higher concentrations will be investigated in further studies.

"We chose to treat periorbital rhytids because of the thinness of the skin at that anatomic site, and we used a low-viscosity hyaluronic acid product since migration of drug through a membrane decreases with increasing viscosity," Dr. Rao explains.

The transdermal drug delivery system is an attachment to the microdermabrasion machine, and it features a vibrating probe that assists with anesthesia and increases circulation to enhance dermal penetration. The drug is released by a liquid dispensing system and delivered at a constant, controlled rate.

At each session, 3 ml of the hyaluronic acid solution was transdermally delivered to the periorbital skin, keeping the electrodes oriented along the rhytids. Each session took between five and 10 minutes and did not require anesthesia, and post-procedure care consisted only of mupirocin ointment application.

Discomfort low

Ratings of intraoperative comfort showed that the average patient considered the procedure only mildly to moderately uncomfortable. After the procedure, almost all patients developed erythema, six had mottled abrasions that lasted a few days and were thought to be related to the rate of pre-treatment microdermabrasion that was performed, and a single patient developed purpura that resolved after one week.

Subject assessments after four weeks showed an average improvement score correlating with moderate to dramatic improvement. Wrinkle severity was rated by the treating dermatologist using a scale of 1 to 5. The average change on the treated side was -1.3 compared with -0.2 on the control side.

In addition, photographic outcomes were assessed by four independent reviewers blinded to treatment. Their ratings indicated the average patient experienced moderate improvement (mean score 3.3 out of 4) and there was a significant difference in mean improvement score favoring the treatment over control (mean score 1.2 out of 4).

Previous animal studies have shown this novel electrophoretic system to be able to transdermally deliver lidocaine, heparin, diclofenac sodium, dexamethasone, carnitine and collagen type I. The additional clinical studies Dr. Rao has undertaken are evaluating its ability to improve the efficiency of penetration of anesthetics, anti-inflammatory drugs and photosensitizers used in photodynamic therapy. **DT**

Disclosure: Dr. Rao has no financial interest in the products he discussed.



Live treatment with the microdermabrasion system.



Live treatment with the TransDerm Ionto.