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Age-related Percutaneous Penetration Part 1: Skin Factors

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ABSTRACT

Changes in the skin that occur in the elderly may put them at increased risk for altered percutaneous penetration from pharmacotherapy along with potential adverse effects. Skin factors that may have a role in age-related percutaneous penetration include blood flow, pH, skin thickness, hair and pore density, and the content and structure of proteins, glycosaminoglycans (GAGs), water, and lipids. Each factor is examined as a function of increasing age along with its potential impact on percutaneous penetration. Additionally, topical drugs that successfully overcome the barrier function of the skin can still fall victim to cutaneous metabolism, thereby producing metabolites that may have increased or decreased activity. This overview discusses the current data and highlights the importance of further studies to evaluate the impact of skin factors in age-related percutaneous penetration.

Key words: transdermal, elderly, dermatopharmacokinetics, percutaneous penetration, cutaneous metabolism

Introduction

Human skin changes with increasing age due to both intrinsic and extrinsic factors. Intrinsic skin aging is primarily determined by genetics and extrinsic aging (photoaging) is primarily caused by environmental exposure to ultraviolet light. In sun-exposed skin, these two processes of aging are superimposed. Age-related skin changes may affect the percutaneous penetration of drugs and ultimately their systemic absorption. Numerous physiological and biochemical changes within the skin have been identified, but it is not clear how these factors have a role, if any, in the degree of percutaneous penetration.[1]

Changes that occur in aged skin include increased stratum corneum dryness,[2,3] reduction in sebaceous gland activity resulting in a decrease in skin surface lipids,[4] flattening of the dermal-epidermal junction,[1,5] and atrophy of the skin capillary network resulting in a gradual attenuation of blood supply to the viable epidermis.[6] This overview provides a basis for understanding the effect of skin aging on percutaneous penetration and discusses the individual skin factors and inherent cutaneous metabolism that may be contributing factors. While this is a relatively new and continually evolving area of investigation, we hope that the data consolidated here will serve as a stepping ground for future studies.

Skin Factors Affecting Age-related Percutaneous Penetration

Humans are exposed to drugs by the oral, pulmonary, or percutaneous routes through intentional or accidental means. The route of exposure as well as other factors can have an impact on the absorption of a drug and its resulting effects either locally or systemically. Percutaneous penetration of a drug occurs with its concentration on the skin's surface as the main driving force for a series of partitioning and passive diffusion steps through the stratum corneum, underlying viable epidermis, dermis, and then finally into the circulatory of lymphatic system. Percutaneous penetration may occur through the intercellular, transcellular, and appendegeal routes. The intercellular route is thought to have a major role in drug penetration, which involves partitioning of the drug into the lipid laden extracellular regions of the stratum corneum. Lipophilic drugs diffuse through the lamellar acyl chains of the lipid, while hydrophilic drugs diffuse through the polar head groups of the lipid. The transcellular route involves the drug going through the corneocytes of the stratum corneum and the appendegeal route involves the drug entering the shunts of hair follicles and sebaceous and sweat glands, effectively bypassing the stratum corneum.

Percutaneous absorption of drugs can be affected by drug, exposure, and skin related factors. Drug-related factors include

ALSO IN THIS ISSUE: **Excimer Laser Therapy for Hairline Psoriasis: A Useful Addition to the Scalp Psoriasis Treatment Algorithm** *(page 6)* & **Update on Drugs** *(page 10)*

molecular weight, lipid solubility, water solubility, vehicle, irritancy, and other drugs that may serve as enhancers. Exposure-related factors include drug concentration, duration, use of protective equipment, climate (temperature and humidity), and the matrix (e.g., soil). Skin-related factors include blood flow, pH, skin thickness, hair and pore density, and the content and structure of proteins, glycosaminoglycans (GAGs), water, and lipids (Table 1).[7,8] Cutaneous metabolism also has a role and will be covered in a separate section. The following sections serve as an overview for how some of these skin-related factors change as a function of increasing age. There is limited data available on how these age-related changes may directly or indirectly affect the percutaneous penetration of drugs.

As we review skin-related factors, keep in mind that percutaneous penetration varies depending on the regional site of the body.[9] There is also considerable variability within a given site as well as within and between individuals, which can result in confounding factors.

Cutaneous Blood Perfusion

Cutaneous blood perfusion has been quantitatively studied *in vitro* using histologic sections stained for alkaline phosphatase or the CD31 antigen. The former is inversely correlated with the degree of blood perfusion and the latter is a marker for endothelial cells.[10,11] *In vivo* methods allow for three-dimensional visualization of cutaneous blood flow and include intravital capillaroscopy (native microscopy and fluorescein angiography), laser Doppler flowmetry (LDF), laser Doppler velocimetry, and photoplethysmography. Intravital capillaroscopy measurements of 26 subjects found a decrease in dermal papillary loops and little change in horizontal vessels with increasing age.[10] Kelly and colleagues used LDF and found little difference in blood flow between young (18-26 years) and elderly (65-88 years) subjects; however, there were only 10 subjects in each group.[10] Another LDF study of 201 people (10-89 years) revealed that areas with high blood flow, such as the lip, cushion of the third finger, nasal tip, and forehead, decreased with age while areas with initially low blood flow, such as the trunk, had no clear variation with age.[12] A photoplethysmographic study including 69 individuals (3-99 years) revealed significantly decreased capillary circulation in forehead skin with advancing age.[13] Despite the many tools and techniques available, age studies are often conflicting in the area of blood flow. Overall trends indicate that blood flow may decrease with age, especially in photo-exposed areas. With topically applied drugs, a reduction in blood flow may enhance local delivery, but diminish systemic delivery.

pH

pH contributes to defense against microbiological or drug insults and plays a role in skin barrier homeostasis and stratum corneum desquamation.[14] Instruments using a glass planar electrode are primarily used for pH measurement and they function based on a

Skin Factor	Age-related Changes	Implication for Percutaneous Penetration
Cutaneous blood perfusion	• Studies are conflicting; overall trends indicate that blood flow may decrease	Enhanced local delivery and diminished systemic delivery
pH	• Studies are conflicting, some report an increased pH	Fluctuation in amount of unionized (lipophilic) drug available for percutaneous penetration
Skin thickness	• Stratum corneum maintains thickness; epidermal, dermal, and whole thickness changes are controversial	Not always an inverse relationship with the degree of percutaneous penetration
Hair and pore density	• Reduction in hair follicles • Sebaceous glands increase in size but produce less sebum • Decreased sweat glands	Decreased percutaneous penetration through the shunt route
Proteins	• Intrinsic: collagen is sparser and less soluble, elastin degrades slower and accumulates damage • Extrinsic: collagen is thickened and more soluble, increased synthesis of abnormal elastin • Increased folding and decreased interaction of proteins with water	Increased xerosis, leading to decreased percutaneous penetration
GAGs	• Increased GAGs but abnormally deposited on elastoic material; cannot interact properly with water	Improper deposition may decrease percutaneous penetration
Water	• More water is found in the tetrahedron form, instead of bound to proteins	Increased xerosis, leading to decreased percutaneous penetration
Lipids	• Studies are conflicting; lipid content appears to decrease	Enhanced percutaneous penetration

Table 1: Skin factors affecting age-related percutaneous penetration

potential difference in H+ concentration between the skin surface and the solution (HgCl + KCl) contained in a reference electrode. Fluhr and colleagues measured 44 adults (21-44 years) and 44 of the adults' children (1-6 years) and found no significant difference in pH between the two groups.[15] However, another study involving 11 anatomic locations in 14 adults (26.7 ± 2.8 years) and 15 aged adults (70.5 ± 13.8 years) found pH was significantly higher in the aged group on the ankle and the forehead. Mean pH varied from 4.8 (ankle) to 5.5 (thigh) in the young group and from 5.0 (forehead) to 5.5 (abdomen) in aged individuals.[16]

Most drugs are weak organic acids or bases and exist in unionized and ionized forms in an aqueous environment. The unionized form is usually lipophilic and the ionized form is hydrophilic. The portion of the unionized form present is determined by the pH and the drug's pK_a (acid dissociation constant). When the pH is lower than the pK_a, the unionized form of a weak acid predominates, but the ionized form of a weak base predominates. Thus, the skin's pH can affect the amount of unionized drug available for percutaneous penetration. At present, it is unclear to what degree the skin's pH changes with advancing age and more studies are needed in this area.

Skin Thickness

While the stratum corneum is generally accepted to maintain its thickness during aging,[17] epidermal, dermal, and whole skin thickness changes are controversial. *In vitro* analyses of images taken from light, scanning electron, and transmission electron microscopies have been used to determine the thickness of various skin layers. Recently, confocal laser scanning microscopy (CSLM) has allowed for direct measurement of stratum corneum and epidermal thickness and is considered to be the "gold standard." A CSLM study of 34 subjects (18-69 years) found that the epidermis on the arm thinned with increasing age.[18] However, a study of 71 people (20-68 years) involved punch biopsies from the dorsal forearm, buttock, and shoulder found no significant difference in epidermal thickness associated with increasing age.[19] Hull and colleagues used scanning electron microscopy to reveal that the corrugated papillary interface between the dermis and epidermis is visible up through the sixth decade and flattens thereafter.[20] Flattening may be associated with decreased proliferative potential and could affect percutaneous penetration.

Pulsed ultrasound has also been used for the determination of whole skin thickness. An ultrasound (B-mode) study of 40 subjects (25-90 years) found an increase in facial skin thickness with age.[21] However, another ultrasound study showed thinning of forehead skin with age.[22] Comparing skin layer thickness is challenging because of significant variation in measurements between individuals and between sites within each individual. The skin thickness of the eyelid is approximately 0.05 cm and that of the palm and sole is about 0.4 cm.[23] Note that percutaneous penetration is not exclusively a function of skin thickness. The skin on the sole or palm has a higher rate of diffusion than the skin of the forearm or abdomen, even though it is much thicker. Furthermore, hormonal differences (e.g., estrogen) during the aging process may confound studies of skin thickness.

Hair and Pore Density

Hair follicles and sebaceous and sweat glands represent an important shunt route into the skin for topical drugs. *In vitro* studies have demonstrated the importance of these skin appendages for percutaneous penetration by hydrophilic drugs.[24] The hair follicle infundibulum also has a large storage reservoir capacity, about 10 times more than the stratum corneum.[25] There may be a reduction in the amount of hair follicles with age, not only in the scalp, but also throughout the body. The mechanism for this hair follicle dropout is unclear, though it may be similar to the programmed hair follicle organ deletion that can occur in mice with age.[26] Sebaceous glands continually secrete sebum, which prevents the loss of water from the skin. In the elderly, sebaceous glands increase in size, but produce less sebum, which may contribute to xerosis. The number of sweat glands also decreases with age, but also shows variation between individuals after adjustment for age and sex.[27] All of these appendegeal changes may contribute to decreased percutaneous penetration in aged skin.

Proteins

Collagen comprises 70-80% of the dry weight of the dermis and is primarily responsible for the skin's tensile strength. The rate of collagen synthesis, activity of post-translational enzymes, collagen solubility, thickness of collagen fiber bundles, and density of the collagen network all decrease in intrinsically aged skin.[28-30] However, extrinsically aged skin is characterized by collagen fibers that are fragmented, thickened, and more soluble.[28] The elastic fiber network occupies 2-4% of dermal volume and provides resilience and suppleness. Elastin is degraded slowly and accumulates damage with intrinsic aging; also, increased synthesis of abnormally structured elastin occurs in extrinsically aged skin.[31] This leads to age-related accumulation of aberrant elastoic material, clumped in the papillary dermis. Age also leads to increased folding and decreased interaction of proteins with water, which may contribute to increased xerosis, and thus, decreased percutaneous penetration.[32]

Glycoproteins (GAGs)

Most GAGs are present in human skin as hyaluronic acid and the proteoglycan family of chondroitin sulfates, including dermatan sulfate. Skin hydration is closely linked to the content and distribution of dermal GAGs, which can bind up to 1000 times their volume in water. Despite increased GAGs in extrinsically aged skin, these are abnormally deposited on elastoic material and cannot interact properly with water.[33] Brown and colleagues found that topical hyaluronic acid significantly enhanced the partitioning of both diclofenac and ibuprofen into human skin when compared to an aqueous control, pectin, and carboxymethylcellulose.[34] This suggests that GAGs, when allowed to interact with water, can enhance the percutaneous penetration of some drugs. The details of their interaction remain to be elucidated.

Water

In young skin, water is usually bound to proteins and is known as bound water, which is important for the structure and mechanical properties of proteins and their interactions. Water molecules not bound to proteins bind to each other and are found in a tetrahedron form. In aged skin, significantly more water is found in the tetrahedron form, which may result in delayed percutaneous penetration, especially for hydrophilic drugs.[35] Diridollou and colleagues utilized an active capacitance imaging

system to investigate the hydration of dorsal and ventral forearm sites and, as expected, found skin dryness to increase with age.[36] Interestingly, they found ethnicity to be a significant factor with elderly African American and Caucasian women (>51 years) having increased skin dryness when compared to their Chinese or Mexican counterparts.

Lipids

Lipids form multilamellar sheets among the intercellular spaces of the stratum corneum and are critical to the stratum corneum's mechanical and cohesive properties, allowing it to function as an effective water barrier. Lipid content appears to decrease with age, although the proportion of different lipid classes seems to remain fairly constant.[37,38] A study of 28 subjects (21-50 years) utilized high performance thin layer chromatography to separate lipid extracts from stratum corneum tape strippings and found a 30% decrease in the face, hands, and legs in older subjects.[39] However, Cua and colleagues studied 11 sites on 29 subjects and noted little relation between skin surface lipid content and age, except on the ankle, where the elderly demonstrated decreased lipid content.[40] These conflicting results may be due to significant regional variation within individuals they studied. It is generally accepted that percutaneous penetration is increased as the percentage of lipid weight in the stratum corneum is decreased. Both *in vitro* and *in vivo* studies have demonstrated enhanced percutaneous penetration following delipidization with polar and nontoxic solvents.[41]

Cutaneous Metabolism

The impact of cutaneous metabolism and how it changes as a function of increasing age is an area of growing interest on percutaneous drug delivery. Skin contains the major enzymes found in other tissues of the body. These enzymes have the ability to metabolize both endogenous drugs (e.g., hormones, steroids, and inflammatory mediators) and topically applied exogenous compounds (e.g., drugs, pesticides, and industrial and environmental agents). This cutaneous metabolism may result in activation of inert compounds to toxicologically active species, detoxification of toxicologically active drugs to inactive metabolites, conversion of active drugs to active metabolites, and activation of prodrugs. If transport through the epidermis is the rate limiting step and the metabolite is less hydrophobic than the parent compound, then percutaneous absorption of the metabolized compound could be faster than the parent compound, resulting in enhanced local and/or systemic toxicity. Examples of some drugs and compounds that undergo cutaneous metabolism are betamethasone 17-valerate, propranolol, nitroglycerin, theophylline, polycyclic aromatic hydrocarbons, butachlor, and atrazine.[42]

The skin contains enzymes that undergo Phase 1 (e.g., oxidation, reduction, and hydrolysis) and Phase 2 (e.g., conjugation) reactions. Although the extent of cutaneous metabolism is modest when compared to hepatic metabolism (0.1-28% of the activities in the liver for Phase 1; 0.6-50% for Phase 2), it is important to consider the effect of cutaneous metabolism on percutaneous drug delivery.[43,44]

Sotaniemi and colleagues measured cytochrome P-450 content in liver biopsy samples from 226 subjects and levels were found to be increased during the fourth decade, declined after 40 years to a level that remained unaltered up to 69 years, then declined further after 70 years.[45] Extrapolating this to the skin, one would expect cutaneous metabolism to follow a similar pattern with increasing age. While a study found a 15-25% decrease in the activity of most cutaneous enzymes,[46] other studies have reported no significant differences in relation to age.[47] Yamasawa and colleagues obtained skin biopsies from the abdomen of 63 subjects (1 month to 90 years) and enzyme activity was assayed using fluorometric methods. Fourteen enzymes, representative of the glycolytic pathway, tricarboxylic acid cycle, the transamination linkages between amino acid and carbohydrate metabolism, the pentose phosphate pathway, and fatty acid metabolism were studied. No significant differences in enzyme activity were observed in relation to age.[48]

The effect of cutaneous metabolism on the biological response to topically applied drugs is only beginning to be investigated. Work has been directed towards the use of topical prodrugs and the design of molecules better able to transport across the stratum corneum and then undergo local enzymatic activation. This task is complicated since skin metabolism is difficult to measure *in vivo* without interference from systemic enzymes. In addition, certain cutaneous metabolic systems, such as cytochrome P-450, have relatively low activity when compared with the liver. Further research in this area requires a more specific quantitative understanding of the metabolic capabilities of human skin *in vivo*.

Conclusion

We are currently facing a dramatic demographic shift as the average age of the population steadily increases secondary to the baby boomer generation and advances in medicine allow for longer life expectancy. Consequently, it is crucial that we gain a better understanding of how age-related changes in the skin affect percutaneous drug penetration. Presently, studies focusing on dermatopharmacokinetics as a function of increasing age have conflicting results. If there is in fact a difference in percutaneous penetration between the young and the elderly, potential skin factors that may have a direct or indirect role have been outlined. Furthermore, cutaneous metabolism may provide an additional variable even if a drug is able to successfully navigate the barrier function of the skin. The crux of these evaluations is the assumption that individuals have similar pharmacodynamics, which may not be the case. In the future, metabolic phenotyping may be able to overcome inter-individual variation.

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Excimer Laser Therapy for Hairline Psoriasis: A Useful Addition to the Scalp Psoriasis Treatment Algorithm

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ABSTRACT

Psoriasis is a chronic, inflammatory skin condition with negative impacts both physical and psychological. Scalp psoriasis, especially around the hairline, can cause significant impairment in quality of life due to its visibility. Options for treatment of facial psoriasis, including hairline involvement, are the use of low potency topical steroids, calcineurin inhibitors, and vitamin D analogues. Though the use of excimer laser for scalp psoriasis has been reported, there are no cases or studies specifically examining excimer laser phototherapy for the treatment of hairline psoriasis. We present a case of rapid improvement of hairline psoriasis using a regimen of 308 nm excimer laser with clobetasol spray and recommend an algorithm for the optimal treatment of scalp psoriasis utilizing currently available antipsoriatic therapies.

Key words: topical corticosteroid, excimer laser, phototherapy, scalp psoriasis

Introduction

Psoriasis is an inflammatory skin disease affecting approximately 2.6% of the U.S. population.[1] Psoriasis tends to remain stable throughout the patient's lifetime or become gradually more widespread. It is associated with a high degree of morbidity, as well as having a negative impact on the lives of patients physically, psychologically, socially, and occupationally.[2,3] As it is a chronic condition, psoriasis often requires lifelong treatment.

Patients suffering from psoriasis have relatively high rates of depression and often report stigmatization, embarrassment, and self-consciousness.[4] Plaques along the hairline and retroauricular regions are visible and resistant to therapy. Treatment of scalp psoriasis with laser has been reported, but this modality presents challenges due to the difficulty of penetration of photons through hair.[5] Hence, such a limitation may discourage the use of excimer laser for scalp psoriasis. It must be noted, however, that because the forehead, hairline, and retroauricular areas are not entirely covered by hair, treatment with laser is a clearly viable option.

Targeted ultraviolet B (UVB) excimer laser phototherapy is one of the most cutting-edge advances in phototherapy. The xenon chloride laser produces a 308 nanometer (nm) monochromatic beam of light that is efficacious for the treatment of psoriasis.[6] In contrast to traditional phototherapy, the UVB laser treats targeted areas while sparing the non-involved skin. Psoriatic plaques can tolerate increased dosimetry compared with non-involved skin, and a supra-erythmogenic dose (multiple times above the minimal erythema dose [MED]) can be delivered, resulting in faster clearance than with traditional UVB phototherapy.[6,7] We first present a case of rapid improvement and maintenance of hairline psoriasis treated with 308 nm excimer laser and clobetasol spray, followed by a discussion of current treatment options, and, finally, offer a recommended algorithm for the treatment of scalp psoriasis.

Case

A 68-year old Filipino female presented with a 16-year history of generalized plaque-type psoriasis. She reported that the most distressing region covered with psoriasis was her hairline because it caused severe pruritus and visible disfigurement. The patient failed past treatment on acitretin and topical therapies, including clobetasol ointment, fluocinonide 0.05% solution, calcipotriene ointment, and fluocinolone acetonide 0.01% oil. She had a past medical history of thyroid cancer with a thyroidectomy, stroke, and coronary artery bypass graft. She had no history of sun or other light sensitivity and no history of skin cancer. Her current medications included levothyroxine, metoprolol, warfarin, atorvastatin, and calcium and vitamin D supplements. She was not on any psoriasis therapies at the time of presentation.

On physical examination, there were thick, well-demarcated plaques of psoriasis with silvery scale over the lower and upper extremities bilaterally, back, abdomen, buttocks, scalp, and hairline, including over the forehead, retroauricular, and occipital area.

As the patient had a past history of cancer, she was not placed on immunosuppressive therapy. Topical therapy alone had not been sufficient for treating her psoriasis. Therefore, the patient was started on twice weekly excimer laser therapy (Photomedex XTRAC® Velocity) in conjunction with clobetasol propionate 0.05% (Clobex®) spray twice daily.

The patient was started on a dose of 400 millijoules per square centimeter (mJ/cm^2) for laser therapy, which was increased to 500 mJ/cm^2 following her first treatment. After 2 weeks of therapy, with a total of 4 excimer laser treatments at a dose of 500 mJ/cm^2 and use of clobetasol spray to affected areas, she demonstrated marked improvement in hairline psoriasis. As the patient responded well to treatment without side effects or irritation, her dose was gradually increased to 666 mJ/cm^2. After 5 weeks

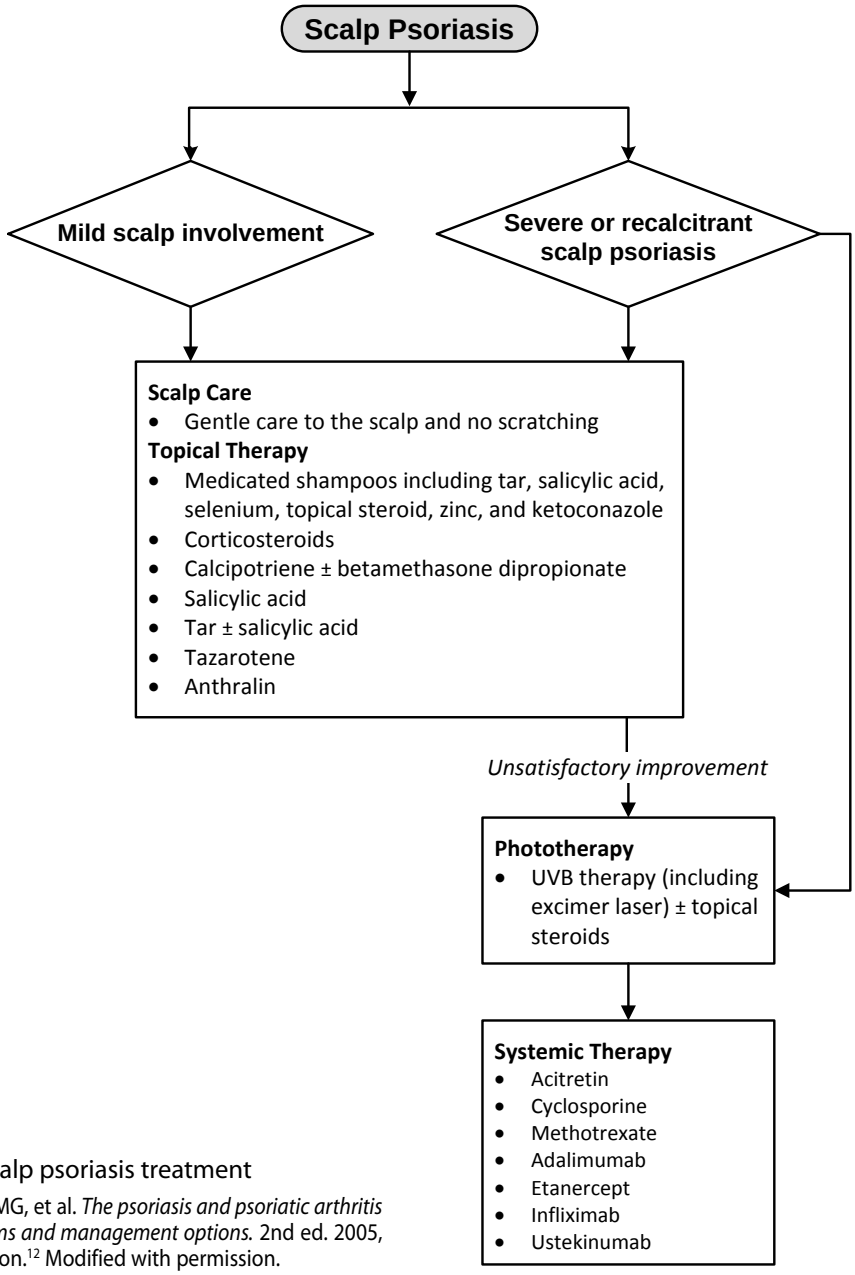

Figure 1 : Algorithm for scalp psoriasis treatment

Feldman SR, Koo JYM, Lebwohl MG, et al. *The psoriasis and psoriatic arthritis pocket guide: treatment algorithms and management options.* 2nd ed. 2005, p.76. National Psoriasis Foundation.[12] Modified with permission.

of therapy (receiving a total of 9 laser treatments and using clobetasol spray twice daily), her hairline psoriasis completely cleared. The patient did not experience any side effects from laser therapy, such as blistering, burning, hyperpigmentation, or erythema. After 3 months without any subsequent therapy, the hairline psoriasis had not returned.

Discussion

Phototherapy can be an effective treatment for generalized plaque psoriasis. However, one major limitation to the aggressiveness of therapy is the MED, which is the lowest dose that causes minimal erythema in non-psoriatic skin.[7] The excimer laser overcomes the barrier of MED, which limits the efficacy of traditional phototherapy. The process by which this is achieved is the excimer laser only irradiates psoriatic plaques that typically require many times more light energy than MED when compared to traditional phototherapy. Thus, the excimer laser provides greater capacity for aggressive therapy, resulting in increased efficacy and significantly reduced number of treatments needed for disease improvement.[7-9]

The medical literature provides a limited number of studies that have been performed for the specific treatment of hairline psoriasis.[10] The Copenhagen Psoriasis Working Group recommended that the first-line treatment of facial psoriasis, including hairline involvement, should be low potency topical corticosteroids, calcineurin inhibitors, and vitamin D3 analogues.[11] However, for general scalp psoriasis, multiple studies have been performed. For mild disease, topical therapies are considered first-line treatments. Topical therapies include gentle care with medicated shampoos, steroids, salicylic acid, tars, calcipotriene/calcipotriol, tazarotene, anthralin, and various combinations of topical agents.[12] In addition, two 52-week studies demonstrated efficacy and safety of calcipotriol/betamethasone

diproprionate gel (Xamiol®, Taclonex® scalp suspension) for scalp psoriasis.[13] More recently, a multicenter, randomized, double-blind study of 81 moderate-to-severe psoriasis patients with scalp involvement evaluated the efficacy and safety of clobetasol spray.[14] Forty-one patients applied clobetasol spray and 40 applied a control vehicle spray twice daily for up to 4 weeks. The study found that 85% (35/41) of the patients using clobetasol spray compared to 13% (5/40) of the control group were assessed as "cleared" or "almost cleared" as measured by the Global Severity Score (GSS).[14]

For severe or recalcitrant scalp psoriasis, systemic therapy is recommended, including acitretin, adalimumab, cyclosporine, etanercept, infliximab, and methotrexate.[12] A recent randomized, placebo-controlled study of 124 patients with stable plaque psoriasis and significant scalp psoriasis evaluated the efficacy and safety of etanercept.[15] Sixty-two patients received etanercept 50 mg twice weekly for 12 weeks, followed by etanercept 50 mg once weekly and placebo once weekly. The remaining 62 patients received placebo twice weekly for 12 weeks, followed by etanercept 50 mg twice weekly for 12 weeks. The study found that etanercept was effective and well-tolerated for scalp psoriasis, showing a statistically significant difference in psoriasis scalp severity index (PSSI) between the experimental and control groups. At week 12, 86% in the experimental group achieved 75% improvement in PSSI in contrast to 11% in the control group.[15]

Despite concern that the efficacy of excimer laser may be limited by hair preventing maximal penetration of photons, two studies have shown improvement of scalp psoriasis with excimer laser. In an open comparative study of 13 patients with scalp psoriasis, patients were treated with a 308 nm excimer laser in conjunction with a hair blower to part the obstructed hair twice weekly for up to 15 weeks.[16] Initial dosage was based on the MED, and subsequent doses were increased by increments of up to 20%. A statistically significant difference in mean decrease in modified Psoriasis Area and Severity Index (PASI) scores between the treated and control sites was found, and scores were 4 and 2.61 respectively.[16] A retrospective study was performed on 35 patients with scalp psoriasis, who were treated by excimer laser using manual separation of the hair to increase exposure of the laser to the scalp.[17] One-half of the scalp was treated, and the other half remained untreated to serve as a control. The results showed that 49% of the patients cleared >95% and 45% of patients cleared 50-95%.[17] However, no studies have examined the use of excimer laser for the specific treatment of hairline psoriasis.

Based on our review of scalp psoriasis treatments and our experience with the excimer laser, we propose an updated algorithm for the treatment of scalp psoriasis, introducing excimer laser as part of the treatment algorithm (Figure 1). For mild scalp psoriasis, the first-line therapy remains topical treatments. However, when psoriasis is resistant to topical therapies or for severe scalp involvement, the combination of excimer laser with topical steroid (i.e., clobetasol spray) could be considered as a viable therapeutic option, as illustrated in our case and in two current studies using excimer laser alone.[16,17] Prior to initiating systemics that carry greater risks to patients, the use of the excimer laser may be an efficacious option for treating recalcitrant plaques along the hairline.

Conclusion

Our case and discussion demonstrates the use of excimer laser in conjunction with topical treatment as an effective and safe method for treating scalp psoriasis. One major limitation of the presented case is that there is a lack of a control arm and, therefore, it is difficult to predict whether the majority of the improvement in psoriasis was attributable to the excimer laser or to clobetasol spray. The clobetasol spray alone may have induced the significant improvements in psoriasis, as the patient had not used clobetasol spray in the past. Furthermore, a study by Sofen et al. showed 85% clearance of psoriasis with clobetasol spray alone.[14] Therefore, the proposed update and addition to the scalp psoriasis treatment algorithm requires more substantiation through a study in which there is a controlled arm, such as comparing the application of clobetasol spray alone to clobetasol spray in conjunction with excimer laser therapy.

Nevertheless, when scalp psoriasis cannot be adequately controlled with topical therapy, the excimer laser can be used effectively to treat hairline plaques, visible lesions that can cause significant psychosocial distress to affected patients. For general scalp psoriasis treatment, clinicians may consider using excimer laser in combination with a topical steroid when topical agents alone do not achieve adequate disease control. This combined therapeutic method may also be considered prior to initiating systemic therapy for severe or intractable cases. Further studies should be performed to establish the safety and efficacy of excimer laser in the treatment of hairline psoriasis. In the future, this novel approach has the potential to become more widely used in clinical dermatology practices.

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Update on Drugs

Name/Company	Approval Dates/Comments
Adapalene 0.3% gel *Differin*® Galderma Laboratories	The US FDA approved a pump dispenser in March 2012 for this retinoid gel formulation for the topical treatment of acne vulgaris in patients 12 years of age or older. A survey study reported that patients found the pump dispenser to be more convenient and easier to use compared with the tube. More than 90% of surveyed patients found the pump to deliver a consistent amount of the gel for application and saved time during treatment application.
Vemurafenib tablet *Zelboraf*® Hoffmann-La Roche Limited	Health Canada approved this oral, small molecule, protein kinase inhibitor in March 2012 for the treatment of adult patients with BRAFV600 mutation-positive unresectable or metastatic melanoma. This BRAF enzyme inhibitor was approved with a companion diagnostic called the cobas® 4800 BRAF V600 Mutation Test, which determines a patient's eligibility for treatment.
Wound care spray *Granulox*® SastoMed GmbH Sangui BioTech	The European Commission granted CE Mark of approval (as a class III medical product) in April 2012 to this hemoglobin spray (also known as HEMO2SPRAY®) for improving the healing of chronic wounds by increasing oxygen supply.

Device News

Laser device for onychomycosis *Harmony® XL* Alma Lasers, Inc.	US FDA clearance was granted to this aesthetic laser device for the treatment of onychomycosis in March 2012. This dual wavelength system utilizes two distinct Q-switched laser technologies, neodymium:yttrium-aluminum-garnet (Nd:YAG) 1064 nm with its potassium titanyl phosphate (KTP) 532 nm tip, to create microcavitations and acoustic shock waves on the surface of the nail plate that are transmitted to the nail bed, causing mechanical damage to the irradiated fungal colony and inducing decapsulation of spores. The green light emitted by the Q-switched KTP 532 nm laser is selectively absorbed by red and brown pigments of the fungal infection, whereas the Nd:YAG 1064 nm laser causes non-specific heat conduction on the entire nail, which induces thermal destruction of the microorganisms.

Drug News

On April 11, 2012, the US FDA announced changes to the labels for finasteride 1 mg (Propecia®) and finasteride 5 mg (Proscar®) to include a wider list of reported sexual adverse events. Such events have been reported to persist after discontinuation of therapy. In 2011, the labels of both finasteride 5 mg and 1 mg formulations were amended to include erectile dysfunction. Proscar® is used to treat benign prostatic hyperplasia, while Propecia® is indicated for treating androgenic alopecia in men, and is also used off-label for hirsutism in women. Revised labelling changes include:

- The Propecia® label will include libido, ejaculation, and orgasm disorders that persist after treatment ends.
- The Proscar® label will include decreased libido that persists post-treatment.
- Both labels will note reports of male infertility or poor semen quality that improved after drug discontinuation.

The FDA states that although "clear causal links between finasteride and sexual adverse events have NOT been established, the cases suggest a broader range of adverse effects than previously reported in patients taking these drugs." Controlled studies showed that a small percentage of men using Propecia® 36 (3.8%) of 945 had reported one or more adverse sexual experiences vs. 20 (2.1%) of 934 on placebo. The FDA recommends that healthcare professionals and patients should consider this new label information when making treatment decisions. More information is available at: http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm299754.htm