Evaluation of the clinical efficacy and safety of “Anti-Dandruff Shampoo” in the treatment of dandruff

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The Antiseptic 2004; 201(1), 5-8
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ABSTRACT
Dandruff (Pityriasis simplex) is a common embarrassing scalp disorder, affecting a large chunk of population. The yeast, Pityrosporum ovale is the causative microorganism of dandruff and due to its lipase activity it releases proinflammatory free fatty acids, causing dermal inflammation and tissue damage. Currently available treatment options have various limitations, either due to poor clinical efficacy or due to the compliance issues. Also, these drugs are unable to prevent recurrence, which is the commonest problem. This study was planned to evaluate the clinical efficacy and safety of “Anti-Dandruff Shampoo” in the management of dandruff.

This study was a prospective, open, non-comparative, phase III clinical trial and was approved by the Institutional Ethics Committee. A total of 35 patients, who were diagnosed as suffering from dandruff, and who were willing to give informed written consent were included in the study. A baseline history was obtained and the baseline assessment included personal data, a description of symptoms and details of past medical history. All the patients were advised to apply the “Anti-Dandruff Shampoo”, twice a week for a period of 6 weeks. The predefined primary efficacy endpoints were reduction in dandruff lesions, reduction in overall scalp inflammation and healing of existing lesions. The predefined secondary safety endpoints measures were incidence of adverse events and overall patient compliance to the drug treatment. All the adverse events either reported or observed by the patients were recorded with information about severity, date of onset, duration and action taken regarding the study drug. Patients were allowed to voluntarily withdraw from the study if they experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment.

This study observed a significant reduction in the mean scores of itching and white scales of dandruff. The subjective evaluation revealed remarkable symptomatic and clinical improvement in 2 weeks period. The excellent antidandruff action of “Anti-Dandruff Shampoo” might have been due to the synergistic antifungal, anti-inflammatory and local immunostimulatory actions of its ingredients. Therefore, it may be concluded that, “Anti-Dandruff Shampoo” is effective and safe in the management of dandruff.
INTRODUCTION
Dandruff (also referred as “Pityriasis simplex”) is a common embarrassing disorder, which affects 5% of the global population. Dandruff mostly occurs after puberty (between ages of 20 and 30 years), and affects males more than females.

Dandruff is characterized by scaling of the scalp, and is frequently associated with seborrhea, and seborrhea is the precursor of seborrheic dermatitis. The yeast, *Pityrosporum ovale* is the causative microorganism of dandruff. *Pityrosporum ovale* feed on the dermal lipids and proteins and facilitates lipase activity, which releases proinflammatory free fatty acids (FFAs) causing dermal inflammation and tissue damage. The lipase activity indicates that in addition to hypersensitivity, *Pityrosporum ovale* releases toxic chemicals, which contribute to the development of a fungal infection.

Currently available treatment options for the management of dandruff include therapeutic use of zinc pyrithione, salicylic acid, imidazole derivatives, glycolic acid, steroids, sulphur and tar derivatives. However, these agents have certain limitations, either due to poor clinical efficacy or due to the compliance issues. Furthermore, these drugs are unable to prevent recurrence, which is the commonest problem.

“Anti-Dandruff Shampoo” is a polyherbal formulation recommended for the treatment of dandruff and contains the extracts of *Rosmarinus officinalis, Vetiveria zizanioides, Nigella sativa, Santalum album, Ficus bengalensis, Citrus limon* and oil of *Melaleuca leucodendron*. This study was planned to evaluate the clinical efficacy and safety of “Anti-Dandruff Shampoo” in the management of dandruff.

Aim of the study
This study was planned to evaluate the clinical efficacy and safety (short- and long-term) of “Anti-Dandruff Shampoo” in the management of dandruff.

Study design
This study was a prospective, open, non-comparative, phase III clinical trial, conducted at the Department of Dermatology at The Apollo Hospitals, Chennai, India, as per the ethical guidelines of Declaration of Helsinki, from June to September 2004. The study protocol, CRFs, regulatory clearance documents, product related information and informed consent forms (in Tamil and English) were submitted to the “Institutional Ethics Committee” and were approved by the same.

MATERIALS AND METHODS
Inclusion criteria
A total of 35 patients, who were diagnosed as suffering from moderate to severe form of dandruff, and who were willing to give informed written consent were included in the study.

Exclusion criteria
Patients with concomitant severe scalp infection, history of hypersensitivity to shampoos/cosmetics, children below eighteen years of age, patients with preexisting severe systemic disease necessitating long-term medication, patients with genetic and endocrinal disorders, and those patients who refused to give informed written consent were excluded from the study. Pregnant and lactating women were also excluded from the study.
**Study procedure**
A baseline history was obtained in order to determine the patient’s eligibility for enrolment in the trial. The baseline assessment included personal data, a description of symptoms and details of past medical history (family history of dandruff and history of possible exacerbating factor/s). All the patients were advised to apply the “Anti-Dandruff Shampoo”, twice a week for a period of 6 weeks. All the patients were asked to adhere to “Anti-Dandruff Shampoo” only as the treatment for dandruff, and no other medicated topical application was allowed.

**Follow-up and monitoring**
All the patients were followed up for a period of 6 weeks and at each weekly follow-up visit, scalp skin examination was done to assess the improvement in the dandruff lesions. At the end of the 6th week, the overall performance of the “Anti-Dandruff Shampoo” was evaluated.

**Primary and secondary end points**
The predefined primary efficacy endpoints were reduction in dandruff lesions, reduction in overall scalp inflammation and healing of existing scalp lesions. The predefined secondary safety endpoint measures were incidence of adverse events and overall patient compliance to the treatment.

**Adverse events**
All the adverse events, either reported by patients or observed by investigators were recorded in the case record forms, with information about severity, date of onset, duration and action taken regarding the study drug. Relation of adverse events to the study medication were predefined as “Unrelated” (a reaction that does not follow a reasonable temporal sequence from the time of administration of the drug), “Possible” (follows a known response pattern to the suspected drug, but could have been produced by the patient’s clinical state or other modes of therapy administered to the patient), and “Probable” (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient’s clinical state).

Patients were allowed to voluntarily withdraw from the study if they experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. Non-compliance was not regarded as treatment failure and reasons for non-compliance were noted.

**RESULTS**
A total of 22 males and 13 females were enrolled in the study. There was a remarkable decrease in the scaling and itching of scalp after a week’s treatment. Subsequently, there was remarkable improvement in the healing of the dandruff lesions from the second week onwards, and the after 4th week, there was complete control of dandruff in all the patients.
At the end of the 6th week, 21 patients (60%) graded the “Anti-Dandruff Shampoo” a “good”, 9 subjects (26%) graded the “Anti-Dandruff Shampoo” as “very good”, and 5 subjects (14%) graded the “Anti-Dandruff Shampoo” as “excellent” (Figure).

There were no clinically significant adverse reactions (either reported by patients or observed by the investigators) during the entire study period. There were no dropouts and the overall compliance to the drug treatment was excellent.

**DISCUSSION**

A person's entire body surface continuously sheds dead skin cells and the skin itself sheds every twenty-four days. Dandruff, the shedding of dead skin cells from the scalp at an excessive rate, is the result of the normal growing process of the skin cells of the scalp.

Dandruff may be caused by several different factors, but the exact underlying cause of dandruff is unknown (at least not agreed upon by the medical fraternity). Dandruff is the visible desquamation of scalp, is the mildest manifestation of seborrheic dermatitis. Dandruff usually is a result of *Pityrosporum ovale* infection combined with multiple host factors. Pityrosporum organisms are linked to T-cell depression, increased sebum levels and an activation of the alternative complement pathway. The age of onset of dandruff also suggests an androgenic influence, as dandruff correlates with peak sebaceous activity. Dandruff can be seasonal, in which it is most severe during winter and mildest during summer (as ultraviolet rays from sunlight counteracts *Pityrosporum ovale*). Poor diet, poor hygiene, genetic disposition, hormonal imbalances and infections contribute to dandruff. Excessive use of hairsprays and hair gels, improper use of hair-coloring products, excessive use of electric hair curlers, dry indoor heating, tight fitting headgears or scarves, infrequent shampooing of the hair, inadequate rinsing of hair, stress, anxiety and tension worsen dandruff.

The most common symptom of dandruff is scalp scaling, and itching with scalp soreness is frequently present. Dandruff scales usually occur as small, round, white-to-gray patches on the top of the head; however, scaling can occur anywhere on the scalp. Clinically, the greyish white flakes of skin are often visible on the hair and shoulders. Unsightly flakes or scales are typically present on the scalp and trapped in the hair. Whether or not these flakes are "oily" or "dry" may provide hints about the underlying cause of the dandruff.

The severity of dandruff varies from mild dandruff to exfoliative erythroderma. Seborrheic eczema is a more severe form of dandruff, which affects the skin around the eyebrows, nose, ears, face and forehead, and the typical scales are yellowish greasy with inflamed skin. The differential diagnosis of dandruff include eczema, atopic dermatitis, candidiasis, contact dermatitis, dermatomyositis, drug eruptions, drug-induced photosensitivity, impetigo, lichen simplex, chronicus lupus erythematosus, nummular dermatitis, pemphigus, pityriasis rosea, tinea capitis, xerotic eczema, and vitamin B and/or zinc deficiency.

The aim of dandruff treatment is to reduce the number of the *Pityrosporum ovale* on the scalp, and the goals of therapy are to reduce morbidity and prevent complications. Dandruff is a natural process, which cannot be eliminated and dandruff can only be managed and controlled. A variety of topical formulations with antipityrosporal activity are available for treating dandruff. Mild dandruff is controlled by regularly shampooing the scalp with a mild, non-medicated shampoo, but when frequent shampooing alone does not control the dandruff, a medicated dandruff shampoo is needed. Common ways to control dandruff is to use agents like imidazoles, selenium sulphide, coal tar and salicylic acid (either alone or in
These shampoos work by slowing down cell turnover and may reduce the number of malassezia (yeast infection of the skin). However, these shampoos have to be used for a long period (usually for few months) and leave scalp skin dry (which leads to frequent scalp irritation), and are also known to discolor light colored hair. Thus, with the available therapies, the problem of complete symptomatic control and clinical cure are not addressed and dandruff usually recurs on stopping these treatments.

This study observed a significant reduction in scalp itching, inflamed scalp and white scales of dandruff. The subjective evaluation also revealed remarkable symptomatic improvement in 2 weeks period and by the 4th week, dandruff was completely controlled. The excellent antidandruff action of “Anti-Dandruff Shampoo” might have been due to the synergistic antifungal, anti-inflammatory and local immunostimulatory actions of its ingredients, which has been well documented by various research workers.

The principle ingredients of *Rosmarinus officinalis* are caffeic acid, phenolic diterpenes (carnosic acid, carnosol and 12-O-methylcarnosic acid), caffeoyl derivatives (rosmarinic acid), and flavones (isoscutellarein 7-O-glucoside and genkwanin). The extract of *Rosmarinus officinalis* has been shown to have potent antioxidant activity, in both aqueous and lipid systems. The principle ingredients of *Vetiveria zizanioides* are valencene, 9-octadecenamide, 2,6,10,15,19,23-hexamethyl-2,6,10,14,18,22-tetracosahexaene, 1,2-benzendicarboxylic acid, di-isooctylester and terpenoids (monoterpenes, sequiterpenes and triterpenes).

*Citrus limon* contains sugars (glucose, fructose, and sucrose), polysaccharides, organic acids, myoinositol, carotenoids, vitamins, flavonoids, limonoids (limonin and nomilin), volatile oil, alpha-terpinene, alpha-pinene, coumarins, mucilage, pectins and bioflavonoids (eriocitrin and hesperidan). *Citrus limon* has strong antioxidant, antibacterial and antifungal effects. Chapel et al. observed clinical benefits of *Citrus limon* in Athlete’s foot, while Alderman et al. documented the antiaspergillus effect of *Citrus limon*. *Citrus limon* is also effective as a natural biocide.

The extract of *Nigella sativa* contains both fixed and essential oils, proteins, alkaloids and saponins; and the biological activity of *Nigella sativa* has been attributed to thymoquinone. *Nigella sativa* has anti-inflammatory, analgesic and antimicrobial activity. Scartezzini et al. and Jagetia et al. documented antioxidant and nitric oxide scavenging activity of *Santalum album*.

Nenoff et al. reported antidandruff activity of *Melaleuca leucodendron*. The antifungal activity of *Melaleuca alternifolia* has also been evaluated against common strains of dermatophytes, yeasts, *Candida albicans*, other Candida species and *Malassezia furfur*. *Melaleuca alternifolia* helps control dermal fungal infections, which are frequently associated with dandruff. The principle ingredients of *Ficus bengalensis* are ketones (tetraatriacontene, 6-heptatriacontene, pentatriacontan, beta-sitosterol-alpha-D-glucose and meso-inositol. *Ficus bengalensis* contributes to the antioxidant potential of the other ingredients.

**CONCLUSION**

Dandruff (“*Pityriasis simplex*”) is a common embarrassing disorder, affecting a large chunk of population. The yeast, *Pityrosporum ovale* is the contributing organism of dandruff and its lipase activity releases proinflammatory free fatty acids, causing dermal inflammation and tissue damage. Currently available treatment options have certain limitations, either due to poor efficacies or due to the compliance issues and these drugs are unable to prevent
recurrence, which is the commonest problem. This study was planned to evaluate the clinical efficacy and safety of “Anti-Dandruff Shampoo” in the management of dandruff.

This study observed a significant reduction in the mean scores of itching and white scales of dandruff. The subjective evaluation revealed a remarkable symptomatic and clinical improvement in two weeks period. The excellent antidandruff action of “Anti-Dandruff Shampoo” might have been due to the synergistic antifungal, anti-inflammatory and local immunostimulatory actions of its ingredients. Therefore, it may be concluded that, “Anti-Dandruff Shampoo” is effective and safe in the management of dandruff.

ACKNOWLEDGEMENT
We are thankful to Dr. Rangesh Paramesh M.D(Ay) for the kind help offered for this project.

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