ORIGINAL PAPER

‘Emollients plus’ with *Vitreoscilla filiformis* in monotherapy and adjunctive therapy in skin diseases in children

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ABSTRACT

Introduction: Emollients are topical preparations, the role of which is to maintain or restore epidermal barrier function, proper hydration, and elasticity of the skin. In recent years, a special range of ‘emollients plus’ enriched with additional active substances has been developed.

Objective: To evaluate the effectiveness of emollient preparations with Vitreoscilla filiformis in patients up to 18 years old with skin diseases that present with dryness.

Material and methods: From October 2022 to January 2023, an observational study was conducted in Poland. A total of 386 children were recruited for the study, primarily suffering from AD (85.2%) and other skin diseases associated with dryness (23.6%).

Results: After 4 weeks of regular usage of emollient products containing Vitreoscilla filiformis in the form of syndet and balm, the severity of the skin disease, dryness, and the surface area of inflammatory changes decreased in 81.8%, 88.0%, and 70.7% of children, respectively. Furthermore, the patient’s overall quality of life associated with experiencing symptoms of skin disease significantly improved across all three factors evaluated; reduction in pruritus and severity of daily discomfort were declared by 81.4% and 80.7% of children, respectively. Sleep quality improved in 65.7% of children. An improvement was also observed among patients who solely used the emollient products with Vitreoscilla filiformis without any prescription (RX) treatment.

Conclusions: The results indicate that emollient preparations with Vitreoscilla filiformis are effective and well-tolerated by patients with skin diseases that present with dryness. They can be used as monotherapy or as an adjunctive therapy.

Key words: emollients, skin barrier, Vitreoscilla.

INTRODUCTION

One of the most common childhood skin diseases is atopic dermatitis (AD), which affects about 20% of children worldwide [1]. According to the ECAP (*Epidemiologia Chorób Alergicznych w Polsce*) study data, 3.91% of children suffer from AD in Poland (6–7 years old: 5.34%, 13–14 years old: 4.3%) [2]. The disease is manifested by characteristic skin changes with the morphology of eczema, located in typical areas often visible to others. It is chronic, with periods of exacerbation and remission, and is accompanied by persistent pruritus and sleep disturbances. AD significantly reduces the quality of life of patients and their fami-

lies. The skin barrier defect, which consists of abnormalities in the stratum corneum lipids, the cornified envelope proteins, tight junctions, and a deficiency of antimicrobial peptides (AMPs), is considered a strategic point for the development of AD [3]. It is responsible for dry skin, increased transepidermal water loss (TEWL), facilitated penetration of allergens and external factors, impaired skin defense response, and disrupted microbiological balance of the skin [3]. The defect of the skin barrier and dry skin are closely related to the patient's perceived pruritus of the skin.

Dry skin also accompanies many other skin conditions such as psoriasis, ichthyosis, and contact dermatitis, but it can also occur as a separate skin condition [4]. Depending on the degree of dryness, dry skin can be clinically marked by flaking, cracking, roughness, dullness, thickening, and redness. Subjective symptoms, in addition to the aforementioned pruritus, also include burning, tingling, and in extreme situations, even pain. Furthermore, dry skin is characterized by decreased elasticity, making it more susceptible to micro-injuries and infection development [5]. It is the result of the interplay between various epigenetic, genetic, environmental, inflammatory, and barrier defect factors, including deficiency of the natural moisturizing factor (NMF), and increased TEWL [4]. The breakdown products of filaggrin (FLG) produced in the stratum corneum form a part of the NMF and are essential for appropriate skin hydration and maintaining its proper pH [6]. Mutations in the gene encoding the structural protein filaggrin, which is attributed to a particular role in the pathogenesis of AD, are also associated with the development of ichthyosis, where the skin is persistently dry due to the abnormal formation and scaling of the epidermis [4]. The abnormal differentiation of keratinocytes and changes in the skin lipids, particularly ceramides, explain the symptoms of dry skin in psoriasis as well [7].

Emollients are topical preparations, the role of which is to maintain or restore proper hydration and elasticity of the skin. They contain occlusive substances such as petroleum jelly, paraffin, or mineral oils, which create a protective layer on the skin, providing protection against adverse external factors and reducing TEWL. Besides occlusive substances, they also contain humectants (e.g. glycerin, urea, sorbitol), which are strong moisturizing ingredients, as well as substances that seal the skin barrier – ceramides, cholesterol, or fatty acids [8–11].

Appropriate emollient therapy, which fills the deficit of essential ingredients building the skin barrier and thus supports its effective regeneration, is applied in many skin diseases, especially those accompanied by dryness and defects in the skin barrier. In the therapy of AD, emollients are fundamental. They are used not only in monotherapy but also in adjunctive therapy for local anti-inflammatory treatment or general treatment [8–11].

A growing understanding of the role of the skin barrier has contributed to the improvement of local moisturizing agents, for example by enriching their composition with certain substances. In recent years, a special range of 'emollients plus' enriched with additional active plant-based substances, such as flavonoids, saponins, non-protein oat extracts, or bacterial lysates from *Vitreoscilla filiformis*, has been developed [8–11]. Thanks to the presence of these ingredients, 'emollients plus' have a multifaceted effect. In addition to helping the reconstruction of the skin barrier, they exert a kind of anti-inflammatory effects by inhibiting some pro-inflammatory cytokines and chemokines, have an anti-pruritic effect, and also support innate immunity by activating toll-like receptors and natural antimicrobial peptides. Additionally, they help to restore the homeostasis of the disrupted skin microbiota [8–11], which appears to play a crucial role in maintaining the function of the skin barrier [12]. Although emollients have a well-established position in the treatment of AD, there is still a lack of studies evaluating their effectiveness in the treatment of other dermatoses that also present with skin dryness.

OBJECTIVE

From October 2022 to January 2023, an observational study was conducted in Poland to evaluate the effectiveness of emollient preparations with *Vitreoscilla filiformis* in patients up to 18 years old with skin diseases that present with dryness. To date, according to our knowledge, no similar studies have been conducted in Poland, making this the first study of its kind involving Polish children.

MATERIAL AND METHODS

A total of 386 children were recruited for the study, primarily suffering from AD (85.2%) and other skin diseases associated with dryness (23.6%). The group of enrolled patients included 216 (56.0%) girls and 168 (43.5%) boys; 2 (0.5%) individuals did not specify their gender. Infants (up to 12 months of age) and toddlers (1–3 years of age) were the dominant age group, accounting for 24.9% and 32.9% of all subjects, respectively. Meanwhile, the percentage of children in preschool age (4–6 years old) and school age (7–18 years old) was 21.5% and 18.7%, respectively. Eight individuals (2.1%) did not provide their age.

The physician assessed the patients with the help of a questionnaire, which was filled out during the initial visit and then again after 4 weeks of using

emollient preparations with *Vitreoscilla filiformis* in the form of syndet and balm during the follow-up visit. The severity of the disease, skin dryness, the percentage of skin area affected by inflammatory lesions, pruritus, sleep quality, and the intensity of daily discomfort were taken into account during the assessment.

A non-parametric test for two dependent samples, the Wilcoxon signed-rank test, was used to determine the differences between the groups.

RESULTS

The skin condition of patients at the initial visit

The severity of the skin disease in children participating in the study was most commonly assessed as moderate (56.2%) or mild (29.3%) at the initial visit. Meanwhile, a severe or very severe skin disorder was diagnosed in 14.2% of children.

Regarding skin dryness, the predominant group of children presented with moderate (57.9%) or mild (25.6%). The percentage of children experiencing severe or very severe skin dryness was 14.8%.

Inflammatory lesions in the majority of children (71.1%) covered up to 30% of the skin surface. More than 30% of the skin surface was affected in 16.3% of children. The remaining ones (12.6%) did not present any signs of inflammation on the skin.

The comfort of life of patients at the initial visit

At the initial visit, mild and moderate pruritus was indicated by 37% and 40.4% of subjects, respectively. Moreover, 14.3% of children complained of severe or very severe pruritus. Only 8.3% of children reported no pruritus.

While the skin disease most often had a mild (33.7%) or moderate (25.8%) impact on sleep quality in children, it had a strong or very strong effect in 13.6% of children. The disease did not interfere with sleep in the remaining 26.9% of subjects.

In 40.8% of children, the skin condition was a cause of mild discomfort in daily life, and in 36.6% it was moderate. Severe or very severe discomfort was experienced by 12.9% of children. A small proportion of patients (9.7%) did not show disturbed comfort in daily life caused by skin disease.

The skin condition of patients at the follow-up visit

After 4 weeks of using regularly emollient preparations with *Vitreoscilla filiformis* in the form of syndet and balm, the skin condition of the patients was significantly improved regarding each of the examined factors (exacerbation of skin disease, skin dryness, inflammatory lesions) ($p < 0.005$).

After 4 weeks, the severity of the skin disease decreased in 81.8% of children; 34.2% of children did not show symptoms of the disease, 53.9% had mild symptoms, and 11.0% had moderate symptoms. Severe symptoms were present in only 0.9% of children.

After 4 weeks, skin dryness decreased in 88.0% of children. Only 0.6% had severe or very severe skin dryness. The remaining percentage of children mostly had mild (46.2%) or absent (46.8%) skin dryness, and 6.4% of children showed moderate skin dryness.

After 4 weeks, the surface area of inflammatory changes was reduced in 70.7% of children. More than half of the children (52.1%) had no inflammatory lesions present, and in 35.2% of children, the inflammatory lesions covered < 10% of the skin surface.

The comfort of life of patients at the follow-up visit

After 4 weeks of using emollient preparations with *Vitreoscilla filiformis* in the form of syndet and balm, the quality of life of patients associated with symptoms of skin disease significantly improved for all three evaluated factors (pruritus, sleep quality, and severity of daily discomfort) ($p < 0.005$).

After 4 weeks, a reduction in pruritus was declared by 81.4% of children. More than half of the children (62.8%) reported no pruritus during the visit, and 31.2% assessed the itching as mild. The remaining 6% of children mostly reported moderate pruritus.

After 4 weeks, sleep quality improved in over half of the children (65.7%). The disease did not interfere with sleep quality in 76.2% of the children. For the remaining children, the disease had a mild (18.7%) or moderate (4.8%) impact on sleep quality.

After 4 weeks, the severity of daily discomfort decreased in 80.7% of the children. For a vast majority of children (69.5%), the disease did not interfere with the daily comfort of life or had a mild impact (23.7%). In the case of the remaining percentage of children (6.8%), the disease mostly caused moderate discomfort in daily life.

Other preparations/medications used by patients during the study (RX)

During the initial visit, one-third of the children (32.6%) received recommendations for using medications and preparations other than emollients with *Vitreoscilla filiformis* in the form of syndet and balm. Among this group of patients, the most common were antihistamines (31.7%) and glucocorticoids (GCs) (27.0%). The remaining patients were recommended to use, among others, skincare products (18.3%) and calcineurin inhibitors (17.5%). Regarding antihistamines, it is worth noting that there is insufficient evidence for their widespread use in treating pruritus in AD. These medications can be used if

standard therapy with topical GCs and emollients is insufficient [8–11].

The group of patients who used only emollient preparations with Vitreoscilla filiformis in the form of a syndet and balm (without RX)

Also in the group of patients who used only emollient preparations with *Vitreoscilla filiformis* in the form of syndet and balm (without RX treatment), a statistically significant improvement was observed after 4 weeks for each of the examined factors (skin disease severity, skin dryness, inflammatory lesions, pruritus, sleep quality, daily discomfort) ($p < 0.005$). The severity of the disease decreased in 82.6% of the children. Reduction in skin dryness and inflammatory lesions were presented by 88.8% and 68.9% of the children, respectively. 80.5% of the children reported a decrease in pruritus, and 79.1% showed a reduction in daily discomfort caused by the disease. As for sleep quality, the percentage of patients who showed improvement was 62.5%.

The vast majority of patients (89%) followed the doctor's recommendations and did not change their treatment during the 4-week study period. 93.6% of the children used emollient preparations with *Vitreoscilla filiformis* every day. The products had a very good tolerance profile. Adverse effects occurred only in a small percentage of the children (3.4%), and it was most commonly a burning sensation after applying the preparation to the area affected by inflammation.

The obtained results indicate the effectiveness and good tolerance of using emollient preparations with *Vitreoscilla filiformis* in the form of syndet and balm in a group of children suffering from AD or other skin diseases associated with dryness.

DISCUSSION

The tested products are emollient preparations 'plus' enriched with patented active ingredients: Aqua Posae Filiformis and Microresyl. The former is produced through the cultivation of the bacterium *Vitreoscilla filiformis* in La Roche-Posay thermal water [13]. *Vitreoscilla filiformis* is a filamentous microorganism naturally occurring in sodium-rich spa waters, which are known for their beneficial effects on the skin [13, 14]. Numerous studies, including randomized controlled trials (RCTs), have demonstrated its anti-inflammatory, anti-pruritic, and skin barrier-restoring effects. It has been shown that *Vitreoscilla filiformis* lysate significantly reduces the severity of AD measured by the SCORAD scale, as well as skin pruritus, thereby improving the quality of sleep. Furthermore, it reduces TEWL and skin colonization by *Staphylococcus aureus,* and has a stimulating effect on the expression of antimicrobial peptides [13–17]. Volz *et al.* obtained interesting results as they have shown that the lysate of *Vitreoscilla filiformis* reduces skin inflammation by activating toll-like receptor 2 (TLR2) on the surface of dendritic cells, which results in the stimulation of these cells to produce immunosuppressive IL-10 [18]. The inhibitory effect of this bacterial lysate on the expression of thymic stromal lymphopoietin receptor (TSLP) and interleukin 31 receptor (IL-31), as well as these cytokines, has also been demonstrated, which may explain the anti-pruritic effect of *Vitreoscilla filiformis* lysate [19]. In addition, in vitro studies have shown that *Vitreoscilla filiformis* lysate induces keratinocyte proliferation, thereby intensifying the restoration of the stratum corneum, and induces the expression of type I and IV collagen [19]. The action of Aqua Posae Filiformis results from the combination of the immunomodulatory properties of *Vitreoscilla filiformis* lysate and the La Roche-Posay thermal water, which contains selenium and strontium that also have anti-pruritic and anti-inflammatory effects [14]. Microresyl is a naturally derived extract from the root of *ophiopogon japonicus*. This extract contains antibacterial compounds that prevent the growth of pathogenic microorganisms and also limit the formation of bacterial biofilm [20]. All these properties put the Aqua Posae Filiformis + Microresyl complex in a positive light. Moreover, the results of this study conducted on a Polish group of children indicate the possibility of effectively applying this substance complex in emollient preparations used both in monotherapy and adjunctive therapy in many skin diseases that involve a defect in the skin barrier.

In the current study, most of the children had a moderate or mild course of the disease, and most of them used the tested emollient preparations in monotherapy. However, the results of the study conducted by Magnolo *et al.* also highlight the positive significance of 'emollients plus' in adjunctive therapy in patients with severe AD requiring systemic treatment. In this randomized controlled trial, the additional use of an emollient preparation 'plus' containing the same substance complex as in the current study significantly improved the effects of AD treatment in patients receiving systemic therapy compared to control emollients. The 'emollient plus' more effectively relieved pruritus and thus improved the quality of life among patients using it [21].

In practice, regular emollient therapy is also a therapeutic challenge. A key element of proper emollient therapy is broad patient education in this area.

Regular emollient therapy alleviates clinical symptoms of AD in both children and adults, prevents disease exacerbations, and prolongs the remission period

between disease exacerbations [8–11]. In addition, emollients exhibit the steroid-sparing effect. It has been shown that they decreased the amount of potent topical GCs required to achieve remission of inflammatory lesions in up to 42% of patients with AD who regularly use emollients, compared to patients not using these preparations. Additionally, emollients increase the safety of using potent topical GCs in the treatment of AD exacerbations, as they reduce their adverse effects [22]. In accordance with the current recommendations, using emollients at least twice a day in the amount of a minimum of 200 g/week in small children and 500 g/week in adults is recommended [8–11].

Emollients have the most established position in the therapy of AD. However, they also have a positive impact on other diseases that involve a skin barrier defect, manifested by dry skin. When used additionally in the therapy of psoriasis, they reduce the severity of scaling and pruritus [23]. Moreover, they are an important element in the treatment of contact dermatitis. They reduce pruritus, relieve inflammation, support the regeneration of the impaired skin barrier, and prevent disease relapse [24]. Regular use of emollients is also recommended to improve skin hydration in ichthyosis, and thus alleviates its symptoms [25].

CONCLUSIONS

'Emollients plus' with *Vitreoscilla filiformis* are applied with clinical effect in the monotherapy of AD and other dermatological diseases that involve dry skin, as well as in adjunctive therapy, as indicated by the above-mentioned research results.

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CONFLICT OF INTEREST

MT has been a speaker and/or consultant and/or investigator and/or participant of the Advisory Board for Abbvie, Bausch Health, Bioderma, Eli Lilly, La Roche-Posay, Leo pharma, Mead Johnson, Novartis, Pfizer, Pierre Fabre, Pfizer, Sanofi Genzyme.

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