MICRO LABS LIMITED

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Greetings from Micro Labs. We are happy to bring you "Derma Today" which contains latest and interesting news in the field of Dermatology.

This issue contains:

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Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited.

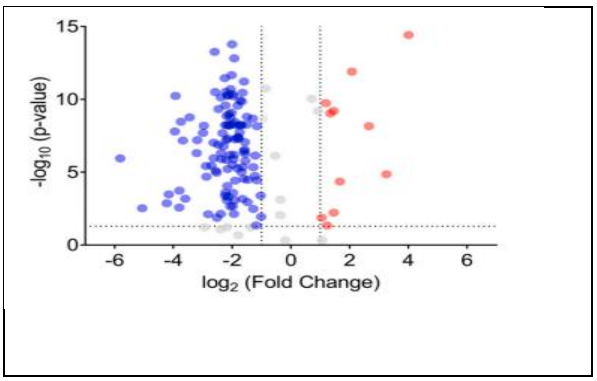
Comparison of metabolites between skin dialysate containing metabolites from the skin Interstitial fluid and venous blood (plasma) samples

Introduction:

Biofluids' metabolites can be used as biomarkers to track bodily conditions and diagnose illnesses. Interstitial fluid (ISF) in the skin is one of the biofluids that is currently available and has attracted a lot of attention because of its benefits, which include its non-clotting nature, ease of skin penetration, and potential for integration with wearable technology.[1] Furthermore, it has been shown by Samant et al. that the levels of caffeine in the skin ISF can be used to monitor levels in the blood. If other metabolites in the skin ISF are closely related to those in the blood, that remains to be ascertained.[2] In this investigation, plasma samples were also acquired with the aim of ascertaining associations between skin dialysate and plasma metabolites, which is essential for comprehending which blood metabolites can be approximated from skin ISF; and recognizing metabolites exclusive to forearm skin ISF in contrast to those found in venous blood.

Methods:

This study included twelve young individuals, six of whom were female. All participants abstained from meals for more than two hours, avoided coffee and alcohol for over twenty-four hours, and refrained from intense physical activity for more than twelve hours. Intradermal microdialysis was used to obtain forearm skin dialysate and venous blood (plasma) samples from these participants. Capillary electrophoresis–Fourier transform mass spectrometry (CE–FTMS) was employed to analyze the samples. The primary outcome was to determine correlations between skin dialysate and plasma metabolites, which was crucial for identifying which blood metabolites can be approximated from skin interstitial fluid (ISF). The secondary outcome was to identify specific metabolites unique to forearm skin ISF as opposed to venous blood.



Results:

Figure 1. Volcano plot illustrating the log2-fold change in metabolite concentrations between skin dialysate and plasma

Out of the twelve young individuals, 138 metabolites found in both skin dialysates and plasma were used for correlation analysis. Among these, 39 metabolites exhibited positive correlations and were categorized using the Human Metabolome Technologies database. The categories included nucleic acids, choline, amino acids, and coffee-related metabolites. Additionally, biomarkers characteristic of forearm skin dialysate was identified, including metabolites involved in acid metabolism (cysteic acid), fatty acids (undecanoic acid), benzoates (benzoic acid, phthalic acid), nucleic acids (inosine 5′-diphosphate, cytidine-3′, 5′-cyclic monophosphate), as well as ascorbic acid (vitamin C) and 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG). A volcano plot illustrating the concentration ratio of metabolites in skin dialysate compared to plasma as shown in Figure 1. The plot represents the ratio of skin dialysate to plasma as a log2-fold change, with a threshold set for significant differences. In comparison to plasma, skin dialysate showed lower concentrations of 111 metabolites (blue circles) and higher concentrations of 11 metabolites (red circles). Metabolites falling below the threshold are depicted as grey circles on the plot.

Discussion:

The current study identified strong correlations between 39 metabolites in forearm skin ISF and venous plasma, suggesting that ISF can reliably reflect blood metabolite levels. In contrast, Samant et al. found similar correlations but used smaller sample volumes and microneedle collection methods. These differences in methodology and sample size may account for variations in the results and the detection of certain metabolites.[3] This study detected metabolites such as MHPG and cystic acid exclusively in skin ISF, potentially due to their local production or stability in ISF. Previous research, however, reported these metabolites in plasma, which could indicate matrix effects or methodological discrepancies in the current study. These differences highlight the impact of the collection method on metabolite detection and quantification.[3]

Conclusion:

There were significant correlations identified between venous plasma and forearm skin dialysate for several metabolites, including trimethylamine N-oxide and 1-methyladenosine. Additionally, 12 distinct metabolites, such as nucleic acids, fatty acids, amino acids, MHPG, cysteic acid, and benzoic acids, were found to be specific to forearm skin dialysate. These findings suggested that forearm skin dialysate or interstitial fluid could potentially serve as indicators for specific venous blood biomarkers.

Analysing metabolites in interstitial fluid through micro dialysis can reveal significant biomarkers and offers a minimally invasive monitoring method.

Reference:

1. Oharazawa A et al. Metabolome analyses of skin dialysate: Insights into skin interstitial fluid biomarkers. J Dermatol Sci. 2024 Jun;114(3):141-147.
2. Samant PP et al. Sampling interstitial fluid from human skin using a microneedle patch. Sci Transl Med. 2020 Nov 25;12(571): eaaw0285.

Effect of mineral-based oil baths on trans epidermal water loss and dry skin through infancy

Introduction:

About 20% of children in developed nations suffer from atopic dermatitis (AD), which is characterized by dry, itchy, and irritated skin that is prone to infections. Both lesional and nonlesional atopic skin exhibit increased transepidermal water loss (TEWL) as a result of the skin barrier function being compromised. Frequent use of emollient bath additives starting at 2 weeks of age did not prevent atopic dermatitis in the general population randomized controlled trial PreventADALL, and its impact on skin barrier function during infancy remains unknown. A skin barrier protein that is necessary for epidermal differentiation, including the formation and operation of the stratum corneum, is encoded by the FLG gene. In contrast to 10% of the general population, approximately 20–50% of AD patients14 have at least one FLG mutation. So, the author sought to evaluate the impact of the skin intervention on TEWL and dry skin during infancy, and then to determine whether carrying FLG mutations could have any bearing on the potential effects. This allowed us to better understand why the skin intervention in the PreventADALL study did not prevent AD.

Methods:

This was an exploratory subanalysis of the PreventADALL study, a multicenter RCT and prospective birth cohort that enrolled 2697 pregnant women and used an electronic questionnaire to gather baseline data. The primary analyses included all 2153 of the 2394 randomized infants whose TEWL was measured on at least one of the clinical follow-up investigations at 3, 6, and/or 12 months of age. Additionally, the author analysed 1683 infants who also had information on their FLG mutation status. Also, the author assessed dry skin from birth, as well as dry skin (1) at any or multiple time-points, (2) at any time-point as moderate or severe, and (3) on cheeks and/or extensor surfaces of the extremities at any time-point for sensitivity analysis. Using mixed-effects regression modeling, the skin intervention's effects on TEWL and dry skin during infancy were evaluated. Weekly diaries, birth records, and electronic questionnaires were used to gather information on background traits and protocol compliance.

Results:

In total, 2153 infants were enrolled and randomized to receive either an oil bath four times a week for two weeks through 8 months as part of the "Skin intervention" (n=995) group or no skin intervention (n=1158) group. Throughout the first year of life, the SI group's TEWL (95% confidence interval) was, on average, 0.42 g m^{-2} h^{-1} (0.13–0.70, P=0.004) higher than that of the NSI group (Figure 1). At 3 months, the levels were significantly higher [8.6 (8.3–9.0) vs. 7.6 (7.3–7.9)], but they were similar at 6 and 12 months. At three months of age (59% vs. 51%) and six months of age (63% vs. 53%), the NSI group was observed to have dry skin significantly more frequently than the SI group; however, at 12 months of age, the difference was no longer significant.

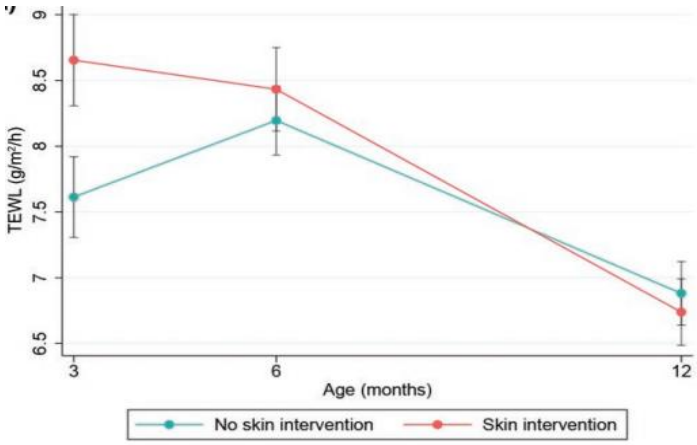


Figure 1. TEWL, in g m^{-2} h^{-1} (95% CI), was calculated using a linear mixed-effects model with random effects on the individual for repeated measurements at 3, 6, and 12 months of age in 2153 infants in the Skin intervention and No skin intervention groups.

Discussion:

This study indicated that infants who received a skin intervention involving face cream and bath oil containing paraffinum liquidum exhibited higher trans epidermal water loss (TEWL) at three months. Likewise, O'Connor C et al. found that infants who were given frequent emollient baths and leave-on emollients starting from day two of life showed significantly increased TEWL at two months of age.[2] This study's finding of reduced skin barrier function at three months in the skin intervention group was also supported by other study, which has reported increased TEWL associated with the use of leave-on emollients.[3]

Conclusion:

Frequent oil baths starting at two weeks of age resulted in lower skin barrier function throughout infancy as compared to controls. This was mostly due to higher TEWL at three months of age, and skin that was less dry at three and six months of age was observed in infants who received the skin intervention

Frequent oil baths starting at two weeks of age resulted in lower skin barrier function through infancy.

Reference:

1 Rehbinder EM et al. Frequent oil baths and skin barrier during infancy in the PreventADALL study. Br J Dermatol. 2024 Jun 20;191(1):49-57
2 O'Connor C et al. Early emollient bathing is associated with subsequent atopic dermatitis in an unselected birth cohort study. Pediatric Allergy and Immunology. 2023 Jul;34(7):e13998.
3 Kelleher MM et al. Skin care interventions in infants for preventing eczema and food allergy. Cochrane Database Syst Rev. 2021 Feb 5;2(2):CD013534.

Capillaroscopic analyses of lesions in patients with scleroderma-spectrum diseases

Introduction:

Nail-fold capillaroscopy is a non-invasive technique for evaluating the microcirculation in nail folds and is especially helpful for diagnosing systemic sclerosis and scleroderma-spectrum diseases, such as dermatomyositis, polymyositis, mixed connective tissue disease, and undifferentiated connective tissue disease, as well as for assessing activity, response to treatment, and the relationship between changes in microvessels and changes in organs.[1] Cutolo et al. defined scleroderma-like pattern microangiopathy as the capillaroscopic alterations typical of systemic sclerosis that occur in scleroderma-spectrum disorders.[2] About 20–40% of patients with idiopathic inflammatory myopathies, particularly DM with Raynaud's phenomenon, have such abnormalities diagnosed. About 50% of patients with MCTD and 5–10% of patients with UCTD have the scleroderma-like pattern. Thus, the capillaroscopic images of the patients with scleroderma spectrum disorders were examined in this study. Additionally, a potential association between the clinical picture and serological profile and capillaroscopic abnormalities was evaluated.[1]

Methods:

In this observational study, 15 patients with scleroderma-spectrum conditions were included. Among them, 7 patients met the European League Against Rheumatism/American College of Rheumatology classification criteria, while 8 patients were diagnosed with mixed connective tissue disease (MCTD) using the Alarcon-Segovia diagnostic criteria. Nailfold capillaroscopy was performed on each subject using a 200× magnification Dino-Lite USB microscope. The first row of nailfold capillaries on fingers 2–5 of both hands was inspected. To prevent Raynaud's episodes, patients were instructed to remain at room temperature for fifteen minutes prior to the assessment. Nailfold microcirculation was evaluated qualitatively, categorizing the images into normal, non-specific lesions, and scleroderma-like microangiopathic patterns. Non-specific changes included twisted capillaries, microhaemorrhages, and dilated loops.

Results:

Out of the fifteen patients in the study, 7 were diagnosed with dermatomyositis (DM) and 8 with mixed connective tissue disease (MCTD). Scleroderma-like microangiopathy was found in 47% of patients with scleroderma-spectrum disorders, including 43% with DM and 50% with MCTD. Vascular abnormalities included early patterns in 42% of MCTD patients, active patterns in 29% (1 with DM and 1 with MCTD), and late patterns in 29% (only in DM patients). Non-specific changes were present in 27% of patients, with 28% in the DM group and 25% in the MCTD group. Normal capillaroscopic images were observed in 27% of patients, including 28% with DM and 25% with MCTD. Comparison between the DM and MCTD groups revealed that MCTD patients had significantly higher levels of muscle enzymes, as well as a significantly higher prevalence of arthritis and Raynaud's phenomenon (Table 1).

Parameters	Study group	DM	MCTD
Number of patients	15	7	8
Raynaud's phenomenon	6 (40%)	3 (43%)	7 (87.5%)
ANA (Antinuclear antibodies)	15 (100%)	7(100%)	8 (100%)
ENA (Extractable nuclear antigen)	13 (87%)	5 (71.4%)	8 (100%)
Arthritis	6 (40%)	1 (14.3%)	5 (62.5%
Creatine kinase	9 (60%)	6 (85.7%)	3 (37.5%)

Table 1. Clinical characteristics of the DM and MCTD groups

Discussion:

In this study, significantly higher muscle enzyme levels in dermatomyositis (DM) patients was noted while mixed connective tissue disease (MCTD) patients had a higher incidence of arthritis and Raynaud's phenomenon. No association was found between scleroderma-like microangiopathy and specific clinical symptoms or capillaroscopic anomalies. The initial scleroderma-like microangiopathy pattern was unique to the MCTD group, consistent with existing study.[3]

Conclusion:

The analysis showed that the incidence of Raynaud's phenomenon and arthritis was statistically significantly higher in patients with systemic connective tissue disease than in those with dermatomyositis, and that the reduced number of vessels correlated with the occurrence of interstitial lung disease.

Monitoring scleroderma-spectrum disorders requires measuring capillary density, and a rapid vascular loss is linked to a higher severity of the condition.

Reference:

1. Wiąk-Walerowicz K et al. The usefulness of nailfold capillaroscopy in scleroderma-spectrum disorders: a single-centre observational study. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii. 2024 Jun 3;41(3):296-300
2. Cutolo M et al. Nailfold capillaroscopy in rheumatology: ready for the daily use but with care in terminology. Clin Rheumatol 2019; 38: 2293-7.
3. Bernardino V et al. A Nailfold capillaroscopy and autoimmune connective tissue diseases in patients from a Portuguese nailfold capillaroscopy clinic. Rheumatol Int. 2020 Feb;40(2):295-301.

Case report on immunocompetent patient experiencing worsening of eczema after herpes zoster infection

Introduction:

The Varicella-zoster virus (VZV), a member of the human herpesvirus family, is the causative agent of both varicella (chickenpox) and herpes zoster (shingles). Herpes zoster represents a reactivation of VZV within the host, and its clinical manifestations are of considerable interest due to their variability, which was essential for differential diagnosis.[1] Various cutaneous reactions have been reported at sites of previous VZV infection, appearing weeks to years after the acute phase. Although the precise pathogenesis of these reactions remains unclear, the detection of VZV DNA in lesions without associated viral cytopathic effects suggested that the virus may induce an atypical, delayed hypersensitivity reaction, which typically does not respond to antiviral therapy.[2] This was a rare case involving a 54-year-old female who developed a severe, widely distributed eczematous rash following a resolved herpes zoster infection.

Case presentation

A 54-year-old woman presented with a bilateral rash affecting her scalp, face, and neck. Her medical history included hypertension, asthma, ovarian and cervical cancer, a heart murmur, and a recent shingles infection. A week prior, she experienced chills, a blistering rash in a dermatomal distribution on the left side of her face, blurry vision in her left eye, and generalized paraesthesia. She was diagnosed with shingles complicated by cellulitis and initially treated with valacyclovir and cephalexin. Examination revealed eczematous lesions on the scalp, face, bilateral ears, neck, and inframammary folds, characterized by crusting, minimal scaling, and minor erosions (Figure 1). There was also minor periorbital edema and watery discharge from both eyes. Laboratory tests showed normal levels of C-reactive protein, rheumatoid factor, and antinuclear antibodies, while the erythrocyte sedimentation rate was slightly elevated at 37 mm/h. HIV testing was negative. A wound culture identified methicillin-resistant Staphylococcus aureus.The diagnosis included allergic contact dermatitis, dermatitis herpetiformis, and eczema exacerbation with a superimposed bacterial infection. Clinical and laboratory findings were most consistent with eczema complicated by a bacterial infection. Treatment included topical hydrocortisone for the eczematous rash, ciprofloxacin eye drops for ocular symptoms, and betamethasone lotion for scalp management. The patient also received a 7-day course of intravenous vancomycin for the bacterial infection and gabapentin to alleviate associated pain and discomfort. The combination of oral, topical, and intravenous treatments significantly improved the patient's symptoms and effectively managed the rash.

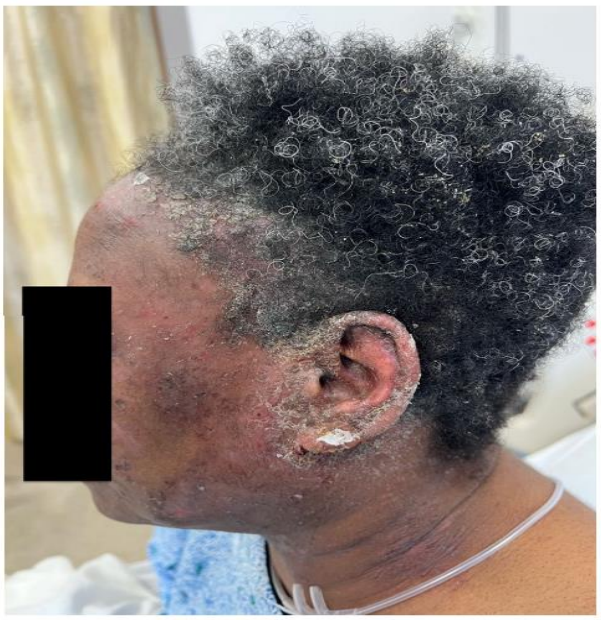


Figure 1. Ill-defined eczematous lesions with crusting, minimal scaling, and some erosions

Discussion:

The study's outcome with valacyclovir contrasts with previous reports where corticosteroids and other antivirals like acyclovir produced mixed results, emphasizing the potential benefit of valacyclovir in managing such lesions.[3] Langenberg et al. and other studies stress the importance of biopsies to exclude neoplastic changes, particularly in patients with underlying conditions. This study corroborates by suggesting the need for careful differentiation between post-herpetic changes and malignancies.[4]

Conclusion:

The study highlighted the challenges in diagnosing and treating cutaneous responses following varicella-zoster virus infection and indicated that a multimodal therapeutic strategy may be beneficial.

Delayed eczematous reactions can occur after herpes zoster and may not respond to antiviral therapy, requiring careful evaluation and management.

Reference:

1. Patil A et al. Herpes zoster: A Review of Clinical Manifestations and Management. Viruses. 2022 Jan 19;14(2):192.
2. Samman L et al. Eczema exacerbation following herpes zoster infection in an immunocompetent patient: A case report. SAGE Open Med Case Rep. 2024 Jun 3; 12:2050313X241259273.
3. Gibney MD et al. Cutaneous reactions following herpes zoster infections: report of three cases and a review of the literature. Br J Dermatol 1996; 134(3): 504–509.
4. Langenberg A et al. Granulomatous vasculitis occurring after cutaneous herpes zoster despite absence of viral genome. J Am Acad Dermatol 1991; 24(3): 429–433.