Topically applied diacerein: Basic pharmacokinetics in generalized/severe epidermolysis bullosa simplex
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Generalized-severe epidermolysis bullosa simplex (EBS-gen sev) is caused by mutations within either the keratin 14 or keratin 5 gene, phenotypically resulting in blistering and wound healing defects. Homozygous membranes significantly differed in reaction to mechanical and chemical stress. For this reason, first clinical trials using gene editing technologies show promising results, systemic treatment is still out of reach, especially due to the autosomal dominant inheritance and the resulting necessity in not only providing sufficient amounts of the wild type allele but also in down regulating the contrary allele. As a result, the topical application of diacerein, previously shown promising results in reducing EBS-gen sev patients blister numbers in a resent phase 2/3 clinical trial. In order to address the safety of this ointment, we analyzed the metabolization of a 1% diacerein ointment both in vitro and in vivo. A Franz diffusion cell setup demonstrated complete conversion into rhein within the skin. Further, uptake and bio-transformation into rhein was also observed in patients upon topical application. Rhein was detected in both urine and faeces at concentrations above 3% of the applied dose. In culture, the surface for four of the cell lines resulted in systemic rhein levels that were approximately 150-fold lower than levels detected 24 hours after single-dose oral intake, as shown by others. In summary, our results demonstrate that the produg diacerein is converted into its active form rhein within the skin, thereby allowing for the exertion of its anti-inflammatory effect in EBS-gen sev patient skin.

Clinical characteristics according to therapeutic efficacy of cyclopore or methotrexate in patients with psoriasis vulgaris
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Psoriasis vulgaris is a chronic, multifactorial, inflammatory skin disease. Either cyclopore (CsA) or methotrexate (MTX) is regarded as most commonly used systemic drugs for the treatment of moderate to severe psoriasis. However, there is no sufficient information related with clinical and laboratory characteristics of patients which might have an influence on the therapeutic efficacy. The goal of this study was to compare clinical and laboratory manifestations among the psoriatic patients treated with either CsA or MTX. Patients with psoriasis vulgaris, who had been treated with either CsA or MTX at the dermatologic clinic of Ajou University Hospital from January 2012 to December 2016, were enrolled. The patients were divided into four subgroups including CsA responders, MTX responders, CsA non-responders, whose CsA was switched to MTX, and MTX non-responders, whose MTX were switched to CsA. The clinical and laboratory information was retrospectively reviewed. Total 488 patients with psoriasis vulgaris were enrolled, including 199 CsA responders, 199 MTX responders, 53 CsA non-responders, 37 MTX non-responders. Disease durations before initial visit were significantly longer in MTX responders, compared to in CsA responders (80.83±17.38 vs. 45.11±5.80 [months], p<0.05). Also, either CsA or MTX non-responders had significantly longer disease duration than either CsA or MTX responders (102.07±12.76 vs. 87.33±4.83 [months], p=0.04). Body mass index was significantly higher in CsA non-responders, compared to in CsA responders (22.15±0.71 vs. 23.65±0.50 [kg/m²], p=0.04). Erythrocyte sedimentation rate was significantly elevated in MTX non-responders, compared to in MTX responders (17.70±3.04 vs. 11.35±0.68 [mm/h], p<0.02). In addition, either CsA or MTX non-responders showed significantly elevated ESR than either CsA or MTX responders (15.46±2.21 vs. 10.75±0.68 [mm/hour], p=0.03). This data showed CsA or MTX non-responders showed longer disease duration, higher BMI and elevated ESR/CRP.

Surgical wound healing in patients with epidermolysis bullosa
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Despite limited evidence to suggest patients with Epidermolysis Bullosa (EB) have more wound healing complications than the general population, we have noted reluctance among some surgeons to operate on these patients. Patients recruited from the Australian National Diagnostic Laboratory Database for EB and the Australasian EB Registry were posted the ‘Surgical Wound and Scar Healing in EB’ questionnaire which contains twenty-two questions about a patient’s experience of having surgery. Forty-six patients reported a total of 94 surgical procedures. The most frequent surgical procedure was the excision of a skin lesion, followed by musculoskeletal surgery, a caesarean section or an appendectomy. Five patients reported blistering at the surgical wound site after seven surgeries. Four patients reported four postoperative wound infections and one reported a postoperative wound dehiscence. Twenty patients had 34 postoperative wounds which they felt healed slower than someone without EB and 30 patients had 55 postoperative wounds which they healed at the same rate as someone without EB. After 67 surgeries, the postoperative scar was reported to heal flat and after 18 it was reported to heal as a keloid scar. It is unlikely that patients with localized EB simplex will develop blistering at the postoperative wound site, but about a quarter of patients with generalised EB may develop blistering which is likely to interfere with wound healing. Postoperative wound infections do not appear to occur any more frequently in patients with EB than in patients within the general population and wound dehiscence is uncommon in patients with EB. Postoperative wounds may heal at a similar or slower rate in patients with EB compared to those within the general population and patients with EB may have a propensity to develop keloid scars. Despite the inherent limitations of a postal survey we feel clinicians should be more confident to refer patients with EB for surgery and surgeons reassured about postoperative wound healing and complications.