Topically applied diacerein: Basic pharmacokinetics in generalized-severe epidermolysis bullosa simplex

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Generalized-severe epidermolysis bullosa simplex (EB-gen sev) is caused by mutations within either the keratin 14 or keratin 5 gene, phenotypically resulting in blistering and wound healing impairments. Numerous members of glucocorticoids are in use, limited invasive mechanical forces, and thus 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 mutated one. Therefore, the aim was to apply the topical diacerein and promising results in reducing EB-gen sev patients blister numbers in a recent 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 serum samples. The peak concentration of 3% of the surface area for four hours 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 EB-gen sev patient skin.

Clinical characteristics according to therapeutic efficacy of cyclosporine or methotrexate in patients with psoriasis vulgaris

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Psoriasis vulgaris is a chronic, multifactorial, inflammatory skin disease. Either cyclosporine (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 psoriasis patients which might have an influence on the therapeutic efficacy. The goal of this study was to compare clinic 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 were 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 (80.8±37.8 vs. 45.1±5.80 [months], p<0.05). Also, either CsA or MTX non-responders had significantly longer disease duration than either CsA or MTX responders (102.0±12.76 vs. 87.3±4.83 [months], p<0.05). 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±2.04 vs. 11.35±0.88 [mm/hour], 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.

Experiences with Smo antagonist vismodegib for the treatment of locally advanced basal cell carcinoma

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Although surgical resection is considered the standard treatment for locally invasive advanced BCC, the use of adjuvant therapy is to be discussed. Gorlin-Goltz syndrome is an inherited disorder which is characterized by the occurrence of multiple BCCs. Vismodegib (Erivedge, Roche) is the first Smo inhibitor agent which is indicated in otherwise untreatable BCC. We treated 11 BCC patients with vismodegib in our department in the last 4 years. 2 male and 9 female patients with mean age of 73.6±15 years were included, 36% of the patients had Gorlin-Goltz syndrome and the rest had locally advanced BCC, there was no metastasis. Vismodegib was given for an average of 15 months. 2 patients showed partial remission, and no relapse had been seen after the discontinuation of the drug. 2 patients passed away from unrelated conditions, such as sepsis from a urinary tract infection and pneumonia. 2 patients first showed remission, then the treatment had to be suspended and 2 patients decided to stop the treatment. When we re-administered the vismodegib to the last group of 5 patients improved considerably, and they are still on-treatment despite the side effects. The main side effects were muscle cramps, thygesia, nausea, loss of appetite and hair loss. The most important side effects were muscle cramps. 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. Forty-six 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 BCC. Among them 12 patients had 55 postoperative wounds with ESR/C6 level of 7.38 vs. 45.11 <C6 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.

The prevalence of periodontitis is increased in psoriasis and linked to its inverse subtype

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Periodontitis and psoriasis are suggested to be co-occurring, chronic inflammatory conditions with overlapping characteristics. However, respective evidence is rare and data on risk factors of periodontitis in psoriasis patients are minimal. The aim of this study was to expand the evidence of psoriasis-associated periodontitis and establish a potential risk profile for periodontitis. The data analyzed in this study were collected at the Department of Dermatology, State Hospital Klagenfurt, Austria, from patients who underwent an inflammatory focus screening, including a dental checkup (DCU), between January 2007 and February 2016. DCU has been routinely performed at this department in patients with psoriasis exacerbation and chronic spontaneous urticaria (CSU). In total data from 2091 patients were consecutively analyzed on recordings of periodontitis and compared with that of 91 chronic spontaneous urticarial (CSU) patients. Analysis showed a significantly increased prevalence of periodontitis in psoriasis compared to CSU patients with an odds ratio of 3.76 [95% CI 1.60-10.27, p=0.001]. Within the psoriatic subtypes the inverse type (affecting intertriginous body areas) was strongly linked to periodontitis with an odds ratio of 5.11 [95% CI 1.36-20.38, p=0.006]. These results are enlarging the evidence for periodontitis-associated periodontitis and identify a link between the inverse type of psoriasis and periodontitis.

Surgical wound healing in patients with epidermolysis bullosa

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Despite limited evidence to suggest patients with Epidermolysis Bullosa (EB) have more postoperative wound complications than the general population, we have noted reluctance among some surgeons to operate on these patients. Patients recruited from the Australian National Diagnostical 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 patients 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. Forty-six 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. Among them 12 patients had 55 postoperative wounds with ESR/C6 level of 7.38 vs. 45.11 <C6 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.