**Comparing the effect of tacrolimus (0.1%) ointment and betamethasone (0.1%) valerate on the epidermal barrier: a twice-weekly maintenance dose**

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**Background:** The proactive use of topical anti-inflammatories is an effective method of addressing the subclinical inflammation associated with the remission phase of atopic dermatitis (AD). To date, the interaction of this treatment dose with the subclinical epidermal barrier defect in AD is yet to be determined.

**Objective:** To compare the effect of a proactive topical corticosteroid dose against an equivalent topical calcineurin inhibitor dose on the biophysical and biological properties of the epidermal barrier.

**Methods:** A randomised, observer-blind, functional mechanistic study was performed in seventeen volunteers with quiescent AD, whereby two fingertip units of betamethasone valerate (0.1%) cream (BMVc) was applied to one forearm, and the same dose of tacrolimus (0.1%) ointment (TACo) to the opposing forearm, twice-weekly for a total duration of eight weeks. Epidermal barrier function, stratum corneum (SC) integrity and cohesion was determined by combining Transepidermal water loss (TEWL) measurements with tape-stripping to 20 discs (TS20). Skin-surface pH and SC hydration was assessed by non-invasive probes. Protease activity in the SC was quantified by a fluorescence cleavage assay from collected tape-strips.

**Results:** Compared to baseline (pre-treatment) measurements, application of BMVc produced a small but significant elevation of skin-surface pH (baseline: 5.099 ±0.05 units, treated: 5.338 ±0.07 units, \**p* = < 0.001) with concomitant loss of SC cohesion represented by the greater mass of SC removed during tape-stripping (TS20) (baseline: Area under the curve [AUC] 1821.4 ±54.55 μg/cm2.TS20, treated: AUC 2064.8 ±75.24 μg/cm2.TS20, \**p* = < 0.05). BMVc preserved epidermal barrier function and SC integrity. By contrast, TACo improved SC integrity, as evidenced by significantly reduced Transepidermal water loss (TEWL) recorded at disc 20 (baseline: TEWL20: 59.99 ±5.13g/m2/h, treated: TEWL20: 45.54 ±3.94g/m2/h, \**p* = < 0.0001). This was coupled with an overall hydrating action on the SC (baseline: 37.29 ±1.23 Relative Capacitance Units [RCU], treated: 43.35 ±1.45 RCU, \**p* = < 0.01). TACo significantly suppressed caseinolytic (baseline: 4.73 ±0.23 nU/μg, treated: 4.21 ±0.27 nU/μg, \**p* = < 0.05) and trypsin-like protease activity (baseline: 1.66 ±0.09 nU/μg, treated: 1.20 ±0.12 nU/μg, \**p* = < 0.05).

**Conclusions:** The differential results observed support the use of TACo to promote reparation of the subclinical barrier defect associated with quiescent AD. Repairing the defective epidermal barrier during long-term treatment regimens could have significant influence on reducing the severity of AD, and be disease modifying.