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Cytokine and chemokine release upon prolonged mechanical loading of the epidermis

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Introduction

At this moment, pressure ulcer risk assessment is dominated by subjective measures and does not predict pressure ulcer development satisfactorily [1]. Objective measures are therefore needed for early detection of these ulcers. The current *in vitro* study evaluates cytokines and chemokines (interleukin 1 α (IL-1 α), interleukin 1 receptor antagonist (IL-1RA), tumor necrosis factor α (TNF- α), and CXCL8/IL-8) as early markers for mechanically-induced epidermal damage.

Loading Experiment

Various degrees of epidermal damage were induced by subjecting epidermal equivalents (EpiDerm, MatTek, USA) to increasing pressures (0, 50, 75, 100, 150, and 200 mmHg) for 24h using a loading device (fig. 1). At the end of the loading experiment, tissue damage was assessed by histological examination (H&E staining) and by evaluation of the cell membrane integrity (lactate dehydrogenase (LDH) release). Cytokines and chemokines were determined in the culture supernatant by ELISA.

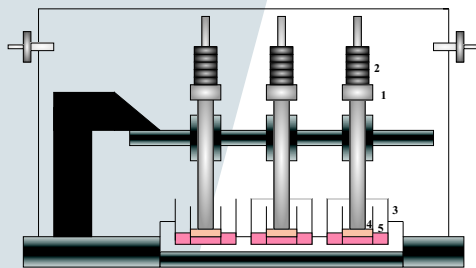


Fig. 1: loading device [2]: (1) indenter, (2) weights, (3) well, (4) EpiDerm, (5) medium.

EpiDermal damage assessment

Three different levels of tissue damage could be observed as a result of prolonged mechanical loading: minor (50 and 75 mmHg), moderate (100 mmHg) and severe (150 and 200 mmHg) (fig. 2 and 3). Minor tissue damage was characterized by a less clear stratum granulosum. Moderate tissue damage was characterized by an increase in the release of LDH, a less compact stratum corneum, and by cell swelling and necrosis in the upper part of the epidermis. The lower part of the epidermis was, furthermore, affected with severe tissue damage.

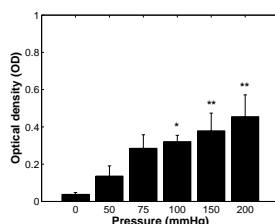


Fig. 2: LDH release in the culture supernatant upon 24h loading.

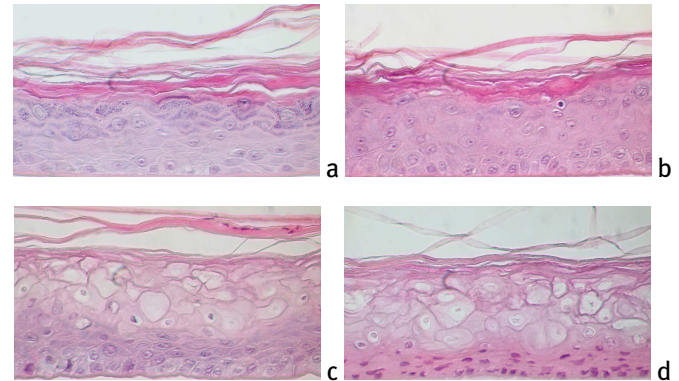


Fig. 3: Epidermal histology after loading: control group (a), minor (b), moderate (c), and severe (d) tissue damage.

Cytokine and Chemokine release

Sustained epidermal loading resulted in an increase in the levels of IL-1 α , IL-1RA, TNF- α , and CXCL8/IL-8 (fig. 4). This increase was first observed at 75 mmHg when tissue damage was only minor.

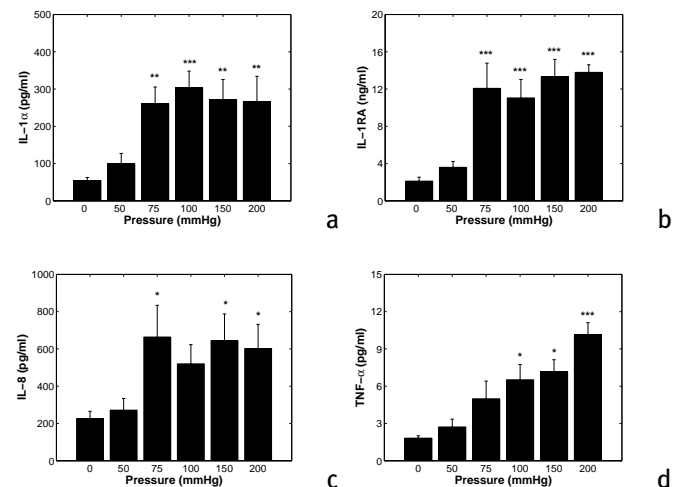


Fig. 4: IL-1 α (a), IL-1RA (b), IL-8 (c), and TNF- α (d) release in the culture supernatant upon 24h loading

Discussion

In conclusion, IL-1 α , IL-1RA, TNF- α , and CXCL8/IL-8 are released *in vitro* as a result of sustained mechanical loading of the epidermis. The first increase in cytokines and chemokines was observed when the epidermal tissue was only slightly damaged. Therefore, these cytokines and chemokines are potential markers for the objective, early detection of pressure ulcers.

References:

- [1] SCHOONHOVEN, L.: *Dissertation*, 2003
- [2] BRONNEBERG, D. ET AL.: *Ann. Biomed. Eng.*, 2006, 34:506-514