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Pilot Study on the effect of Daptomycin on IL-6, MMP-9 and TIMP-1 in patients with MRSA-infected diabetic foot stage 2 and 3

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The clinical and economic relevance of the diabetic foot ulceration (DFU) is well known. The elevated bacterial load and increased inflammatory reaction lead to increased levels of proinflammatory cytokines and proteases. Also the rate of MRSA-contaminated or infected foot lesions increases. Typical anti-MRSA antibiotics like glycopeptides (Vancomycin) show increasing minimally inhibitory concentrations (MIC) with a minor clinical efficiency and inappropriate side effects (e.g. nephrotoxicity). Studies with the new lipopeptide Daptomycin demonstrated a sufficient healing rate (approx. 77%) in severe infections of skin and/or tissue.

The presented non-interventional study investigated the profile of cytokines and proteases in MRSA-infected DFU during Daptomycin therapy. **Methods:** We included 8 patients with Stage 2 or 3 lesions (Wagner/Armstrong classification) and documented MRSA infection. Wound fluids (new filter paper method and flush) and microbiological swabs were collected (at day 0, 7, 14, 21 and 28). Additional laboratory analyses (creatinine, urea, white blood cell count, HbA1c, CRP and blood glucose) were performed as well as a daily wound documentation. Wounds were treated with standard care. MMP-9, TIMP-1 and IL-6 were analyzed by ELISA technique; all measurements were done in double settings and calculated as ng/ml or pg/ml. **Results:** IL-6 levels decreased during Daptomycin therapy and the wound healing course. Our data show also a reduction of the MMP-9 paralleled by an increase of TIMP levels during the sufficient antibiotic treatment. Wound fluid data obtained by filter paper method or flush were comparable. **Conclusion:** Our results demonstrate for the first time the MMP/TIMP modulation capacity of an antibiotic treatment in patients with DFU and severe MRSA infection. Both local levels of proteases and cytokines might be useful for the monitoring of infection (diagnosis and treatment).