

Cytokines as Predictors of Multiple Organ Dysfunction Syndrome of Polytrauma Patients: Osteoprotegerin and Lipocalin-2 Better than Interleukin-6?

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Background/Purpose: Multiple organ dysfunction syndrome (MODS) is with its unchanged high mortality is still one of the most severe complications in the posttraumatic course of severely injured patients. Thus an early detection of patients with an increased risk of developing MODS is crucial to help avoiding lethal courses. Interleukin (IL)-6 is, in this context, corresponding to its central role in regulation of posttraumatic inflammation, one of the gold-standard parameters for estimating individual risk profile. The paracrine osteoprotegerin (OPG) is part of the tumor necrosis factor superfamily and mediates various biologic effects including increased cytokine and chemokine synthesis. Lipocalin-2 (LCN) as an acute phase protein is among other things also of regulative importance within posttraumatic immune response. The primary end point of this study is the analysis of prognostic value of OPG and LCN for developing of posttraumatic MODS compared to IL-6.

Methods: A standardized arterial blood sample for plasma cytokine measurement was gathered from polytrauma patients (ISS = 16) between 16 and 65 years at days 1, 2, 3, 5, 7, and 14. A 10-mL probe was immediately centrifuged with 500g for 10 minutes. The plasma was extracted and preserved at -80°C. Cytokine analysis (IL-6, OPG) was made with flow cytometry/FACS, measurement of LCN/NGAL with ELISA (enzyme-linked immunosorbent assay). Clinical parameters were collected parallel. Diagnosis of MODS depended on the Marshall score. Statistical analysis included chi-squared test as well as Mann Whitney U test for nonparametric data with significance set at a P value < 0.05. Evaluation of the diagnostic value of IL-6, LCN, and OPG as MODS predictors was performed with ROC (receiver operating characteristic curve) analysis and the AUC (area under the curve). Cutoff points were defined on the basis of Youden's index.

Results: Altogether 234 samples from 39 patients (32 male, 7 female) with a mean age of 41.4 ± 20.4 years and a mean ISS of 34 ± 11 were analyzed. 7 patients (18 percent) died in the course of the treatment, 14 (36%) developed MODS. IL-6 as well as OPG and LCN were significantly increased within the MODS group ($P < 0.001$). According to ROC analysis, OPG and LCN were better predictors for MODS compared to IL-6. In addition, OPG distinguished best especially in the early phase.

Conclusion: OPG as well as LCN had a higher predictive value for developing MODS compared to IL-6 and were already significantly increased in the early phase. Thus, measuring OPG and LCN could help to identify patients with imminent multiple organ dysfunction syndrome earlier and hence contribute to further decrease mortality of polytrauma.