Surfactant Proteins A and D – New Diagnostic and Prognostic Biomarkers of Acute Respiratory Distress Syndrome in Septic Patients

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Acute Respiratory Distress Syndrome (ARDS) is a noncardiogenic pulmonary edema, in the basis of which lies an alteration (dystrophy, necrosis, apoptosis) of alveolar epithelium, pulmonary microcirculation endothelium, and their basal membranes (including structures of aerothematic barrier) by endogenous and exogenous aggressive factors, leading to a vascular permeability growth and development of acute respiratory failure [1-3].

A multicenter investigation at the V.A. Negovsky scientific research institute of general reanimatology in 2000-2011 confirmed that the non-cardiogenic pulmonary edema is the crucial element of the pathogenesis of early ARDS stage and a key for its detection in the clinical setting. The modern approach of ARDS early diagnosis was developed at the V.A. Negovsky scientific research institute of general reanimatology. These criteria provided clinicians with a possibility to diagnose an early, reversible stage of ARDS, start prompt treatment, decrease the duration of artificial pulmonary ventilation by 4-7 days, the intensive care unit stay by 5-6 days, the hospital stay by 10 days, the rate of pulmonary complications by 31.9% and the mortality – by 29.6% [1-4].

But this diagnostic approach does not provide us with a possibility to detect the injury of the alveolar epithelium. Biomarkers of the alveolar epithelium injury give an enormous prospect in the field of ARDS early diagnosis, prognosis and monitoring of the treatment efficacy [5].

Clinical investigations at the V.A. Negovsky scientific research institute of general reanimatology in 2012-2013 have confirmed that plasma surfactant proteins A (SP-A) and D (SP-D) may be used as biomarkers of ARDS in septic patients with severe intraabdominal surgical infections [6].

Plasma SP-D is a sensitive and specific diagnostic biomarker of ARDS and its early stages in septic patients. Plasma SP-D levels are significantly higher in patients with ARDS, than in patients without ARDS and have a good diagnostic capacity for the ARDS (any stage): SP-D on the day of sepsis diagnosis ≥ 115, 8 ng/ml yields a sensitivity of 82,5% and specificity of 80,0% (AUC 0,87; 95% CI 0,778-0,984; =0,0026) for the diagnosis of ARDS (any stage). Moreover, plasma SP-D is significantly higher in patients with the 2nd stage of ARDS than in patients with the 1st stage of ARDS (day 0 - 154,6 ± 125,2 ng/ml vs. 451,8 ± 299,2 ng/ml; day 3 - 129,3 ± 74,9 ng/ml vs. 362,9 ± 202,0 ng/ml; day 5 - 167,8 ± 120,4 ng/ml vs. 428,5 ± 372,4 ng/ml; day 7 - 186,2 ± 127,1 ng/ml vs. 415,5 ± 337,0 ng/ml). Plasma SP-D on the day of sepsis diagnosis ≤ 253,0 ng/ml yields a sensitivity of 90,0% and specificity of 74,0% (AUC 0,83; 95% CI 0,631-0,951; p=0,0001) for the diagnosis of the 1st stage of ARDS [6].

Plasma SP-A is a sensitive and specific prognostic biomarker of ARDS in septic patients. Plasma SP-A is significantly higher in patients who died of ARDS. Plasma SP-A has a good prognostic capacity for the lethal outcome in ARDS patients: SP-A on the day of sepsis diagnosis ≥ 38, 8 ng/ml yields a sensitivity of 65,0% and a specificity of 80,0% (AUC 0,74; 95% CI 0,577-0,866; p=0,0026). Plasma SP-A on the day of sepsis diagnosis has a good prognostic capacity for the development of ARDS on days 4-5 in septic patients: SP-A on day 1 ≥ 24,5 ng/ml yields a sensitivity of 60,0% and a specificity of 85,0% (AUC 0,74; 95% CI 0,527-0,871; p=0,0034).

Therefore, plasma surfactant proteins are sensitive and specific diagnostic and prognostic biomarkers of ARDS. There research data should be implemented into the daily clinical practice, which will provide us with an early ARDS diagnosis, a more prompt and effective treatment and outcomes improvement. Our future research will be focused on the investigations into other candidate biomarkers of ARDS and severe infections (Clara cell protein, bacterial permeability increasing protein, neutrophil elastase, etc.).

References

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