MICROCIRCULATORY ALTERATIONS IN PATIENTS WITH SEVERE SEPSIS: IMPACT OF TIME OF ASSESSMENT AND RELATIONSHIP WITH OUTCOME

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Abstract

Objectives: Sepsis induces microvascular alterations that may play an important role in the development of organ dysfunction. However, the relationship of these alterations to systemic variables and outcome is still not well defined. We investigated which factors may influence microcirculatory alterations in patients with severe sepsis and whether these are independently associated with mortality.

Design: Analysis of prospectively collected data from previously published studies by our group.

Setting: A 36-bed, medicosurgical university hospital Department of Intensive Care.

Patients: A total of 252 patients with severe sepsis in whom the sublingual microcirculation was visualized using orthogonal polarization spectral or sidestream dark-field imaging techniques.

Measurements and main results: Microcirculatory measurements were obtained either early, within 24h of the onset of severe sepsis (n = 204), or later, after 48h (n = 48). When multiple measurements were obtained, only the first was considered. Although global hemodynamic variables were relatively preserved (mean arterial pressure 70 [65-77] mm Hg, cardiac index 3.3 [2.7-4.0] L/min.m, and SvO2 68.3 [62.8-74.7]%), microvascular variables were markedly altered (proportion of perfused small vessels 65 [50-74]%, microvascular flow index 2.15 [1.80-2.60], and heterogeneity of proportion of perfused small vessels 35 [20-50]%). Among microcirculatory variables, proportion of perfused small vessels was the strongest predictor of outcome (receiver operating characteristic curve area 0.818 [0.766-0.871], $p < 0.001$). Survival rates decreased markedly with severity of alterations in the proportion of perfused small vessels (70% and 75% in the two upper proportion of perfused small vessel quartiles compared with 3% and 44% in the two lower quartiles, $p < 0.0001$). Multivariable analysis identified proportion of perfused small vessels

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and sequential organ failure assessment score as independent predictors of outcome. Microcirculatory alterations were less severe in the later than in the earlier (proportion of perfused small vessels, 74 [57-82]% vs. 63 [48-71]%, p = 0.004) phase of sepsis. In multivariable analysis focused on the early period of sepsis, proportion of perfused small vessels and lactate were independent predictors of outcome.

Conclusions: Microcirculatory alterations are stronger predictors of outcome than global hemodynamic variables.

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THE APC TREATMENT IMPROVES MICROCIRCULATION IN SEVERE SEPSIS/SEPTIC SHOCK SYNDROME

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Abstract

Background: The role of recombinant activated protein C (aPC) during sepsis is still controversial. It showed anti-inflammatory effect and improved the microvascular perfusion in experimental models of septic shock. The present study was aimed at testing the hypothesis that recombinant aPC therapy improves the microcirculation during severe sepsis.

Methods: Prospective observational study on patients admitted in a 12-beds intensive care unit of a university hospital from July 2010 to December 2011, with severe sepsis and at least two sepsis-induced organ failures occurring within 48 hours from the onset of sepsis, who received an infusion of aPC (24 mcg/kg/h for 96 hours) (aPC group). Patients with contraindications to aPC administration were also monitored (no-aPC group).At baseline (before starting aPC infusion, T0), after 24 hours (T1a), 48 hours (T1b), 72 hours (T1c) and 6 hours after the end of aPC infusion (T2), general clinical and hemodynamic parameters were collected and the sublingual microcirculation was evaluated with sidestream dark-field imaging. Total vessel density (TVD), perfused vessel density (PVD), De Backer score, microvascular flow index (MFIs), the proportion of perfused

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vessels (PPV) and the flow heterogeneity index (HI) were calculated for small vessels. The perfused boundary region (PBR) was measured as an index of glycocalyx damage. Variables were compared between time points and groups using non parametric or parametric statistical tests, as appropriate.

Results: In the 13 aPC patients mean arterial pressure (MAP), base excess, lactate, PaO2/FiO2 and the Sequential Organ Failure Assessment (SOFA) score significantly improved over time, while CI and ITBVI did not change. MFIs, TVD, PVD, PPV significantly increased over time and the HI decreased ($p < 0.05$ in all cases), while the PBR did not change. No-aPC patients ($n = 9$) did not show any change in the microcirculation over time. A positive correlation was found between MFIs and MAP. TVD, PVD and De Backer score negatively correlated with norepinephrine dose, and the SOFA score negatively correlated with MFIs, TVD and PVD.

Conclusions: aPC significantly improves the microcirculation in patients with severe sepsis/septic shock (BMC Anesthesiol. 2013 Sep 26;13(1):25. doi: 10.1186/1471-2253-13-25).PMID:24070065

Trial Registration:
NCT01806428

CARDIOVASCULAR BENEFITS OF PHLEBOTOMY: RELATIONSHIP TO CHANGES IN HEMORHEOLOGICAL VARIABLES

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Abstract

Renewed interest in the age-old concept of "bloodletting", a therapeutic approach practiced until as recently as the 19th century, has been stimulated by the knowledge that blood loss, such as following regular donation, is associated with significant reductions in key hemorheological variables, including whole blood viscosity (WBV), plasma viscosity, hematocrit and fibrinogen. An elevated WBV appears to be both a strong predictor of cardiovascular disease and an important factor in the development of atherosclerosis. Elevated WBV through wall shear stress is the most direct physiological parameter that influences the rupture and erosion of vulnerable plaques. In addition to WBV reduction, phlebotomy may reduce an indi-

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vidual's cardiovascular risk through reductions in excessive iron, oxidative stress and inflammation. Reflecting these findings, blood donation in males has shown significant drops in the incidence of cardiovascular events, as well as in procedures such as percutaneous transluminal coronary angioplasty and coronary artery bypass grafting. Collectively, the available data on the benefits of therapeutic phlebotomy point to the importance of monitoring WBV as part of a cardiovascular risk factor, along with other risk-modifying measures, whenever an increased cardiovascular risk is detected. The development of a scanning capillary tube viscometer allows the measurement of WBV in a clinical setting, which can prove to be valuable in providing an early warning sign of an increased risk of cardiovascular disease.

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