Sulfonated immunoglobulin improves cardiopulmonary functions by promoting IGF-I production in ARDS patients with severe sepsis

ISS scale was 35 ± 14, on a scale of APACHE II was 26 ± 6, and on the SOFA scale was 7 ± 4. We investigated the serum markers of apoptosis: sAPO-1/Fas (soluble Fas receptor, sFas), sFas-L (soluble Fas ligand), Bcl-2 and p53 (Bender MedSystems, Austria). Data are presented as mean ± standard deviation.

Results In patients with severe injury on the first day determined by the initial high level of sAPO-1/Fas (410.9 ± 89.7 pg/ml), which decreased on the second day, while remaining significantly above control values, the component for sAPO-1/Fas was 108 ± 12 pg/ml (P = 0.001). The level of sAPO-1/Fas increased, reaching a maximum on the fifth day (419.5 ± 94.5 pg/ml). The level of sFas-L was initially almost three times higher than the reference values at 48 ± 14 pg/ml, and on the third day rose in parallel to sAPO-1/Fas, reaching a maximum on the fifth day. In response to increased Fas-L, sFas is released. With increased expression of FasL and sFas lack of apoptosis leads to the development of multiple organ failure, and an excess of sFas massive death of lymphocytes may cause immunosuppression. The level of Bcl-2 in serum on the first day was significantly higher than in the control group (7.11 ± 5.55 ng/ml, P = 0.001) and amounted to 26.5 ± 6.3 ng/ml. On the fifth day there was a significant increase in the concentration of Bcl-2 to 39.8 ± 8.8 ng/ml, but by the seventh day the level of Bcl-2 decreased to 22.8 ± 4.3 ng/ml. Increased levels of p53 induced by hypoxia lead to increased concentrations of Bcl-2.

Conclusions The progressive development of multiple organ dysfunction syndrome in polytrauma is associated with serum concentrations of sAPO-1/Fas and sFas-L ratio, Bcl-2 and p53.

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Sulfonated immunoglobulin improves cardiopulmonary functions by promoting IGF-I production in ARDS patients with severe sepsis

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Introduction It has been emphasized that severe sepsis often leads to shock and ARDS in critically ill patients. We reported previously that sulfonated immunoglobulin (sIG) administration significantly inhibited the increase of in lung MPO activities and the increase of pulmonary vascular permeability. In the present study, we examined whether sIG improves not only ARDS but also cardiovascular dysfunction in patients with severe sepsis.

Methods ARDS patients with severe sepsis were divided into two groups, the sIG administrated group and the polyethylene glycol-treated immunoglobulin (pIG) administrated group. We evaluated them by measuring the value of IGF-1, lactate, PF ratio, cathecholamine index, septic severity score (SSS) and SOFA score.

Results The serum IGF-1 levels in the sIG group were increased at the seventh day significantly (P <0.05). PF ratios in the sIG group were increased significantly at the seventh day (P <0.05). The serum lactate levels and catecholamine index in the sIG group were decreased significantly at the seventh day (P <0.05). The total score of SSS and SOFA also significantly improved in the sIG group at the seventh day (P <0.05).

Conclusions These observations suggest that sIG might improve cardiopulmonary functions by promoting IGF-I production in ARDS patients with severe sepsis.

References

1. Okajima K, *et al.*: Activation of sensory neurons may contribute to reduction of endotoxin-induced hypotension by releasing CGRP, which is capable of promoting endothelial production of prostacyclin. *Crit Care Med* 2005, **33:**847-854.
2. Harada N, *et al.*: Capsaicin-induced sensory neuron activation, which leads to release of CGRP, might increase IGF-I production, thereby reducing reperfusion-induced liver injury by reducing apoptosis. *Neuropharmacology* 2007, **52:**1303-1311.
3. Asakura H, *et al.*: Plasma levels of TNF and IL-6 could be significantly suppressed by immunoglobulin in the LPS-induced DIC model. Moreover, hemostatic abnormality, organ dysfunction, and glomerular fibrin deposition in this model were all ameliorated by immunoglobulin. *Crit Care Med* 2006, **34:**2421-2425.
4. Harada N, *et al.*: Stimulation of FcγRI on primary sensory neurons increases insulin-like growth factor-I production, thereby reducing reperfusion-induced renal injury in mice. *J Immunol* 2010, **185:**1303-1310.

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Fluorinated groups mediate the immunomodulatory effects of volatile anesthetics in acute pulmonary inflammation

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Introduction Volatile anaesthetics are known as immunomodulatory substances in inflammatory as well as in ischemia/reperfusion processes [1,2]. We investigated in a model of acute pulmonary inflammation whether these immunomodulatory effects arise from the ether basic structure or from characteristics in their halogenation.

Methods Inflammatory response in pulmonary epithelial and endothelial cells as well as in neutrophils after co-exposure to endotoxin and sevoflurane, diethyl-ether or various water-soluble molecules carrying trifluorinated carbon groups (CF3) was evaluated. Expression of monocyte chemotactic protein-1 and cytokine-induced neutrophil chemoattractant protein-1, IL-6, and IL-8 as a measure of inflammatory activity were analyzed by ELISA. Chemotactic activity of supernatants regarding neutrophil recruitment was assessed. Flow cytometric analysis of neutrophil activation was performed measuring CD11b and CD62L expression. Viability was observed using fluorescence DNA quantitation. Cytotoxicity was evaluated by measuring lactate dehydrogenase in supernatants.

Results Expression of inflammatory mediators to lipopolysaccharide stimulation in epithelial and endothelial cells was dose-dependently decreased upon exposure to sevoflurane and other molecules with CF3 groups. This was not observed for diethyl-ether or structure-similar nonfluorinated molecules. In neutrophils, chemotactic activity as well as expression of surface CD11b and CD62L was decreased by molecules carrying CF3 groups. Cytotoxicity could be excluded.

Conclusions These findings show that the immunomodulatory effects are not limited to volatile anesthetics, but are associated with a much broader class of CF3 group-containing molecules. The immunomodulatory effects could now be provided in a hydrophilic, injectable formulation for the future treatment of patients suffering from acute pulmonary inflammation in environments not suitable for volatile anesthetics.

References

1. Ross S, *et al.*: *Br J Anaesth* 1999, **82:**622-632.
2. Voigtsberger S, *et al.*: *Anesthesiology* 2009, **111:**1238-1248.

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Soluble triggering receptor expressed on myeloid cells as a marker of non-infectious systemic inflammatory response syndrome

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Introduction The objective was to determine the diagnostic significance of soluble triggering receptor expressed on myeloid cells (sTREM-1) as a marker of the systemic inflammatory response syndrome (SIRS) in ischemia/reperfusion (extracorporeal circulation).

Methods Eighty-nine patients were included in the study. All patients were divided into: group 1 (n = 41) – coronary heart disease (CHD), group 2 (n = 47) – acquired heart diseases (AHD). All the operations were performed with normothermal nonpulsatile extracorporeal circulation (EC) with cold blood cardioplegia (coronary artery bypass surgery in the group with CHD and prosthetics/plastic valves for the group with AHD). Systemic inflammatory response (SIRS) was defined by Bone and colleagues [1]; ischemia and reperfusion by lactate and oxygen status of arterial and mixed venous blood (StatProfile). We studied by enzyme immunoassay level (ELISA): high-sensitivity C-reactive protein (hsCRP), procalcitonin (PCT-Q) and sTREM-1, using