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A co-culture model that simulates Cardiopulmonary Bypass induced systemic inflammation: From bench to bedside

Wollersheim S. (1), Miera O. (1), Fedarava K. (1), Berger F. (1,2), Schmitt K.R.L. (1)
Deutsches Herzzentrum Berlin, Germany (1)
Charité - Universitätsmedizin Berlin (2)

Background: Cardiopulmonary bypass (CPB) is known to induce a postoperative inflammatory response that is influenced by various factors. However, the underlying mechanisms are complex and not fully understood. To get more insights into the cellular mechanisms we developed an in vitro co-culture model that reflects the clinical situation. For evaluation of this model we compared the effect of hypothermia on the inflammatory response in the co-culture model with a clinical prospective study.
Methods: The co-culture model consisted of endothelial cells (HUVEC) and monocytes (THP-1). The cells were stimulated with 500 U/mL TNF-alpha to simulate CPB in pediatric open- heart surgery and exposed to moderate hypothermia (20°C) or normothermia (37C°). During the experiment, cell morphology (fluorescence microscopy), cell vitality (MTT-test) and cytokine release of IL-6 and IL-8 (ELISA) were investigated. In the prospective clinical trail, 20 patients (median age 3.3 months) undergoing CPB for ventricular septum defect (VSD) were randomized to receive either normothermic (37°C) or mild hypothermic (32°C) CPB. Dry blood spots (DBS) were obtained preoperatively, directly after weaning from CPB and after 24 h. IL-6 and IL-8 cytokines levels of the DBS samples were analysed by multiplexed sandwich immunoassays.
Results: We observed a significant IL-6 and IL-8 release in the co-culture model 2 h and 24 h after TNF-□ stimulation. Clinically, the cytokine release was also seen directly after weaning from CPB and remained elevated until 24 h. Interestingly, the IL-6 secretion in the co-culture 2 h after TNF-alpha stimulation was significantly decreased under hypothermia. After 24 h the IL-6 and IL-8 release of the co-culture model and the clinical data were similar and temperature independent.
Conclusions: These results demonstrate that our co-culture model is compatible to the clinical setting of pediatric CPB during VSD closure. The cytokine increase starts about the same time and is temperature independent after 24 h in both, the in vitro co-culture and the prospective clinical trail. This may suggest that our co-culture model could be used for further studies on the mechanisms of CPB induced inflammation.