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Letter to the Editor

Anti-inflammatory response and cardiopulmonary bypass

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We read with a great interest the excellent article by Onorati and co-workers demonstrating that pulsatile cardiopulmonary bypass (PCPB) and off-pump coronary artery bypass (OPCAB) surgery markedly reduced endothelial activation and inflammatory response as compared with linear CPB [1]. What about anti-inflammatory cytokines (except interleukin (IL)-10 already investigated in this study)? Studies have demonstrated that both inflammatory/anti-inflammatory cytokines and growth factors/anti-growth factors are released during conventional CPB [2—5]. Anti-inflammatory cytokines and anti-growth factors (sFlt-1) are considered as an anti-inflammatory response against CPB-induced inflammatory changes. The authors might use their collected blood samples to search for IL-4, IL-13, soluble IL-6 receptor and soluble vascular endothelial growth factor (VEGF) receptor (sFlt-1) and to identify whether the anti-inflammatory response is also impaired during PCPB and OPCAB as compared with linear CPB.

References


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Reply to the Letter to the Editor

Anti-inflammatory response and cardiopulmonary bypass: reply to Denizot and Nathan

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We thank doctors Denizot and Nathan for their appreciation and comments about our article investigating endothelial activation and inflammatory response after different types of perfusion [1].

There is compelling evidence that off-pump surgery is associated with reduced circulating levels of inflammatory mediators, some of which, such as interleukin (IL)-6, are still expected to occur as consequences of the surgical trauma, whereas others, such as IL-8 (with a key-role in neutrophil trafficking and myocardial injury), are related to cardiopulmonary bypass (CPB)-induced ischaemia–reperfusion injury [2]. With the advances of scientific research, a progressive increase of pro-inflammatory/anti-inflammatory markers and growth/anti-growth factors are daily discovered and tested in the clinical practice. However, the cost/benefit ratio on the advancement of knowledge must always be kept in mind. We have already investigated the endothelial/cytokine response to CPB with different laboratory assays available at our Institution, and found IL-6, IL-8, IL-10, MCP-1 and vascular endothelial growth factor (VEGF) to dramatically change during cardiac operations [2]. Therefore, we decided to transpose this set of biochemical assays also to off-pump surgery.

On the other hand, the interest of the scientific community to circulating biomarkers and triggers of the systemic inflammatory response dates back to decades [3]. A vast amount of literature data have been stored during these years, all demonstrating a significant burst of pro-inflammatory activation with a parallel activation of different anti-inflammatory pathways. Of the vast amount of anti-inflammatory markers activated during a cardiac operation, Misoph and Babin-Ebell [3] demonstrated that the degree of the observed modulation of cytokine patterns during and after CPB was patient-dependent, since large inter-individual variations
in cytokine levels were observed preoperatively, during and following CPB. However, IL-10 showed the least interindividual variation, suggesting that this cytokine may give reliable information regarding modulation of the immune response following CPB and its consequences for the patient’s outcome [3]. Since then, different studies have confirmed the key role of IL-10 on the anti-inflammatory response activated by the CPB-related pro-inflammatory burst [2–4]. Giomarelli et al. recently confirmed the crucial activation of the IL-10 pathway during the anti-inflammatory response to CPB [4]. Nathan et al. already showed limited changes of IL-4 compared with significant changes of IL-10 serum levels after CABG [5].

Finally, there are ongoing studies at our institutions aimed at analysing the release of different anti-inflammatory biomarkers, such as IL-4 and interferon (IFN)-gamma, as well as of other growth factors, such as epidermal growth factor (EGF). Preliminary data of these biochemical markers, in a limited cohort of patients enrolled up to date, show slightly higher leakage of anti-inflammatory IL-4 in pulsatile CPB, without significant changes of serum levels of this cytokine in off-pump and linear CPB, thus confirming a higher anti-inflammatory activity after pulsatile CPB (IL-4 linear-CPB = T0:6.1 ± 4.5 pg ml⁻¹; T1:4.9 ± 4.3; T2:5.0 ± 4.4, T3:5.5 ± 4.6, T4:6.2 ± 4.6 — pulsatile-CPB = T0:6.3 ± 4.9; T1:5.9 ± 4.6; T2:8.6 ± 5.1, T3:9.1 ± 4.8, T4:9.2 ± 6.2; off-pump coronary artery bypass grafting (OPCABG) = T0:6.3 ± 5.1; T1:5.8 ± 4.6; T2:5.8 ± 4.5, T3:6.4 ± 4.5, T4:6.6 ± 4.3; within group p = 0.09 for linear CPB, 0.001 for pulsatile CPB, 0.11 for OPCABG; between-groups p = 0.01). However, IFN-gamma and EGF levels were below the detection limit of the assay at all time points.

References


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