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Gut permeability and myocardial damage in paediatric cardiac surgery

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SUMMARY

Cardiopulmonary bypass (CPB) induces a systemic inflammatory response syndrome (SIRS) in patients following cardiac surgery that can lead to major organ injury and postoperative morbidity. Initiation of CPB sets in motion an extremely complex and multifaceted response involving complement activation along with activation of platelets, neutrophils, monocytes, and macrophages. This in turn initiates the coagulation, fibrinolytic, and kallikrein cascades, increasing blood concentrations of various endotoxins and cytokines and increasing endothelial cell permeability.

The basic physiological insults caused by CPB have been associated with major postoperative morbidity, including neurological, pulmonary adrenal dysfunction, and/or haematological abnormalities. Additional clinical manifestations associated with the SIRS include increased metabolism (fever), fluid retention, myocardial oedema, and detrimental haemodynamic alterations.

The use of steroids to minimize or prevent the consequences of SIRS in the postoperative period has been extensively investigated in adults. Clinical investigations in the paediatric population are scarce. Our aim was to investigate how dexamethasone could influence the associated side effects of CPB in two organs, the small intestine and the heart. To that effect we chose two surrogate markers, gut permeability and cardiac troponin T production.

Intestinal mucosal ischaemia, although transient, can occur in infants and children during and after CPB. Gut permeability had not been previously investigated in children undergoing cardiac surgery. In *chapter two* we describe, in an observational study, the natural course of gut permeability in patients undergoing cardiac surgery with and without CPB. Gut permeability has been investigated in healthy children and neonates not undergoing surgical or medical interventions during the study period. Patients with congenital cardiac diseases have preoperative gut permeability values up to seven times what we could expect in healthy children of similar age.

In patients operated without CPB gut permeability was reduced in the postoperative period returning to near normal values 24 hours after surgery. On the other hand, in patients undergoing surgery with CPB gut permeability deteriorated even further in the postoperative period.

In *chapter three* we report the results of a study designed to test the hypothesis that dexamethasone has beneficial effects on intestinal permeability during the postoperative period. Dexamethasone given before CPB starts reduced intestinal permeability within 24 h after surgery. The differences are highly significant when compared to control patients not given dexamethasone. In the investigation reported in *chapter four* we studied the changes in intestinal permeability in patients undergoing stage I of the Norwood procedure.

Neonates with hypoplastic left heart syndrome (HLHS) undergo surgical repair in three stages. These patients suffer from an imbalanced circulation potentially exposing the intestine to chronic ischaemia. The surgical repair requires a period of circulatory arrest. It comes as no surprise, therefore, that HLHS patients are at high risk of developing necrotizing enterocolitis in the postoperative period, with devastating consequences. We found that HLHS patients have abnormal intestinal permeability before and after surgery.

Rhamnose is one of the four sugars used to test intestinal permeability. For the last thirty years it has been assumed that rhamnose is an inert sugar not metabolized by the human body. We have found this not to be the case, and the results are presented in *chapter five*.

The type of anaesthetic agent used during adult coronary bypass surgery may influence considerably the postoperative production of cardiac troponin T (cTnT), a protein that reflects the extent of myocardial damage after a period of hypoxia. In particular halogenated ethers may exert its effect through a process called anaesthetic preconditioning, a phenomenon similar to ischaemic preconditioning.

Anaesthetic preconditioning has not been investigated in paediatric cardiac surgery to the same extent as in adult cardiac surgery. In *chapter six* we present a study of the effects of three different anaesthetic agents, propofol, midazolam and sevoflurane, on the postoperative production of cTnT in paediatric cardiac surgical patients. Contrary to what happens in adult patients we could not find significant differences in the postoperative production of cTnT when midazolam, propofol or sevoflurane were used as anaesthetic agents.

In *chapter seven*, we report on a study designed to test the hypothesis that dexamethasone given before CPB starts may have myocardial protective effects as assessed by the postoperative production of cTnT. Subgroup analysis in cyanotic and neonatal patients was also evaluated for the same hypothesis.

We found that dexamethasone did reduce postoperative cTnT concentrations. However, the reduction was short lived and was not accompanied by improvements in any of the other clinical parameters measured.