THE ROLE OF LEUKOCYTE DEPLETION IN THE PREVENTION OF REPERFUSION INJURY ASSOCIATED WITH OPEN HEART SURGERY

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SUMMARY

Reperfusion injury (RI) is a term used to describe tissue injury associated with revascularization after a period of ischaemia. This phenomenon may occur in open heart surgery and result in considerable morbidity. The mechanism of RI is thought to be an interaction between activated leukocytes, and reperfused endothelium, resulting in the release of variety of substances, such as activated oxygen species or proteolytic enzymes, with potential for parenchymal damage.

Leukocyte activation occurs during cardiopulmonary bypass and strategies to minimize RI include minimizing organ underperfusion, improving the surfaces of the extracorporeal circuit so as to reduce cellular and protein activation, pharmacological agents such as steroids, radical scavengers or enzymes which remove activated oxygen species and leukodepletion of re-infused blood.

Leukodepletion of re-infused autologous blood or transfused allogeneic blood has become possible using in-line filtration. Leukodepletion of autologous blood can be achieved in both the extracorporeal perfusion circuit and the cardioplegia delivery system. Several early clinical studies indicated benefit of this approach in reducing postoperative morbidity, length of stay in the intensive care unit (ITU/ICU) and ventilation times.

INTRODUCTION

Reperfusion injury, as the name implies, describes the sequence of pathological events which occurs after blood flow is restored to an organ.
or tissue after a period of flow reduction or cessation.1 In this regard, reperfusion injury, as such, is not restricted to cardiac surgery, but may be associated with many surgical specialties involving the application of tourniquets or indeed crush injury.2 Leukocytes are considered to be important in the mediation of reperfusion injury.

Despite the uneventful progress of most patients undergoing open heart surgery, there remain a number of patients who exhibit a profound adverse reaction to the procedure, which is particularly apparent in the postoperative recovery phase. Reperfusion injury has been recognized for some time as a significant factor in the morbidity of such patients undergoing open heart surgical procedures. The cellular dysfunction attributed to this phenomenon ranges from mild neurological disruption3-6 to moderate sequelae such as the “wet lung” syndrome to, in extreme cases, death due to severe cardiopulmonary injury.7 These sequelae were observed even in the very early days of cardiac surgery. Cleland et al published their observations describing an increase in extravascular fluid and pulmonary insufficiency in patients who had undergone cardiopulmonary bypass procedures in 1966.8 In cardiac surgical practice, the wide ranging spectrum of adverse events associated with this injurious mechanism are known as the post-perfusion syndrome reflecting the major importance of cardiopulmonary bypass in its etiology. Before considering the various methods, both pharmacological and mechanical, which have evolved to reduce or limit the adverse clinical reactions associated with reperfusion injury, it is important to understand the pathogenesis of the reperfusion injury syndrome as it exists in the cardiac surgical field.

As already stated, reperfusion injury occurs when blood flow is restored to a region of tissue after a period of low or no-flow. This is in contrast to ischemic injury which may be characterized as cell death mediated by long term deprivation of nutrients under conditions of reduced or eliminated blood flow. This nutrient starvation results in cell death due to a reduction in metabolism leading to an accumulation of toxic metabolites. Reperfusion injury is thought to be the consequence of activated leukocytes attacking otherwise healthy tissues by the uncontrolled release of mechanisms normally employed as a host defense system. In this regard, reperfusion injury differs from ischemic injury. Reperfusion injury does not require a reduction or elimination of cellular metabolism as is the case in ischemic injury. However the ischemic phenomenon and the release of toxins and mediators are essential prerequisites for the reperfusion syndrome. Gotlick elegantly described the difference between ischemic cell death and reperfusion injury as being a passive mechanism versus an active and violent one. What is clear from the literature is that the leukocyte (in particular the neutrophil) has a very important role to play in the development of reperfusion injury and that flow restriction following periods of no flow or reduced flow is necessary for the development of the syndrome. It is essential, therefore, to characterize why the conditions present during cardiopulmonary bypass offer the required combination of leukocyte activating processes and altered hemodynamics required for this phenomenon to occur.

HEMODYNAMICS DURING CARDIOPULMONARY BYPASS

The cardiac surgical patient is placed on a cardiopulmonary support system which performs the function of the patient’s heart and lungs during the operative procedure. This is essential in order that the surgical team can operate on a static heart. The use of cardiopulmonary bypass (CPB) has been associated with an increase in peripheral vascular resistance index (PVRI) (Fig. 11.1) indicating a reduction in perfusion to peripheral tissues.9 The use of “core cooling” to reduce the metabolic requirements of the tissues during the perfusion period and the vasoconstriction associated with hypothermia compound this phenomenon.10 A reduction in tissue oxygen uptake during this phase of