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CARDIAC SURGERY ANESTHESIA AND SYSTEMIC INFLAMMATORY RESPONSE

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Abstract: Cardiac surgery is associated with the development of a systemic inflammatory response. Inflammation represents the response of the body to tissue injury and in normal circumstances is a controlled humoral and cellular response that will lead to control of infection and wound healing. In some instances this response may become exaggerated, ultimately leading to additional tissue injury and the development of organ dysfunction. In this paper we discuss about relationships between cardiac surgery anesthesia and systemic inflammatory response.

Key words: Cardiac surgery, Anesthesia, Agent, Systemic inflammatory response

INTRODUCTION

Inflammation represents the response of the body to tissue injury and in normal circumstances is a controlled humoral and cellular response that will lead to wound healing and control of infections. In some instances this response may become exaggerated, ultimately leading to additional tissue injury and the development of organ dysfunctions. Cardiac surgery may provoke such an inflammatory response with important clinical implications, in up to 20% of the operated patients. Such a response may be activated by the extent of the surgical trauma, by hypothermia, blood loss and blood transfusion, and so on. In the case of cardiac surgery additional factors such as contact activation, ischemia-reperfusion injury, and possibly endotoxemia may contribute to the development of a systemic inflammatory response (MacCallum *et al.,* 2014).

Deleterious effects of a systemic inflammatory response may occur at any organ level. Major cardiac events such as acute myocardial infarction, cardiac death, and heart failure appear to occur in up to 10% of coronary surgery patients. Pulmonary complications such as acute lung injury occur in up to 3% of the patients, while frequencies of up to 13% for renal dysfunction and even up to 45% for hepatic dysfunction have been reported (Gil-Gomez *et al.,* 2014).

Several anesthetics appear to alter the systemic inflammatory response. It is likely to be a direct effect on the inflammatory mediators or indirectly by reducing myocardial reperfusion injury and associated inflammatory response or both (Prieto *et al.,* 2013). Unfortunately this subject is likely to remain controversial for the time being, as clinical studies investigating various anesthetic regimen on systemic inflammatory response and myocardial injury during CPB cardiac surgery are few.

Systemic Inflammatory Response

The inflammation is body's response to tissue injury and is a rapid, highly amplified, controlled cellular and humoral responses. While the term 'sepsis' has classically been utilized to imply a clinical response to infection, a similar response may arise in the absence of infection also.

In fact, patients who appear to have sepsis but have negative microbial cultures have similar morbidity and mortality rates to the respective culture-positive population. This has led to the understanding that this process is a nonspecific, generalized inflammatory response to injury and prompted a diagnostic reclassification of these events into a pathophysiologic continuum by the

American College of Chest Physicians–Society of Critical Care Medicine Consensus Conference Committee in 1991 (Table 1) (Bone *et al.,* 1992).

The term systemic inflammatory response syndrome (SIRS) has been proposed to describe the entry point to this continuum, an entity that overlaps with normal postoperative physiology (Warltier *et al.,*

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2002). SIRS is a generalized, nonspecific inflammatory process, independent of the causative factors, and is of importance for several reasons also. It is a sensitive if nonspecific indicator of injuries. The classification of severity of SIRS into uncomplicated SIRS, sepsis, severe sepsis, and septic shock based on the existence of documented infection or hypotension has prognostic purporst. A frequent complication of SIRS is the development of organ dysfunction, including acute lung injury, renal failure, shock, and MODS (multiple organ dysfunction syndrome). Finally, long-term survival in patients developing SIRS can be adversely affected also. This is well documented in the context of sepsis, with the risk of death increased for up to 5 years after the septic episode (Quartin *et al.,* 1997).

Table 1: Criteria for Diagnosis of SIRS, MODS, and Sepsis

SIRS: Presence of two or more of the following are required for diagnosis: Temperature > 38°C or < 36°C Heart rate > 90 beats/min Respiratory rate > 20 breaths/min or $PaCO_2$ < 32 mmHg Leukocytes > 12,000, < 4,000/mm^3 or > 10% immature (band) forms
Sepsis: SIRS with documented infection
Severe sepsis: sepsis associated with organ hypotension, dysfunction or hypoperfusion
MODS: state of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention

MODS = multiple organ dysfunction syndrome; SIRS = systemic inflammatory response syndrome.

Cardiac Surgery and the Inflammatory Response

Cardiac surgery provokes a vigorous inflammatory response that has important clinical implications and effects. In the report from the Society of Thoracic Surgeons National Database, 20% (22,000 patients) of 'low-risk' patients developed postoperative complication. The incidence of MODS following cardiopulmonary bypass (CPB) was 11%, with a mortality rate of 41% in these patients in another experiment. Acquired multiple organ dysfunction is the best predictor of mortality in cardiac surgical patients who require prolonged postoperative mechanical ventilations. Many aspects of a patient's risk of serious perioperative complications are perceived as being relatively fixed (preoperative health status, genotype, surgical difficulty, *etc.*), but the degree to which these may be improved (for example hemodynamic optimization using mechanical or pharmacologic support) is still under assessments. The contribution of the inflammatory response to patient outcome is potentially remediable and thus deserves attentions. Factors influencing severity, incidence, and clinical outcome of the inflammatory response, and particularly the reasons why certain patients develop life-threatening perioperative complications, are currently not well understood. Three separate perspectives contribute to our understanding of the link between the inflammatory response and adverse clinical pursuant. First, the complex interaction of humoral proinflammatory and anti-inflammatory molecules may influence the clinical presentation and course of SIRS, with the balance of proinflammatory and anti-inflammatory cytokines determining the clinical course following cardiac surgeries.

Alternatively, changes in the time course, magnitude, or patterns of cytokine release following CPB may contribute to abnormalities in the inflammatory response to cardiac surgeries.

Second, a 'multiple-hit' scenario may be seen, whereby serious sequelae develop after cardiac surgery as a result of adverse events, like ongoing organ hypoperfusion or infection. The combination results in the conversion of an inherently self-limiting, tightly controlled homeostatic response to an uncontrolled destructive process resulting in organ dysfunction (Bone, 1996). Potential mechanistic insights into the pathophysiologic basis for multiple hits include the ability of CPB to 'prime' neutrophils, causing pulmonary leukosequestration and enhanced cytotoxin release following subsequent insults.

Third, it has been suggested that there may be a fundamental misconception about the inflammatory responses. The proinflammatory state, SIRS, may be only one aspect of a multifaceted response. The converse has been termed the compensatory anti-inflammatory response syndrome. CPB-induced generalized immunosuppression may play an important role in the development of infectious complication. Thus, these responses represent the body's attempt to reestablish homeostasis and may clinically manifest as predominantly proinflammatory (SIRS), anti-inflammatory (compensatory anti-inflammatory response syndrome), or an intermediate mixed response. (Welters *et al.,* 2011)

Factors That Activate the Inflammatory Response: Nonspecific activators of the inflammatory response include surgical trauma, hypothermia, and blood loss or transfusion. Furthermore, CPB may specifically activate the inflammatory response *via* at least three distinct mechanisms. (Figure 1) One mechanism involves direct 'contact activation' of the immune system following exposure of blood to the foreign surfaces of the CPB circuit. A second mechanism involves ischemia–reperfusion injury to the brain, heart, lungs, liver and kidney as a result of aortic cross-clamping.

The restoration of perfusion on release of the aortic cross-clamp is associated with activation of key indices of the inflammatory response (Davies *et al.,* 1993). Endotoxemia may indirectly activate the inflammatory cascade. A common finding during and following CPB, Splanchnic hypoperfusion, may damage the mucosal barrier, allowing gut translocation of endotoxin in this case. Systemic endotoxin concentrations correlate closely with the degree of cardiovascular dysfunction following CPB, while low preoperative serum immunoglobulin M antiendotoxin core antibody concentrations predict poor outcomes. However, the importance of endotoxin in stimulating the inflammatory response to cardiac surgery remains in doubt, with conflicting evidence regarding the importance of gut translocations. (Welters *et al.,* 2011) In fact, endotoxin may be a contaminant of fluids, such as cardioplegia and circuit priming fluid, routinely used during cardiopulmonary bypass. The sole study to examine the incidence and time sequence of splanchnic hypoperfusion (as measured by intramucosal pH), gut permeability, and endotoxemia during CPB found no association between mucosal acidosis and either endotoxemia or intestinal permeability (Riddington *et al.,* 1996).

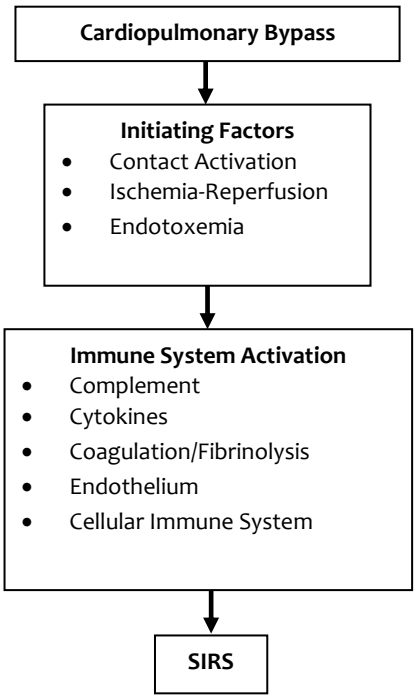

Figure 1: Schematic diagram of the sequence of events by which cardiopulmonary bypass (CPB) may lead to the development of SIRS (systemic inflammatory response syndrome).

Anesthesia, Anesthesiologist and Inflammatory Response to Cardiac Surgery

As perioperative physicians, anesthesiologists contribute to the management of the patient when adverse sequelae of CPB may pose a significant threats. Anesthesiologists are well positioned to minimize the risk of adverse sequelae resulting from the inflammatory response to CPB by reducing perioperative risk factors. Many drugs administered during the perioperative period, particularly for the purposes of anesthesia and sedation, possess potentially important immunomodulatory effect. Anesthesiologists may be best placed to properly evaluate and eventually implement therapeutic strategies, particularly as many potentially useful therapies seem poised to enter the clinical stage. A thorough knowledge of all aspects of the inflammatory response to CPB is mandatory if the anesthesiologist is to realize the goal of minimizing perioperative risks.

Cytokines Associated with Cardiopulmonary Bypass: Cytokines are a wide and swiftly growing group of polypeptides manufactured by several diverse cell types and necessary for optimum function of the immune system. (El Azab *et al.,* 2002) Interleukin-1β (IL-1β), IL-6, IL-8, and TNF-α are the major pro-inflammatory cytokines response to cardiac surgery. (Welters *et al.,* 2011) The proinflammatory cytokine response is balanced by a phased anti-inflammatory cytokine response with soluble cytokine receptors, anti-inflammatory cytokines, and cytokine receptor antagonists. The prime anti-inflammatory cytokines are interleukin-10 (IL-10), interleukin-1 receptor antagonist (IL-1ra), and TNF soluble receptors 1 and 2. (TNFsr 1 and 2)

TNF-α is made by activated monocytes and mononuclear phagocytes, and it has a significant role in inflammation. Plasma levels of TNF-α increase with CPB and increase faster than other cytokines, showing its role as a pioneer in the inflammatory responses. It has a big role in rised microvascular permeability and is liable for the post CPB weight gain, worse respiratory index and prolonged hospital stay. (Ozawa *et al.,* 2000) TNF-α can engender hypotension, coagulopathy and renal dysfunction and its increased levels are closed with multiple organ dysfunction syndrome/systemic inflammatory response syndrome (MODS/SIRS). (Khabar *et al.,* 1997)

IL-6 is a proinflammatory cytokine and is one of the prime mediators in the acute phase response causing a host of organ involvement, chiefly including the respiratory system and the central nervous system. It is the major predictor within the pro-inflammatory cytokines of LV systolic dysfunction, myocardial ischaemic episodes, reduction in systemic vascular resistance, need for vasopressor support, and cardiovascular abnormalities and associated with mortality rates in inflammatory states like sepsis. High levels of IL-6 are also significantly associated with

hepatic and renal dysfunctions (Kapoor and Ramachandran, 2004).

IL-8 is a proinflammatory cytokine, and its level increases in cardiac surgeries with CPB. Elevated IL-8 levels associated with respiratory dysfunction, length of inotropic support and were inversely related to the ratio of PaO_2 to FIO_2.

Thoracic Epidural Anesthesia: Thoracic epidural anesthesia combined with general anesthesia for CABG decreased the perioperative stress response, as measured by plasma epinephrine, and may decrease pulmonary injury and postoperative myocardial. However, thoracic epidural anesthesia does not significantly alter the cytokine response to CPB (Brix-Christensen *et al.,* 1998).

Lung Management during CPB: Apnea during CPB may lead to activation of lysosomal enzymes in the pulmonary circulation, which in turn are correlated with the degree of postoperative acute lung injury (ALI). This may be attenuated by a vital capacity maneuver performed before termination of the bypass; however, continuous positive airway pressure applied during CPB appears ineffective.

High Dose Opioid Anesthesia: Since the 1980s, high-dose opioid methods have been used in cardiac anesthesia due to their good circulatory stability and stress reduction characteristics. However pure high-dose opioid anesthesia (for example sufentanyl, 15-25 mcg/kg, or fentanyl, 50-100 mcg/kg) performs longer postoperative respiratory depression (12-24 h) and is associated with an unacceptably high incidence of patient awareness during surgery. Muscle rigidity during induction and prolonged postoperative ileus, also are undesired effects of this regimen. Furthermore, simultaneous administration of benzodiazepines with large doses of opioids may produce hypotension with myocardial depression. When short acting agents, like remifentanil or sufentanil are used instead of fentanyl, patients generally regain consciousness and can be extubated sooner (Butterworth *et al.,* 2013).

Opioids have many effects and results on the immune system, intervened indirectly over the central nervous system or through direct interactions with the cellular immune system.

Guggenberger *et al.,* (2006) compared the effects of remifentanil with sufentanil on pulmonary function and showed remifentanil anesthesia was better in improving pulmonary function in CABG patients.

Total Intravenous Anesthesia (TIVA): The drive for cost containment in cardiac surgery was a major impetus for development of anesthesia techniques with short acting agents. This method utilizes induction with propofol (0.5-1.5mg/kg followed by 25-100mcg/kg) and small doses of fentanyl (total doses of 5-7mcg/kg) or remifentanyl (1mcg/kg bolus followed by 0.25-1 mcg/kg/min). (Butterworth *et al.,* 2013)

Propofol may boost the anti-inflammatory response to surgery by several mechanisms. Propofol may maintain hepato splanching blood flow during cardiopulmonary bypass. It not only changes the balance between proinflammatory and anti-inflammatory cytokines, increasing production of anti-inflammatory cytokine IL-10 and IL-1ra while decreasing neutrophil IL-8 secretion, and also cleans reactive oxygen species either. Also propofol with low doses decrease neutrophil uptake in the coronary circulation following myocardial ischemia and reperfusion. Propofol reduces free-radical-mediated lipid peroxidation and systemic inflammation in patients with impaired myocardial function undergoing CABG.

Several studies have investigated the effects of different anesthetic managements on the immune response during and after cardiac surgery, and have suggested that propofol may have beneficial effects on post-traumatic immune changes. Moreover, it has been showed that propofol may alleviate the cytokine response observed during septic shock in rodents. El Azab *et al.,* (2002) compared the effects of three different anesthesia regimens on the cytokine response during cardiac surgery. They showed that the cytokine response was similar after volatile anesthetics, midazolam/suffentanil anesthesia and propofol /sufentanil anesthesia. (El Azab *et al.,* 2002)

A study comparing desflurane with propofol in patients undergoing offpump CABG surgery showed that postoperative troponin was lower and hemodynamic function was better in patients receiving desflurane. In contrast, a small study that administered high-dose propofol (120mcg/kg/min), low-dose propofol (60 mcg/kg/min) while on pump or titrated isoflurane throughout surgery improved troponin levels and gave better hemodynamic function in the large-dose propofol group compared to the isoflurane or low-dose propofol group. Baki *et al.,* (2013) studied the effect of propofol versus desflurane anesthesia on systemic immune modulation and the central nervous system in cardiac surgery patients with CPB. They showed that the immune reaction was less in patients exposed to desflurane anesthesia when compared to propofol anesthesia, as showed by lower plasma concentrations of IL-8 and IL-6.

Mixed Intravenous / Inhalation Anesthesia: Renewed interest in volatile agents came about following studies demonstrating the protective effects of volatile agents on ischemic myocardium and an increased emphasis on fast track recovery of cardiac patients. Etomidate (0.1-0.3 mg/kg) or Propofol (0.5-1.5 mg/kg) is often used for anesthesia induction. Opioids are given in small doses together with a volatile agent with 0.5-1.5 minimum alveolar concentration (MAC) for maintenance anesthesia. The opioid may be given in small intermittent boluses, by continuous infusion, or both. (Butterworth *et al.,* 2013) The most commonly used volatile anesthetics are sevoflurane, desflurane and isoflurane. Nitrous oxide is generally not used during the time interval between cannulation and decannulation because of its tendency to expand any intravascular air bubbles that may form. (Butterworth *et al.,* 2013) Sevoflurane, enflurane and isoflurane reduce IL-1β, TNF-α release by human peripheral mononuclear cells *in vitro*. Halothane, isoflurane, and enflurane minimize free radical–mediated myocardial injury. Isoflurane decreases alveolar macrophage phagocytosis and microbicidal function more than propofol.

Winterhalter *et al.,* compared the effects of continuous infusion of remifentanyl with intermittent fentanyl on the endocrine stress response and inflammatory activation during CABG surgery. They used propofol for induction and also maintenance with sevoflurane in their study. They showed that remifentanyl group patients were extubated earlier than the fentanyl patients in their study. Stress hormones (ADH, ACTH, cortisol) and interleukins (TNF-α, IL-6, IL-8) were higher in the fentanyl group compared to the remifentanyl group.

Other Techniques: Patients with hemodynamic instability the combination of ketamine with midazolam is a useful technique for induction and maintenance of anesthesia.

Midazolam has little effect on host defense mechanisms and decreases neutrophil IL-8 secretion in response to lipopolysaccaride. Midazolam decreases postischemic uptake of neutrophils in the coronary circulation following myocardial ischemia and reperfusion.

Ketamine decreases the increased levels of IL-6 concentrations during and following CPB and decreases coronary uptake of neutrophils following myocardial ischemia and reperfusion. High concentrations of ketamine affects *E.Coli* clearance and neutrophil and monocyte phagocytosis *in vitro*. Ketamine in subanaesthetic doses was shown to have beneficial effects on the immune response during and after surgery. Welters *et al.,* (2011) investigated the plasma levels of inflammatory markers with an anesthetic regimen based on ketamine as the sole analgesic. They showed that anesthesia with ketamine may have beneficial effects in attenuating the CPB-induced systemic inflammatory response.

Adjuvant Drugs

Many of the drugs used to produce anesthesia and maintain postoperative sedation and analgesia possess immune modulatory effects (Table 2). The clinical implications of such effects, particularly in the context of CPB, remain unknown, with most data in this area to date confined to *in vitro* experiments. Nevertheless, developments in this emerging field are worthy of consideration in the light of their future therapeutic potential.

Propofol may enhance the anti-inflammatory response to surgery by several mechanisms. Propofol may preserve hepatosplanchnic blood flow during CPB, thereby aiding maintenance of mucosal barrier. This alters the balance between anti-inflammatory cytokines and proinflammatory, increasing production of anti-inflammatory cytokine IL-1ra and IL-10, while decreasing secretion of neutrophil IL-8, and scavenges reactive oxygen species. It can be said that low concentrations of propofol reduce neutrophil uptake in the coronary circulation following myocardial ischemia and reperfusion. However, this effect is abolished at higher propofol concentrations; this may be due to the propofol solvent Intralipid (Kabi Pharmacia, Uppsala, Sweden) (Szekely *et al.,* 2000). Propofol impairs several aspects of monocyte and neutrophil function, including the respiratory burst, chemotaxis, polarization, phagocytosis, and oxygen radical generation. Certain immunomodulatory effects of propofol, such as suppression of respiratory burst of neutrophils by propofol, may be caused by the solvent Intralipid, while other actions, such as its ability toscavenge free radicals, appears to be a property of propofol itself.

Sodium thiopental impairs the neutrophil respiratory burst, chemotaxis, adherence, polarization, phagocytosis and killing, and coronary uptake of neutrophils following myocardial ischemia and reperfusion. At the therapeutic concentrations, thiopental inhibits the monocyte respiratory burst. In high concentrations thiopental affects *Escherichia coli* clearance *in vitro* and neutrophil and monocyte phagocytosis. Effect of thiopental on the respiratory burst of neutrophils appears less pronounced compared to propofol.

Ketamine attenuates the increase of serum IL-6 concentrations during and following CPB and reduces coronary uptake of neutrophils following myocardial

ischemia and reperfusion. Ketamine also affects *E. coli* clearance and neutrophil and monocyte phagocytosis *in vitro*, although just in high concentrations. Methohexitone only has minimal effects on the respiratory burst of neutrophils *in vitro*. Opioids have multiple effects on the immune system, mediated indirectly *via* the central nervous system or through direct interactions with the cellular immune system. While the precise cellular mechanisms underlying the immunomodulatory effects of opioids are largely unknown, emerging evidence indicates that opioids share many properties with cytokines. Ultrahigh affinity novel δ, μ and κ opioid receptors have been demonstrated on inflammatory cells. Granulocytes contain both opioid peptide selective δ2 receptors (which stimulate chemotaxis) and opiate alkaloid-selective, opioid peptide-insensitive receptors (which inhibit cytokine-induced activation and chemotaxis).

Table 2: Anti-inflammatory Effects of Anesthetic Drugs Used during Cardiac Surgery

Agent	Anti-inflammatory Effects	In Cardiac Surgery
Propofol	Enhances production of IL-10 Enhances production of IL-1ra Decreases neutrophil IL-8 secretion Scavenger of free radicals of oxygen-derived Impairs neutrophil respiratory burst Impairs neutrophil polarization Impairs neutrophil chemotaxis Impairs neutrophil phagocytosis Impairs neutrophil oxygen radical generation Inhibits monocyte oxidative burst and phagocytosis	
Sodium thiopental	Inhibits neutrophil polarization, chemotaxis, and adherence Inhibits neutrophil killing and phagocytosis Inhibits neutrophil respiratory burst Inhibits monocyte respiratory burst Inhibits monocyte phagocytosis Inhibits *E. coli* clearance	
Ketamine	Suppresses IL-6 concentrations Decreases *E. coli* clearance Decreases neutrophil phagocytosis Decreases monocyte phagocytosis Inhibits respiratory burst of neutrophils	Suppresses the increase of serum IL-6 concentrations, both during and following CPB
Methohexitone Morphine	Inhibits the activity of lymphocytes, macrophages, and granulocytes Suppresses the antibody response Inhibits the lymphocyte proliferation in response to T- and B-cell mitogens Inhibits the production of IL-2 and interferon γ Increases the secretion of anti-inflammatory substances, such as CRH, ACTH, and glucocorticoids	
Fentanyl	Increases concentrations of IL-1ra	Increased CD11b Reduced lymphocyte HLA-DR expression Attenuated the increase in monocyte HLADR expression
Midazolam Volatile anesthetic agents	Decreases extracellular IL-8 accumulation Decreases release of IL-1β, TNF-α Decreases microbicidal function and alveolar macrophage phagocytosis Protect against myocardial free radical injury	

IL = interleukin; IL-1ra = interleukin 1 receptor antagonist; CPB = cardiopulmonary bypass; CRH = corticotrophin-releasing hormone; ACTH = adrenocorticotrophin hormone; TNF-α = tumor necrosis factor α.

Morphine down-regulates the activity of granulocytes, lymphocytes, and macrophages, and suppresses the antibody response. Microinjection of morphine into lateral ventricle of the rat induces pronounced, dose dependent reductions in lymphocyte proliferation to T- and B-cell mitogens, natural killer cell cytotoxicity, and also the production of IL-2 and interferon-γ. Morphine also increases the secretion of ACTH, CRH, and glucocorticoids, for example substances with inhibitory effects on the immune system. Specific immune modulatory actions of morphine, including release of NO and inhibition of cell adhesion, appear to be mediated particularly *via* the μ3 receptor.

Fentanyl increases concentrations of IL-1ra in *in vitro* monocyte cultures. In one isolated blood primed CPB circuit, fentanyl increased CD11b, augmented reduction in lymphocyte HLA-DR expression, and attenuated increase seen in monocyte

HLA-DR expression. Unlike morphine, Fentanyl appears to lack the ability to bind to the μ3 receptor, diminishing its ability to down-regulate the inflammatory response to CPB.

Midazolam, the best studied benzodiazepine, has a little influence on host defense mechanism. Midazolam decreases neutrophil IL-8 secretion in response to lipopolysaccharide but does not alter IL-8 production. Midazolam reduces neutrophils' postischemic uptake in the coronary circulation following myocardial ischemia and reperfusion. Midazolam, at the clinically relevant concentrations *in vitro*, doesn't attenuate neutrophil polarization and has minimal effects on the neutrophil respiratory burst, clearance of *E. coli*, and neutrophil phagocytosis. Enflurane, sevoflurane, and isoflurane decrease proinflammatory cytokine (TNF-α, IL-1β) release by human peripheral mononuclear cells *in vitro*. Here Isoflurane decreases alveolar macrophage phagocytosis and microbicidal function to a greater extent compared with propofol. Halothane, enflurane, and isoflurane attenuate free radical–mediated myocardial injuries. Halothane and isoflurane (but not sevoflurane) appear to attenuate hydroxyl radical production in the ischemic rat heart (El Azab *et al.*, 2002). Halothane and sevoflurane and isoflurane reduce neutrophil and platelet uptake in the coronary circulation and preserve cardiac function following myocardial ischemia and reperfusion. Such effect is mediated at least in part *via* reduced neutrophil expression of the adhesion molecule CD11b. (Welters *et al.*, 2011).

CONCLUSIONS

Cardiac surgery evocates generalized inflammatory response in all patients with serious clinical results in a minority, despite advances in cardiovascular monitoring, pharmacology, surgical and anesthetic techniques and perfusion technology. It is obviously evident regarding to cardiovascular dysfunction and postoperative pulmonary. The etiology of such events maybe is a composite of unstable peribypass hemodynamics, suboptimal organ perfusion during cardiopulmonary bypass, immune events related to exposure to extracorporeal circulation, and global myocardial ischemia. A controlled, balanced inflammatory response is potentially beneficial, aiding host defenses against infection and facilitating wound healing, but loss of control of the inflammatory response may herald the onset of systemic inflammatory response syndrome and multiple or single organ dysfunctions. Anesthesiologists, as perioperative physicians, contribute to the management of patient when adverse sequelae of CPB may pose a significant menace. Several drugs administered during the perioperative period, especially for the purposes of anesthesia and sedation, possess potentially important immunomodulatory effects and results. Anesthesiologists might be best placed to properly evaluate and eventually implement therapeutic strategies, especially as many potentially useful therapies seem poised to enter the clinical arenas.

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