ISSN 3060-4567

MECHANISMS OF SYSTEMIC INFLAMMATORY RESPONSE IN CARDIAC SURGERY

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Abstract. *Recent data show that artificial circulation, myocardial and pulmonary ischemia-reperfusion, contact activation of leukocytes, anticoagulation, artificial ventilation, surgical trauma and other factors are powerful triggers of the inflammatory response after cardiac surgery. The combination of these factors leads to uncontrolled synthesis of various pro- and anti-inflammatory mediators, which in turn directly or indirectly cause dysfunction of endothelial cells, increased vascular permeability and manifestation of systemic inflammatory response syndrome with the development of organ dysfunction. The purpose of this literature review is to consider and systematize the main causes of the systemic inflammatory response after cardiac surgery with artificial circulation.*

Keywords*: artificial circulation, cardiac surgery, systemic inflammatory response, cardiovascular diseases.*

МЕХАНИЗМЫ СИСТЕМНОГО ВОСПАЛИТЕЛЬНОГО ОТВЕТА ПРИ КАРДИОХИРУРГИЧЕСКИХ ОПЕРАЦИЯХ

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Аннотация. *Последние данные показывают, что искусственное кровообращение, ишемия-реперфузия миокарда и легких, контактная*

ISSN 3060-4567

активация лейкоцитов, антикоагуляция, искусственная вентиляция легких, хирургическая травма и другие факторы являются мощными триггерами воспалительного ответа после кардиохирургических операций. Совокупность данных факторов приводит к неконтролируемому синтезу различных про- и противовоспалительных медиаторов, которые в свою очередь прямо или опосредованно вызывают дисфункцию эндотелиальных клеток, повышение сосудистой проницаемости и манифестацию синдрома системного воспалительного ответа с развитием органной дисфункции. Целью настоящего обзора литературы является рассмотрение и систематизация основных причин системного воспалительного ответа после кардиохирургических операций с искусственным кровообращением.

***Ключевые слова**: искусственное кровообращение, кардиохирургия, системный воспалительный ответ, сердечно-сосудистые заболевания.*

Relevance of the research

Cardiac surgery, especially with the use of artificial circulation (AC), along with sepsis, remains the most common cause of the systemic inflammatory response. Contact of blood with the surface of the perfusion circuit is recognized as the main mechanism triggering the systemic inflammatory response during cardiac surgery. Several interconnected pathways of contact activation of the inflammatory cascade during AC are distinguished. Activation of neutrophilic leukocytes increases the production of proinflammatory cytokines and elastase [1], tumor necrosis factor alpha (TNF-α) and interleukins (IL)-1β, IL-6, IL-8 [2]. Thus, the most important cytokine and interleukin cascades of inflammation are inextricably linked with the leukocyte link of the systemic inflammatory response. On the other hand, activation of neutrophils and monocytes leads to a systemic inflammatory response, releasing active oxygen radicals, hydrogen peroxide, cytotoxic enzymes: elastase, myeloperoxidase, etc. [3].

An important element of the inflammatory reaction is contact activation of the coagulation and anticoagulation systems of the blood [8]. In general, contact

ISSN 3060-4567

activation of the inflammatory cascade has many diverse, but closely interconnected cellular and humoral pathways. The final link in all these processes is the systemic inflammatory response.

Ischemic and reperfusion injury to the myocardium can be a significant and specific trigger for the systemic inflammatory response in cardiac surgery. This is an integral stage of most operations performed with CPB. Cardioplegic protection of the myocardium does not completely prevent myocardial injury, and with emergency myocardial revascularization, its acute ischemia develops initially. Previously, the systemic inflammatory response was described as a possible complication of myocardial infarction [4], which can be extrapolated to some extent to intraoperative myocardial injury. Myocardium can be a source of proinflammatory mediators, such as TNF-α, IL-6 and IL-8 [5].

The scheme of CPB is naturally accompanied by pulmonary ischemia. With the outflow of venous blood into the cardiotomy reservoir from the vena cava or the right atrium and its injection into the aorta, the blood flow in the pulmonary circulation is reduced. During CPB, the lungs are supplied with blood mainly only from the bronchial branches of the aorta. The resulting pulmonary ischemia and their subsequent reperfusion can lead to pulmonary dysfunction and serve as a trigger for the systemic inflammatory response. Artificial ventilation of the lungs (AVL) can injure the lung parenchyma with the release of proinflammatory mediators [2, 3].

Risk factors for the development of a systemic inflammatory response may include lung trauma due to their overstretching, and, conversely, atelectasis [1] with the formation of non-ventilated pulmonary zones vulnerable to the development of infection and damage during their subsequent “opening” (atelectotrauma) [3]. An important pulmonary factor in the development of a systemic inflammatory response in cardiac surgery patients remains concomitant pneumonia - in more than 6% of cardiac surgery patients [4]. Thus, the lungs can be both a trigger factor and a “target” of a systemic inflammatory response during cardiac surgery, closing the pathophysiological vicious circle.

ISSN 3060-4567

Transient mesenteric ischemiaIntestinal ischemia during CPB is associated with non-pulsatile mesenteric blood flow, spasm of mesenteric arterioles, and hemodilution. Tissue acidosis and permeability of the intestinal mucosa, together with depression of the liver reticuloendothelial system function, lead to translocation of intestinal flora and penetration of cytokines, IL, and TNF-α into the bloodstream against the background of loss of intestinal barrier function. Endogenous production of nitric oxide (NO) from L-arginine via calcium-dependent NO synthases (NOS) is the most important mechanism for regulating vascular tone. Vasodilation due to NO is a common final pathway for numerous regulatory humoral processes [16]. At the same time, pathological hyperproduction of NO under the action of inducible calcium-independent isoform of NO synthase (iNOS) causes vasoplegia and peripheral arteriovenous shunting during systemic inflammatory response [5].

The mechanism of NO action is cyclic guanosine monophosphate (c-GMP)-dependent decrease in intracellular calcium concentration [2]. Hyperproduction of NO is a common link in various pathophysiological processes, the most important cause of vasoplegia. The problem of systemic inflammatory response in cardiac surgery, despite numerous studies and development of various therapeutic measures, remains unresolved. An analysis of the current state of the issue gives grounds to believe that the most important areas of further work may be the prediction and prevention of the development of a systemic inflammatory response after CPB, the use of alternative (“non-catecholamine”) vasopressors and means of correcting the endogenous metabolism of nitric oxide, and finally, the improvement of rehabilitation measures after a systemic inflammatory response and its various clinical manifestations, primarily respiratory.

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ISSN 3060-4567

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