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SURGICAL STRESS RESPONSE

Tarasenko S.V.[1], Morozova E.A.[2], Zhuravlev A.N.[3], Diachkova E.Yu.[4]

[1] M.D., PhD., Professor, Chief of Department of Surgical Dentistry of Sechenov University, Russia, Moscow, Mojaiskii val, h.11, 121059, E-Mail.: prof_Tarasenko@rambler.ru

[2] PhD., Professor of Department of Surgical Dentistry of Sechenov University, Russia, Moscow, Mojaiskii val, h.11, 121059, E-Mail.: lemua@yandex.ru

[3] Postgraduate Student of Department of Surgical Dentistry of Sechenov University, Russia, Moscow, Mojaiskii val, h.11, 121059, E-Mail.: sanekzhu@ya.ru

[4]PhD, Associate Professor of Department of Surgical Dentistry of Sechenov University, Russia, Moscow, Mojaiskii val, h.11, 121059, E-Mail.: secu2003@mail.ru ,

Phone cell number: +7-926-519-93-42

Abstract:

The main cause of postoperative complications is considered to be the surgical response, which is a complex of changes in the neuroendocrine, metabolic and inflammatory developing due to the surgical trauma. With the high degree of surgical trauma these changes initially with compensatory-adaptive character become overweight, acquiring, thus, a clearly defined pathological direction. Surgical stress response is a major cause of postoperative dysfunction of various organs and systems (pain syndrome, immune system disorders and hemostasis, dysfunction of the lungs, gastrointestinal tract, cardiovascular system), which dictates the need to find approaches to correct it. In the basis of this kind of stress reaction we can find different mechanisms of general and local response of the organism, including humoral, endocrine and central nervous systems through changing of level bioactive substances such as enzymes. Despite the existence of many ways of the correction of individual parts of the surgical stress response, the most promising possibility of its limitation is the use of laser radiation. The most significant mechanism of the stress-limiting effect of laser radiation is the minimally invasive effect on the tissues of the surgical field.

In this paper the main components of surgical-induced stress reaction are described, also with methods of its correction.

Key words: ***oral surgery, stress response, surgical treatment, trauma, cytokines***

Corresponding author:

Diachkova E.Yu,

PhD, Associate Professor of Department of Surgical Dentistry of Sechenov University, Russia, Moscow, Mojaiskii val, h.11, 121059, E-Mail.: secu2003@mail.ru , Phone cell number: +7-926-519-93-42

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INTRODUCTION:

In recent years, there has been a perception that traumatic surgical interventions were accompanied by unacceptably high rates of complications and mortality. The main cause of postoperative complications is the surgical stress response, which is a complex of neuroendocrine, metabolic and inflammatory changes developing as a result of surgical trauma. With the high trauma of surgical intervention these changes of primary compensatory-adaptive character become overweight, acquiring, thus, a clearly defined pathological focus. Surgical stress response becomes the main cause of perioperative dysfunction of various organs and systems (pain syndrome, immunity and hemostasis disorders, lung, gastrointestinal, cardiovascular system dysfunction), which necessitates the search for ways of its correction. The severity and duration of the surgical stress response are determined primarily by the trauma of the intervention.

Awareness of the pathological nature of the surgical stress response led to the use in the perioperative period of a number of methods and tools aimed at the correction of its individual components.

Recently there are several methods of surgical treatment using different techniques (cutting, rotating) and laser radiations, which have different levels of stress on the patient's body that still remains a subject of debate.

This review is devoted to the current state of the problem of evaluation and correction of the main components of the surgical stress response in oral surgery using different tools.

Characteristics of surgical stress response

Modern ideas about surgical stress-response have developed at the end of XX century. It is understood as a set of changes of endocrine, metabolic and inflammatory nature, developing in the body in response to surgery.

It is well known that any surgical intervention depending on its volume and condition of homeostatic systems of the patients' body affects their immune system even to the development of secondary immunodeficiency, which results in the appearance of purulent-inflammatory and septic complications, often leading to death. M. A. Dolgov and A. Yu. Ryabchenko (2013) tell that any irritation (external or internal) leads to the emergence of a complex set of reactions aimed for adapting the body to the changed conditions, preventing or smoothing a possible shift in the composition of the internal environment [1].

The main factor determining the severity of surgical stress response is the traumatic nature of surgical intervention.

Studies of the pathophysiology of the surgical stress response led to the conclusion that changes in homeostasis, which were initially protective and adaptive in nature and aimed at mobilizing the compensatory resources of the body and the localization of damage, with excessive severity (associated with excessive surgical trauma), had pathological orientation and become the cause of postoperative dysfunction of various organs and systems. Pain syndrome increased myocardial oxygen demand, microcirculation disorders, respiratory dysfunction, paresis of the gastrointestinal tract; hemostazis disorders can cause complications and slow down postoperative rehabilitation, which determines the need to find ways to correct surgical stress response.

Pathophysiological assessment of the stress response of the body by determining the level of blood plasma stress hormones can be used to evaluate the clinical effectiveness of any method of anesthesia, surgical methods and tools, that's why it has great practical importance [2].

There are many studies pointing to the importance of stress triggers in the central nervous system (CNS), its emotional sphere, realizing influence through the hypothalamic centers and the corresponding endocrine glands. Under stress, there is a mobilization of almost all physiological systems, as a result of which the body's resistance increases. Stress is based on the tension of the hypothalamic-pituitary-adrenal system. The leading role of CNS in the development of stress, in the nature and severity of changes of physiological functions caused by stress effects was proofed.

From the point of view of physiology, each individual stimulus causes a complex neuroendocrine response aimed at overcoming extraordinary circumstances. Recently it is known that the sympathoadrenal and pituitary-adrenal axis, forming a nonspecific response to exposure, are common and necessary elements in a wide range of stimuli [3].

In response to the emotional tension, pain, surgical trauma, the activation of adrenergic structures occurs, which increases the level of catecholamines circulating in the blood. Both adrenaline and norepinephrine are released into the blood, but the first of them is dominant, as its metabolic activity is 8 times higher. Heart rate increases, as well as myocardial

contractility and peripheral vascular resistance; all this leads to increase of blood pressure and oxygen consumption.

The high concentration of catecholamines and glucocorticoids leads to a temporary decrease in resistance due to the parallel activation of catabolic processes: stimulation of protein breakdown, tissue destruction by activated proteo-and lipolytic enzymes. These changes depend on the strength, duration and nature of the stress factor [4].
Many forms of pathology are accompanied by pain syndrome, the origin and mechanisms of which are not clear enough and that's why they are the subject of modern research. There are works in which it is shown that the experimentally induced neuropathic pain syndrome is accompanied by the formation of antibodies to serotonin, noradrenaline and dopamine, and the immunization of animals with these conjugated mediators increases the symptoms of neuropathic pain. Yu.B.Abramov (2009) says about the influence of immune status on the value of pain thresholds. In infection, inflammation or trauma the immune cells of periphery produce cytokines, which reinforce pain and cause the release of proinflammatory active substances in the brain through glial cells [5].

But not only the immune system can affect the formation of pain, but pain may have an impact on the immune system, including innate immunity [6].

Thus, the pain syndrome and operational stress during and after surgery can have a significant impact on the course of free radical processes [7].

The reaction of the immune system in response to the alteration
Already in the 60-70 years of the last century, it was firmly established that regardless of the initial general condition of the patient and the level of his immunoreactivity, the surgical operation itself had an adverse effect on the immune system and causes the development of immunodeficiency, the main manifestation of which are infectious postoperative complications.

Almost all surgical operations damage the main components of the immune system: phagocytosis, humoral immunity, cellular immunity.

During surgical stress nociceptive impulses initiate endocrine response and production of inflammatory cytokines, which is accompanied by activation of sympathetic-adrenal, hypothalamic-pituitary-adrenal and renin-angiotensin-aldosterone systems. The result is an increase of the concentration of stress hormones [8].
The development of surgical stress response in high-trauma operations is directly related to clinically significant and requiring correction of homeostasis disorders, as well as to the occurrence of serious complications associated with changes in neuroendocrine status, metabolism and immunity [9].

Hormonal secretion
Surgical interventions at the stages of hospitalization in congenital and acquired pathology of the maxillofacial region lead to stress reaction of the organism, which is characterized by multifactorial side effects. Endogenous stress factors associated with infectious and inflammatory processes are joined by exogenous components such as surgical trauma. Any kind of the last is accompanied by the activation of the function of the hypothalamic-pituitary-adrenal system, followed by an increase in the blood content of stress hormones cortisol and adrenaline corticotropic hormone (ACTH), which have a powerful depressive effect on the immune system and pose a threat to the development of postoperative complications.

Surgery is one of the most powerful activators of ACTH and cortisol secretion, the increase in plasma concentrations of both hormones can be measured a few minutes after the start of the operation [10] .

Proper assessment of the immune status, taking into account the stress immunodeficiency, is important for predicting the course and outcome of the disease, as well as for substantiating new, more effective schemes of correction, which will be aimed not only at increasing the functional activity of the system (which is not always resultative due to the continued immunosuppressive action of stress hormones), but also at decreasing effect of glucocorticoids [11].

Under the influence of stress, there is an active release of corticoliberin from the hypothalamus, which leads to increased secretion of ACTH and, accordingly, glucocorticoids from the adrenal glands. At the same time, under the influence of the psychological component in the perception of the stressor, the activation of the corticoliberine system of the amygdala complex occurs [12].

Thus, at the primary stage of stress development, corticoliberin plays a key role launching a cascade of biochemical reactions and integrating further protective adaptation processes by interacting with all hormonal mediators, stress-activation generators and stress-limiting systems [13].

Under conditions of minor secretion of ACTH and glucocorticoids the hypothalamus releases a large amount of somatomedin, whereby the pituitary gland secretes a greater amount of somatotropic hormone (STH) and thus triggers the body system preventing stress-associated immunosuppression [14].

Cortisol plays the most important role in the body's response to surgical trauma. A significant increase in cortisol concentrations during and after various surgical interventions has also been confirmed by many authors. The level of plasma concentration of cortisol is an adequate reflection of the body's response to surgical stress. During the operation the level of cortisol in the blood increases, exceeding the norm; it can remain elevated for several days after the intervention [15].

Cortisol has a complex effect on the intermediate metabolism of carbohydrates, fats and proteins, stimulates gluconeogenesis, proteolysis and enhances the synthesis of alanine, sensitizes adipose tissue to the action of lipolytic hormones (growth hormone and catecholamines). In addition, cortisol has an anti-inflammatory effect, suppressing the synthesis of leukotrienes.

Cortisol lowers peripheral vascular resistance, increases cardiac output and improves tissue blood flow, leads to fluid and sodium retention with kidneys and inhibits the action of insulin. All this combined with gluconeogenesis in the liver causing hyperglycemia. Elevated concentration of cortisol in the blood can suppress the immune system, which increases the risk of infection and worsens wound healing.

Determination and evaluation of cortisol levels in the blood can serve as a marker of surgical stress and antinociceptive protection of the body.

According A. T. Crozier et al. (1994) plasma cortisol level is independent of the degree of emotional stress and the type of anesthesia, while for most other hormones the effect of anesthesia is significant. Hyperoperations stress of coronary surgery overcomes the inhibition of cortisol synthesis caused by etomidate anesthesia-fentanyl [16].
Mirjana Kendrisic et al. (2016) in their studies found that during surgery on the hip joint the level of stress hormones were changed besides it has depended on the used kind of the anesthesia [17].

Metabolic effects of endocrine response
The general metabolic effect of hormonal changes caused by surgical trauma is contained in the enhancing of the processes of catabolism with the mobilization of energy substrates, as well as water and salt retention.

Water-electrolyte changes are aimed at maintaining of the adequate volume of circulating fluid. Stimulation of anti-diuretic hormone (ADH) provides water retention by increasing the concentration function of the kidneys. Elevated levels of ADH are maintained for 3-5 days after surgery and depend on its traumatic volume.

As a result of the combined action of catecholamines, cortisol, glucagon and reduced insulin secretion during and after surgery, glucose utilization by peripheral tissues is reduced, gluconeogenesis and glycogenolysis are activated. As a result, hyperglycemia develops, the severity and duration of which are dependent on the trauma and duration of operation.

A typical reaction of water-electrolyte metabolism to surgical trauma is water and sodium retention, aimed at maintaining the volume of circulating blood. This comes at the expense of increase of secretion of vasopressin with posterior lobes of the pituitary gland and the sympathetic activation of the renin-angiotensin-aldosterone system.

The negative nitrogen balance during the catabolic phase of the postoperative period is the result of the disturbed balance between protein synthesis and decomposition. The shift of this balance towards decay appears because of the activation of one or more elements of the classical hormonal stress response [18].

Systemic inflammatory response
Any injury is accompanied by the development of local inflammation, which leads to limit and eliminate irreversibly damaged tissues being the basis of the recovery process.

The inflammatory response is a systemic reaction of the body to tissue damage or other pathogenic factor, as well as a necessary condition for the structural and functional recovery of damaged tissue. However, it is a "double-edged sword". Excessive generation of proinflammatory impulses, which occur in a number of clinical situations, exacerbates the processes of tissue damage due to the massive release of

inflammatory mediators. The release of vasoactive mediators (histamine, leukotrienes) from mast cells, as well as platelet and plasma components (bradykinin), causes vasodilation and increases vascular permeability with the formation of classical signs of inflammation (redness, edema, pain etc.).

The local inflammatory reaction is manifested by vasodilation, infiltration of the liquid part of the blood from the capillaries, appearance of thrombus, release and mobilization to the wound a significant amount of lysosomal enzymes, vasoactive amines, prostaglandins, granulocytes and mononuclear cells.

Activated leukocytes, particularly monocytes, as well as local fibroblasts and endothelial cells produce cytokines. In addition, neutrophils generate active oxygen metabolites (active radical of oxygen, peroxide etc.) using nicotine adenine dinucleotide phosphate (NADP) oxidase or myeloperoxidase enzyme complexes. The formation of free radicals increases oxygen consumption, this phenomenon is called "re-helical surge".

Cytokines have pleiotropic biological effects on various types of cells, mainly participating in the formation and regulation of protective reactions of the body. Synthesized in the focus of inflammation cytokines affect almost all cells involved in the development of inflammation, including granulocytes, macrophages, fibroblasts, endothelial cells and epithelium, and then T - and B-lymphocytes. Within the immune system cytokines carry out the relationship between nonspecific protective reactions and specific immunity, acting in both directions. At the level of the body cytokines carry out communication between the immune, nervous, endocrine, hematopoietic and other systems and serve to involve them in the organization and regulation of a single protective reaction [19].

Cytokine production reflects the trauma of surgery [20].

Opportunities of correction of surgery-induced stress reaction

Taking into account the dependence of the intensity of the surgical stress response on the trauma of the operation the most obvious way to its limitation is to reduce the invasiveness of surgical interventions.

Attempts are made to influence the surgical stress response using different methods of surgery and different types of anesthesia.

In connection with the introduction of laser technologies in surgical dentistry, interest is to consider the effect of laser on surgical stress response.

The use of laser in surgical dentistry can improve the efficiency of treatment of patients. Surgical laser technologies are increasingly used in surgical dentistry, because they have a number of advantages over traditional methods of treatment [21].

When laser light interacts with biological tissues, a large number of physical and biological effects are observed.

Different lasers interact differently with tissues of the organism. Depending on the absorption coefficient, the laser beam has features that lead to variable interaction with the target tissue and absorption of its radiation.

Operations performed with a laser do not contradict the standard procedures used in surgical treatment. However, using a surgical laser there are a number of advantages proven by previous clinical studies. According to the researches, the use of laser radiation has a positive effect on the course of surgical operations and subsequent healing of the wound surface [22].

The authors note that during laser operations there is a coagulation of vessels, bactericidal effect, reducing of swelling, hyperemia and pain in the postoperative area, which improves the quality of life of patients in the postoperative period. In addition, the laser beam has an immunomodulatory effect and accelerates the regeneration of the oral mucosa [23].

According to clinical studies, nearly all patients report no or less pain after laser surgery compared to patients who had undergone surgical intervention with standard surgical instruments.

CONCLUSION:

The development of surgical stress response in high-trauma operations is directly related to clinically significant and requiring correction of homeostasis disorders, as well as to the occurrence of serious complications associated with changes in neuroendocrine status, metabolism and immunity. Despite the existence of many ways of the correction of individual parts of the surgical stress response, the most promising possibility of its limitation is the use of laser radiation. The most significant mechanism of the stress-limiting effect of laser radiation is the minimally invasive effect on the tissues of the surgical field. At the same time, the question of the optimal degree of limitation of the surgical

stress response and accordingly the criteria for the adequacy of the stress-limiting effect of laser radiation remains open.

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Abbreviation
ACTH – adrenocorticotropic hormone
ADH – anti-diuretic hormone
CNS – central nervous system
NADP – nicotine adenine dinucleotide phosphate

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