Section 6. Medical science

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ERECTILE DYSFUNCTION AS A LOCAL MANIFESTATION OF SYSTEMIC HORMONAL AND METABOLIC DISORDERS

Abstract: This article presents the latest research data on erectile dysfunction. It addresses the issues of mitochondrial dysfunction, leading to increased oxidative stress and progression of endothelial dysfunction. Systemic hormonal and metabolic disturbances are considered to be hypothalamic dysfunction, and erectile dysfunction is a local manifestation.

Keywords: erectile dysfunction, mitochondrial dysfunction, hypothalamus dysfunction.

The well-known pattern of erectile dysfunction (ED) is a polyetiological organic progressive chronic disease of the cavernous bodies of the penis with a multifactorial neuro-vasculo-hormonal pathogenesis due to endothelial dysfunction [1]. ED is defined by the development of the inability of a man to maintain and achieve an adequate erection of the penis for full sexual intercourse. The key mechanisms of the pathogenesis of ED are psychoneurogenic (non-vascular)/arterial infringement disorders/impaired venous outflow [2]. It is regrettable that in the most cases a narrow approach to ED (viewing it as an organ pathological process) still dictates main pharmaceutical principles of ED treatment. Moreover, mainly selective drugs that affect local symptoms (phosphodiesterase-PDE inhibitors; E1 prostaglandins; α -1 and α -2- adrenoblockers, herbal medicinal products, bioregulatory peptides, biologically active food supplements). One of the ED paradoxes is the symptomatic treatment. Why do not we use effective pathogenetic drugs to treat patients with ED, when we know that ED is only a local manifestation of a systemic pathological process?

The second ED paradox is that modern data shows whole ED development occurs in conditions of progressive endothelial dysfunction, then there are no screening and screening of oxidative stress and mitochondrial disorders in any of the modern guidelines for managing patients with ED?

The researches have established the involvement of damaged mitochondria in the development of endothelial dys-

function, activation of programmed cell death processes in atherosclerotic plaques, which leads to a violation of their stability and the initiation of local thrombogenesis. Objective data were obtained indicating the development of structural and functional disorders in the mitochondria of endothelial cells, smooth muscle cells, monocytes and macrophages in the atherogenic process [3; 4].

It has been established that mitochondrial dysfunction is a major factor in the formation and maintenance of a wide range of urological diseases (shrinking processes in the urinary bladder, chronic prostatitis with chronic pelvic pain syndrome, renal failure, erectile dysfunction, male infertility, hyperactive bladder, etc.) [5].

Mitochondrial dysfunction is accompanied by excessive formation of free radicals and oxidative stress. Today, it is proven that oxidative stress is the universal mechanism of many diseases [6; 7].

Mitochondrial dysfunction is a typical pathologic process that develops in presence of many different pathologies caused by various pathogenic factors. They do not have etiological and nosological specificity and are a special concept in relation to a particular disease, being included in it as one of its elements and mechanisms, and may develop in many different diseases [8].

The most common factors that cause secondary mitochondrial dysfunction are hyperglycemia, dyslipidemia, the formation of protein aggregates in cells, tissue ischemia/re-

perfusion, and toxic damage [9–11]. As a result of mitochondrial dysfunction, the level of adenosine triphosphate acid in the cell decreases, the production of reactive oxygen species increases, and the cell death mechanisms are activated.

It is known that hormonal metabolic homeostasis (integration and regulation of autonomic, metabolic, endocrine and trophic functions) is controlled by the hypothalamus. This part of the brain has the most developed vascular system, with a strong capillary network, characterized by the highest permeability for large-molecule protein compounds. The hypothalamus is very sensitive to various kinds of disorders: intoxication, infections, disorders of circulation and cerebral fluids circulation, as well as pathological impulses from other parts of the central nervous system.

Those noxas cause mitochondrial dysfunction of the hypothalamus cells. Over time, unidirectional disorders with a reduced or elevated tone of the autonomic nervous system are added to progressive dysfunction of the hypothalamus. Increased tone of the neurohormonal system is characterized by the predominance of the sympathetic orientation of the vegetative reactions; lowered tone – by the predominance of parasympathetic vegetative reactions. The state of balance between these two systems determines the body's response to various factors.

Hormonal imbalances caused by hypothalamic dysfunction develop not at the same time and in a long period.

Hormonal imbalances caused by hypothalamic dysfunction develop have two ways of development based on tone of neurohumoral systems:

- changes in the tone in the hypothalamus are primary – as a result of these noxas, an organ dysfunction develops;
- changes in the functions of the organs are primary – as a result of constant irritating impulses from the organs, dysfunctions of the hypothalamus develop.

Psychologic, somatic and emotional overloads, high amount of xenobiotics and toxins in the body, violation of intestinal microflora – all these factors that affect a man's body for months and years lead to functional disorders of the hypothalamus. Without elimination of these factors in time, by the age of 30 many modern men can detect endothelial dysfunction of the cavernous arteries, which at this age in most cases remains asymptomatic, and therefore undiagnosed and untreated. The progression of dysfunction of the hypothalamus with hormonal imbalance leads to the predominance of the sympathetic vegetative reactions. This is linked with an increase in the synthesis and release of the tropic hormones of the pituitary and an increase in the release of the catecholamines of the adrenal cortex.

It is known fact that catecholamines activate muscle and liver glycogenolysis, as well as stimulate lipolysis in adipose tissue, which increases glucose and fatty acids content in the blood plasma. Hyperglycemia increases insulin secretion (hyperinsulinemia), which leads to the growth of vascular endothelium and hyperplasia of smooth muscle cells of the vascular wall, which narrows the lumen of the vessels and the violates microcirculatory hemodynamics. The erosion of insulin concentration in time at the periphery occurs, which increases the duration of hyperglycemia. Through the control system, the pancreas receives a signal to increase insulin synthesis, which leads to prolonged hyperglycemia and hyperinsulinemia. A deeper violation of hemodynamics (vicious circle) and the emergence of relative insulin deficiency occur.

Hypothalamic dysfunction causes a progressive increase in the frequency of hormonal-metabolic and psychosomatic disorders in modern men. Hypodynamia and improper diet causes obesity development, which nowadays affects even younger people and has become the most important mechanism for the pathogenesis of most diseases, including metabolic syndrome, type 2 diabetes, cardiovascular diseases [12–15].

Later, the deepened noxas (psychologic, somatic and emotional overloads, xenobiotics, toxins, intestinal dysbiosis) at the age of 40–45 years some new hormonal imbalances develop. These are age-related androgenic deficiency, accompanied by estrogen balance disorders, as well as the age-related phenomenon of hyperinsulinemia/insulin resistance. Their synergism causes obesity progression, endothelial dysfunction worsening, systemic chronic inflammation, cellular and tissue hypoxia increase. As a result, many men of 40–45 years can already show organic signs of ED.

Conclusion

In summary, an integrative approach to ED, based on an analysis of modern mechanisms of disease pathogenesis, makes it possible to clearly understand that all local pathological processes accompanying ED are inextricably linked with systemic age-related neuro-hormonal imbalances, which have a simultaneous effect on the cavernous metabolism of the penis, so on systemic aging men in general. This approach makes it necessary for modern urology to form a new interdisciplinary view of ED as a hormonal and metabolic disease with systemic pathogenesis and local clinical manifestations. This will require fundamental changes in traditional narrow approaches to pharmacotherapy and prevention of this common age-related disorder.

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