THE ROLE OF 24-HOUR AMBULATORY BLOOD PRESSURE MONITORING IN THE ASSESSMENT OF ARTERIAL HYPERTENSION IN PATIENTS WITH ULCERATIVE COLITIS

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Abstract

Cardiovascular diseases, including atherosclerosis and arterial hypertension, are a priority for the World Health Organization. Indeed, cardiovascular disease is the leading cause of death, accounting for one third of deaths worldwide. A growing body of evidence shows that the pathogenesis of hypertension is closely linked to dysbiosis of the intestinal microbiota. When the intestinal barrier function is normal and intestinal permeability is low, it can effectively prevent the leakage of intestinal pathogens, enteroendotoxins and other substances into the body, thus reducing acute and chronic inflammation in all organs. Ulcerative colitis, which is an inflammatory bowel disease, is believed to occur in people with a genetic predisposition after exposure to environmental factors; defects in the intestinal epithelial barrier, changes in the microbiota and dysregulation of the immune response.

Given the relevance of the topic, this article describes the mechanisms that affect the intestinal microbiota in patients with hypertension and ulcerative colitis, as well as the 24-hour ambulatory blood pressure monitoring to understand the cause of high blood pressure in patients with ulcerative colitis.

Keywords: cardiovascular system, cardiovascular diseases; blood pressure; arterial hypertension; 24-hour ambulatory blood pressure monitoring; intestines; ulcerative colitis.

Main text.

Arterial hypertension (AH) remains the most common risk factor for cardiovascular disease (CVD) [1]. It affects more than one billion adults worldwide, and 10% of global healthcare costs are directly related to hypertension and its complications [2].

The prevalence of AH among adults is higher in low- and middle-income countries (31.5%, 1.04 billion people) than in high-income countries (28.5%, 349 million people) [3]. AH is a complex disease that is influenced by genetic and environmental factors, such as physical inactivity, obesity, alcohol consumption, smoking, stress, diet, and microbiome [4]. Both genetic and environmental factors act through changes in the regulatory systems of the cardiovascular system (CVS), leading to an increase in systemic vascular resistance, which is a characteristic feature of the haemodynamic abnormality responsible for the increase in blood pressure (BP) in almost all patients with AH. Over the past few years, important new evidence has been obtained for the genetically determined development of AH, with the identification of biochemical and pathophysiological pathways through which they act. Environmental factors such as polluted air and noise can influence the development of AH. In addition, new experimental and clinical studies have confirmed that changes in several major cardiovascular control systems can contribute to chronic AH [5].

A growing body of evidence suggests that the pathogenesis of AH is closely linked to dysbiosis of the intestinal microbiota [6]. The human microbiome refers to the community of microorganisms that live in or on the human body. They influence human physiology by interfering with a number of processes, such as the provision of nutrients and vitamins. The gut microbiota contributes to blood pressure homeostasis and the pathogenesis of AH by producing, modifying, and degrading various microbial bioactive metabolites [7]. Metabolites derived from the microbiota are either beneficial (e.g., short-chain fatty acids and indole-3-lactic acid) or

harmful (e.g., N-trimethylamine oxide) and can activate several signalling pathways through G-protein-coupled receptors or by direct activation of immune cells [8]. When the function of the intestinal barrier is normal, intestinal permeability is low, which can effectively prevent intestinal pathogens, enteroendotoxins and other substances from leaking into the body, thus reducing acute and chronic inflammation in all organs [9], and to a certain extent reducing inflammatory damage to blood vessels and lowering blood pressure. Intestinal barrier dysfunction refers to an abnormal change in intestinal permeability and structural damage to the intestinal mucosa caused by various causes, which leads to the movement of bacteria and toxic products into the bloodstream and causes systemic inflammation [10]. These changes lead to endothelial cell dysfunction and vascular sclerosis, thus causing or exacerbating the development of AH [11]. In addition, intestinal barrier dysfunction can affect the growth of beneficial gut microflora, leading to an imbalance in the gut microbiota and an increase in intestinal pathogenic bacteria and lipopolysaccharides. These harmful substances can enter the bloodstream through the mesentery, which further increases blood pressure [12].

The mucous layer and intestinal epithelium are the first physical and chemical barriers against intestinal bacteria, pathogens and food antigens. Dysregulation of the mucosal immune response, characterised by changes in the innate immune system, activation of effector T-cells, increased presence of B-cells and antibody production, and increased production of pro-inflammatory mediators, plays an important role in the pathogenesis of inflammatory bowel disease (IBD) [13].

IBD is a chronic, progressive immune-mediated inflammatory condition of the gastrointestinal tract. Environmental risk factors play a role in the development of any type of IBD, Crohn's disease and ulcerative colitis (UC) [14]. Although the exact cause of IBD is still unknown, it is hypothesised that individuals with a genetic predisposition may develop IBD when exposed to environmental factors, altered gut microbiome and dysregulated immune response [15].

UC is a lifelong inflammatory disease that affects the rectum and colon to varying degrees. In 2023, the prevalence of UC was estimated at 5 million cases worldwide, and the incidence is increasing. It is believed that UC occurs in people with a genetic predisposition after exposure to environmental factors; defects in the intestinal epithelial barrier, changes in the composition of the microbiota and dysregulation of the immune response [16]. Thus, the intestinal microbiota plays an important role in the homeostasis and functioning of the immune system. It is currently believed that various environmental and genetic factors may contribute to changes in this microbiota. The formation of pathogenic microflora in genetically predisposed individuals is associated with changes in epithelial function, impaired gastrointestinal immune function and persistent intestinal inflammation, and the entry of toxins into the vascular bed through defects in the intestinal epithelial barrier [17].

The development of AH is often triggered by stress. Stress controls the autonomic response by stimulating the sympathetic nervous system, which causes the adrenal medulla to secrete excess adrenaline and norepinephrine, subsequently causing central and peripheral tissues to over-secrete inflammatory mediators, or pro-inflammatory cytokines. The intestine is well innervated, which is called the enteric nervous system. Neurons of the sympathetic and parasympathetic nervous system communicate with the nerves of the intestine, forming a complex neural network called the brain-gut axis. The enteric nervous system contains a large number of neurons that are responsible for regulating many functions of the gastrointestinal tract. Stress-induced activation of the sympathetic nervous system excites the enteric nervous system and increases the density of nerve fibres and the number of cholinergic neurons in the intestinal mucosa, which leads to increased permeability of the intestinal epithelium. Clinical studies have shown that lesions in patients with UC have a greater number of submucosal nerve plexuses and increased epithelial permeability [18].

Thus, AH and UC share some common etiological factors, genetic predisposition, and environmental influences. Stress worsens the course of each other, which is due to an increase in the permeability of the intestinal epithelium, leading to a vicious circle.

Current guidelines for AH recommend using the average of several blood pressure (BP) readings obtained both in and out of the office for the diagnosis and treatment of hypertension. In-office BP measurement using an upper arm cuff is the evidence-based reference method for current BP classification and treatment goals. However, out-of-office BP assessment using ambulatory BP measurement or home BP monitoring is recommended by all major medical associations to obtain additional information about a person's BP profile and its relationship to daily activities [19].

This study complies with international regulations and laws of Ukraine: «Fundamentals of Ukrainian Healthcare Legislation» (1993), «On Medicines» (1996), «On Personal Data Protection» (2010). The clinical trial was approved by the Ethics Committee of the Shupyk National Healthcare Institution of Ukraine (protocol № 6, dated 03.10.2022).

All patients were explained the essence and stages of the study, and patients signed informed consent to participate in the clinical trial. The study was conducted in compliance with the principles of bioethics and legal requirements: The Declaration of Helsinki (2000) and Ukrainian legislation, and participation was voluntary and anonymous. It was possible to refuse to participate in the study at any stage, with the subsequent receipt of the necessary medical care. The presented research is a fragment of the dissertation for the degree of Doctor of Philosophy at the Department of Therapy of the Shupyk National University of Health of Ukraine on the topic: «Minimally invasive methods of diagnosis and evaluation of the effectiveness of treatment in patients with ulcerative colitis and concomitant arterial hypertension».

The dissertation is a fragment of the research work of the Department of Therapy of the Shupyk National

University of Health Care of Ukraine on the topic: «Clinical and pathogenetic aspects of diagnosis and treatment of patients with combined pathology of internal organs (diseases of the cardiovascular system, digestive system, endocrine system)», state registration number 0119U101507, term of implementation 2019-2025.

This study included 142 patients and 30 healthy individuals. In 96 patients, UC was confirmed clinically, endoscopically and pathologically. During 24-hour ambulatory blood pressure monitoring, 95 patients were diagnosed with AH. Of these, 49 patients had UC + AH and 46 patients had AH without UC. 47 patients out of 142 had UC without concomitant AH. Table 1 shows the patients' age and blood pressure values.

Table 1.

Patients' age and blood pressure values

Parameter	Group	N	M	Me	SV	MIN	MAX
Age, years	UC + AH	49	39,90	38	12,49	19	59
	UC without AH	47	40,17	41	10,82	19	59
	AH without UC	46	40,41	40,5	11,97	20	57
SBP, mmHg	UC + AH	49	153,02	153	7,25	142	170
	UC without AH	47	126,49	127	8,43	110	137
	AH without UC	46	151,28	150	5,81	142	165
DBP, mmHg	UC + AH	49	96,02	95	4,25	85	107
	UC without AH	47	80,98	83	6,59	65	95
	AH without UC	46	95,17	95	4,05	84	106

Notes:
SBP – systolic blood pressure
DBP – diastolic blood pressure
M – arithmetic mean
Me – median
SD – standard deviation
MIN – minimum value
MAX – maximum value

In 95 patients, 24-hour ambulatory blood pressure monitoring was successful: the number of reliable measurements (31 during the day and 8 at night, 93% in total) was satisfactory. In the UC+AH group, a rise in blood pressure was more often observed during tenesmus and during defecation. The manifestations of UC included bloody diarrhea with or without mucus, rectal urgency, tenesmus, and abdominal pain of varying degrees, which often decreased during the defecation. Patients recorded their poor health and the feeling of high blood pressure in a notebook. In the group of AH without UC, blood pressure rose more often during emotional overload and the white coat effect was observed.

Conclusions.

AH is an important public health problem because it is associated with a number of serious diseases, including CVD and stroke. The importance of assessing hypertension taking into account different BP profiles and BP variability is becoming increasingly important. Daily BP monitoring is the gold standard for diagnosing AH and assessing 24-hour BP and provides data on several important parameters that cannot be obtained using any other form of BP measurement [20]. Given the close relationship between the development of hypertension in patients with UC, careful monitoring of BP in IBD is necessary. In the present observations, we found a close relationship between the rise in BP directly during the act of defecation in UC. Given the frequent urge to defecate and the feeling of stress in patients with UC, dynamic monitoring of BP and timely correction of hypertension treatment along with the achievement of remission in UC are necessary.

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