Orthostatic Hypotension in Older Adults

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Preface

Orthostatic hypotension (OH) is defined as a certain amount of decrease in blood pressure in the first 3 min of transition from the supine position to the upright position. The prevalence, which increases with advancing age, varies between 20% and 30% in patients over 65 years of age. Besides, it is a medical problem resulting from the deterioration of the adaptation ability of the body with advancing age.

OH is associated with various adverse health outcomes, such as coronary heart disease, congestive heart failure, stroke, falls, dementia, and all-cause mortality. On the other hand, a range of comorbidities, which are common in older adults, and several medications may also play a role in the development of OH.

With multiple etiologies, OH is a significant cause of morbidity and mortality in the elderly. Therefore, it may be referred to as a geriatric syndrome that affects daily life activities and impairs quality of life. For this reason, in order not to overlook OH in the elderly, postural blood pressure changes should be evaluated routinely, as an essential part of the comprehensive geriatric assessment.

We decided to prepare the book *Orthostatic Hypotension in Older Adults* in order to examine OH in all aspects, which is such an important health problem for geriatric patients and to discuss the most rational approaches in this regard. It is our greatest happiness that the book will complement an important deficiency in geriatric practice.

We would like to thank all the scientists for their valuable contributions to the creation of the book by preparing the relevant chapters in the light of their knowledge and experience.

We wish that the book *Orthostatic Hypotension in Older Adults* will be beneficial to scientists and health professionals related to the subject.

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Fatma Sena Dost Gunay and Ozge Dokuzlar

1.1 Introduction

Orthostatic tolerance is a term that defines the ability to prevent hypotension during gravity stress. [1]. First, maintaining postural balance and homeostasis requires the integration of sensory information through proprioception, visual and vestibular pathways [2]. Visual and vestibular stimulation is confounded by proprioceptive input from stretched legs and joint and this integration is important for postural stability, blood pressure, and muscle activity [3]. The regulation of blood pressure (BP) depends on the proper function of the muscle pump, cardiac, renal, neural (parasympathetic and sympathetic nervous systems, baroreflex), and endocrine systems [4, 5].

1.2 Mechanisms of Orthostatic Tolerance

1.2.1 Cardiac Mechanism

In the upright position due to the gravity, 500–700 mL of blood translocates from the upper body to the lower limbs and splanchnic circulation and approximately 10% of the intravascular plasma shifts towards the extravascular space [6, 7]. Venous return and ventricular filling decrease because of that mechanism. Reduction of ventricular filling results in decreased cardiac output and BP. Ventricular filling pressure (end-diastolic volume) indicates the left ventricular end-diastolic diameter. Changes in leftventricular end-diastolic diameter alter the ability of the leftventricular force and thereby stroke volume (SV) [8]. This situation is based on Frank-Starling relationship. Increased end-diastolic volume causes increased sarcomere

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length and powerful contraction of the left ventricle. There is a relationship between stroke volume and sarcomere length to a degree [9]. In the upright position due to reduced venous return, end-diastolic volume decreases. Decreased end-diastolic volume and sarcomere length causes diminished stroke volume. The normal heart maintains its output by several mechanisms, such as Frank-Starling relationship, increasing heart rate, peak force, and elevation of afterload [10]. There is a two-part increase in BP, one of which is splanchnic vasoconstriction and the other is increased heart rate [11]. Increased heart rate is due to increased adrenaline secretion [12].

1.2.2 Parasympathetic and Sympathetic Nervous Systems (Baroreflex)

Baroreceptor stimuli cause baroreflex (BR). Baroreceptors are sensitive to pressure and strain and are located in the heart's auricles, heart fat pads, vena cava, aortic arch, and carotid sinus wall. As a result of baroreceptor stimulation, the parasympathetic nervous system is activated, while the sympathetic nervous system is inactivated [13]. In the upright position, the ventricular wall tension decreases as a result of the decrease in the ventricular volume. In this case, BR is a typical compensatory reflex mechanism to a reduction in stroke volume, which is manifested by increased heart rate, cardiac contractility, and peripheral vascular resistance [3]. Cardiac BR is responsible for the heart rate and sympathetic BR for BP [14]. Vagal withdrawal and activation of the sympathetic nervous system are the basis of the baroreflex. This mechanism helps restore cardiac output and BP for a few beats [15]. After this short-term compensation, the muscle pump mechanism is activated to maintain blood pressure.

1.2.3 Muscle Pump Reflex

During upright position, skeletal muscles (especially lower extremity muscles) help to maintain venous return by compressing the veins, which is called a skeletal muscle pump mechanism. The muscle pump mechanism is very effective, so a single muscle contraction may direct more than 40% of the intramuscular blood volume to the venous return [16]. Even while standing silently, the lower limb muscle tension and this rhythmic activity act to maintain balance and reduce the amount of blood redistributed due to gravity [17]. In the upright position, muscle pump mechanism after short-term cardiac compensation is the most important mechanism for the maintenance of BP.

1.2.4 Renal and Endocrine Systems

When blood pressure drops below normal, decreased blood pressure directly affects the kidneys, increasing water and salt retention. A decrease in arterial pressure causes an increase in the secretion of aldosterone.

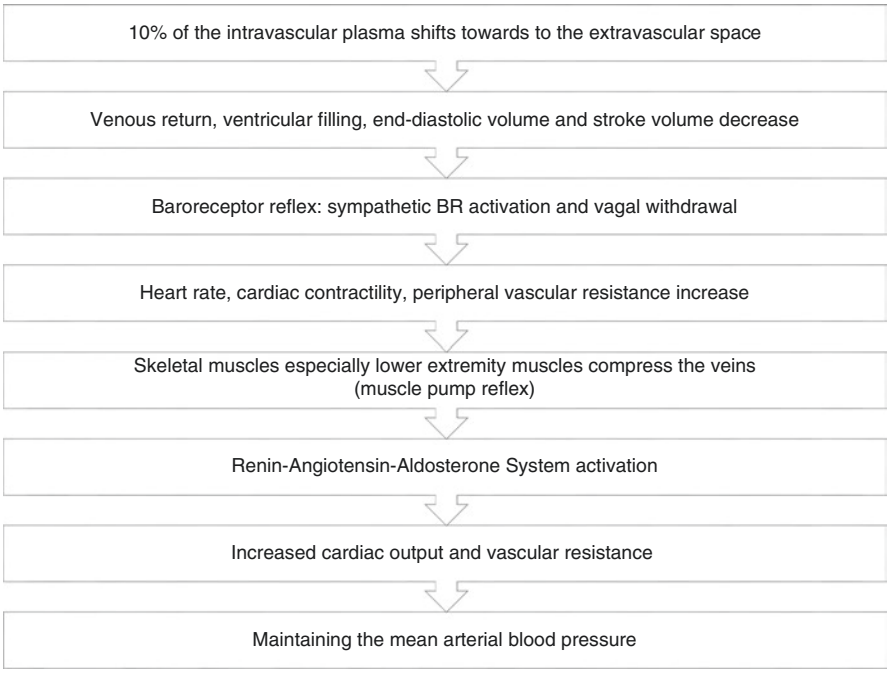

Fig. 1.1 Response mechanism in the uprightposition

First of all, arterial pressure drop increases renin release from juxtaglomerular cells. Renin increases the secretion of angiotensin, which stimulates aldosterone secretion from the adrenal gland. A decrease in blood pressure also directly causes aldosterone secretion which increases water and salt retention from renal tubules. Increased salt absorption increases water retention by increasing antidiuretic hormone (ADH), leading to vasoconstriction with the action of ADH. The increase in body fluid volume, in turn, returns the arterial pressure toward normal [18] (Fig. 1.1).

1.3 Age-Related Changes in Orthostatic Challenge

Aging brings about many physiological differences in the body that cause both structural and functional changes. Therefore, with advancing age, it is difficult to provide the homeostatic balance against stress factors [19]. Age-related decreases are observed in orthostatic tolerance mechanisms as in many other systems [20]. Vision and vestibular systems are of great importance in the upright position. With aging, the deterioration of visual functions affects perception and the activities of older adults [21]. Vestibulosympathetic reflex also deteriorates in older adults, and maintaining arterial blood pressure in the upright position becomes more difficult [22]. All three phases of the orthostatic challenge: [1] an initial heart rate rise and

blood pressure drop, [2] an early phase of stabilization, and [3] a phase of prolonged stabilization are influenced by aging [23].

There is a progressive decline in cardiovagal baroreflex sensitivity with aging, which leads to an inadequate heart rate response to a change in blood pressure. Although all of the underlying mechanisms are not clear, arterial stiffness in the baroreceptor-containing segments (such as carotid artery and aorta), decreased cardiac cholinergic response, and oxidative stress are some of the causes. In contrast to this decline in vagal baroreflex sensitivity, no age-related changes were observed in the baroreflex-mediated sympathetic outflow [24]. However, in older age, the number of pacemakers in the sinoatrial node decreases. Also, a decrease in beta-adrenoreceptor-mediated response to norepinephrine is observed. This may be due to beta-adrenoreceptor downregulation caused by high norepinephrine levels. Another cardiac change is decreased diastolic filling due to a decrease in cardiac compliance and preload. In the absence of compensatory cardioacceleration, the reduction of preload may cause a remarkable reduction in cardiac output [20, 25, 26].

In an upright position, a concurrent increase in peripheral vascular resistance is important to maintain blood pressure regulation additively to baroreflex-mediated cardiac compensation. However, another impaired orthostasis mechanism in older adults is the reduced vasoconstrictor response to alpha 1-adrenergic stimulation and the absence of an expected increase in peripheral vascular resistance. Although the responsible mechanisms are not clear, a decrease in vascular compliance due to atherosclerosis, deterioration in norepinephrine re-uptake and release, and a decrease in the number of alpha receptors in vascular smooth muscle are the possible causes [27] (Fig. 1.2).

Aging impairs not only autonomic regulation but also skeletal muscle function. While standing, in addition to the autonomic control of blood pressure, the lower leg muscles play an important role in maintaining blood pressure by pumping the pooled venous blood back to the heart. Also, according to known mechanical muscle pump knowledge to push venous blood back into the heart, activation of leg muscles has been shown to depend on blood pressure fluctuations, i.e.,

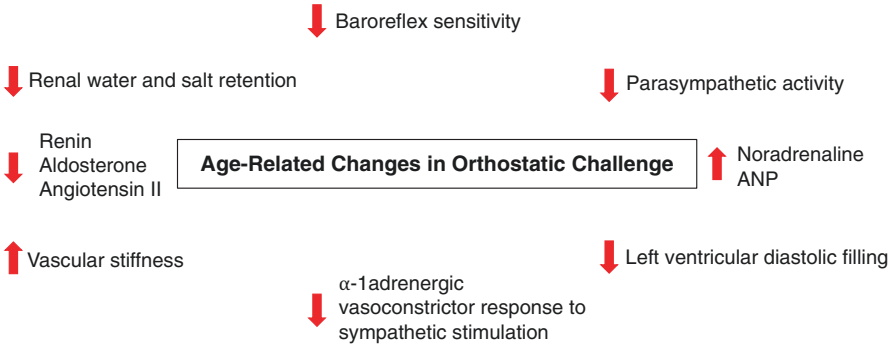

Fig. 1.2 Mechanisms of age-related changes in orthostatic challenge

muscle-pump baroreflex. Therefore, the postural system (leg muscle activation) also contributes to orthostasis while standing. However, studies have found that in older adults, muscle pump baroreflexes, especially in lateral gastrocnemius and soleus muscles, are lower than younger ones. These findings can be important to improve specific exercise or training strategies to restrain aging-related impairment in muscle-pump baroreflexes [28]. Neuroendocrine changes are the other compensator mechanisms for hemodynamic homeostasis, especially in long-term maintenance. However, it is known that the activity of RAAS decreases with advancing age. Both absolute levels and responses to stimulation of plasma renin and angiotensin II concentrations decrease. Some reasons for the decrease are nephrosclerosis, reduced renal mass, and impaired juxtaglomerular cell function in the aging kidney. On the other hand, a strong renin and aldosterone secretion inhibitor ANP plasma levels increase with advancing age. This is another cause of RAAS inhibition [29]. In addition, the feeling of thirst decreases with age, and the aging kidney reduces the ability to concentrate urine; therefore, older adults become inclined to dehydration. Of course, dehydration is an important risk factor for orthostatic intolerance [20, 29].

Orthostatic hypotension (OH) is common in older adults due to the inadequacy of the mentioned mechanism, and OH is closely related to mortality and morbidity [30].

1.4 Conclusion

Aging is a risk factor for orthostatic intolerance with its physiological changes. Therefore, we should avoid additional interventions and treatments that could adversely affect homeostatic mechanisms maintained at the border to protect older adults from orthostatic hypotension.

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Orthostatic Hypotension: A New Geriatric Syndrome

2

Pinar Soysal and Ahmet Turan Isik

The life expectancy and world population have started to increase significantly in parallel with the developments in science, technology, and health since the mid-nineteenth century and led to the emergence of geriatrics discipline in the early twentieth century. In addition, due to age-related changes that occur with advancing age, general Hippocratic medicine has been replaced by syndromal medicine and the concept of "geriatric syndromes" has emerged [1]. Unlike the concept of "disease," geriatric syndromes occur due to multifactorial causes.So far, dementia, delirium, depression, incontinence, falls, polypharmacy, malnutrition, pressure sores, sarcopenia, and frailty have been accepted as geriatric syndrome [1]. In a study involving 2816 older patients, it was found that prevalence was 54.5% for polypharmacy, 47.6% for urinary incontinence, 9.6% for malnutrition, 35.1% for depression, 21.6% for dementia, 33.6% for falls, 31.7% for sarcopenia, 28.3% for frailty, and 1.1% for pressure ulcers. In the same study, all geriatric syndromes, except for depression and pressure ulcers, were determined to be significantly more common with advancing age [1].While the rate of having four or more syndromes in the same person was 27.1%, 12% had no geriatric syndrome, 22.9% had one syndrome, and 21% had two syndromes. In particular, the frequency of having three or more syndromes in the same age group at ≥80 years was calculated as 68.8% [1].

Common Features of Geriatric Syndromes

1. The frequency increases with age.
2. Multiple pathological processes accompany the event.

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3. Many causes play a role in etiology and are easily complicated.
4. Multiple organs are affected.
5. The clinic can be quite faint and atypical presentation is common.

Considering the common features of geriatric syndromes, the question arises whether orthostatic hypotension (OH) can also be a geriatric syndrome.

2.1 Is OH a Geriatric Syndrome?

1. Does the frequency increase with age?

   In a review that examined the age-related increase of OH prevalence and the results of two separate epidemiological studies, it was stated that changes such as increase in age and vascular stiffness associated with age, decrease in baroreflex sensitivity, and decrease in beta adrenoreceptor response may increase OH development [2].The first of these studies was conducted by Rose et al. involving 12,433 people between the ages of 45 and 65, and it was shown that the frequency of OH increased compared to the five-year age ranges and after 6 years of follow-ups, it was found that cardiovascular mortality was higher in those with OH. In the second study by Rutan et al., it was found that in 5201 people over 65 years of age, OH increased with age (that it has increased exponentially especially after the age of 80) and the presence of OH was associated with the development of cardiovascular events when followed for 3 years [2–4]. There are many similar study results in the literature.
2. Do more than one pathological process accompany the event?

   Numerous factors play a role in the development of OH, just like other geriatric syndromes: [2, 5].

   - In arteries and veins, stiffness and curvature increase, and baroreceptor sensitivity decreases.
   - Cardiac hypertrophy due to old age and diastolic filling defect due to hypertension occur.
   - Renal sodium retention decreases.
   - Renin–angiotensin–aldosterone level decreases.
   - Sensitivity to hormones such as arginine and vasopressin decreases.
   - The maximum increase in heart rate expected during hypotensive maneuvers decreases with age. (In other parts of the book, the pathogenesis of OH is explained in more detail.)

3. Why are multiple factors involved in etiology and are they easily complicated?

   In addition to the numerous pathophysiological changes that occur with aging, some other factors may increase the severity of OH or cause the development of OH in someone who does not have OH before. These situations are generally evaluated under two headings as acute and chronic. Acute OH causes usually develop in a short time and are symptomatic, of which adrenal insufficiency, myocardial ischemia, drug applications, sepsis, and dehydration are