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Innovations Influencing Physical Medicine and Rehabilitation

Is Technology for Orthostatic Hypotension Ready for Primetime?

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Abstract

Spinal cord injury (SCI) often results in the devastating loss of motor, sensory, and autonomic function. After SCI, the interruption of descending sympathoexcitatory pathways disrupts supraspinal control of blood pressure (BP). A common clinical consequence of cardiovascular dysfunction after SCI is orthostatic hypotension (OH), a debilitating condition characterized by rapid profound decreases in BP when assuming an upright posture. OH can result in a diverse array of insidious and pernicious health consequences. Acute effects of OH include decreased cardiac filling, cerebral hypoperfusion, and associated presyncopal symptoms such as lightheadedness and dizziness. Over the long term, repetitive exposure to OH is associated with a drastically increased prevalence of heart attack and stroke, which are leading causes of death in those with SCI. Current recommendations for managing BP after SCI primarily include pharmacologic interventions with prolonged time to effect. Because most episodes of OH occur in less than 3 minutes, this delay in action often renders most pharmacologic interventions ineffective. New innovative technologies such as epidural and transcutaneous spinal cord stimulation are being explored to solve this problem. It might be possible to electrically stimulate sympathetic circuitry caudal to the injury and elicit rapid modulation of BP to manage OH. This review describes autonomic control of the cardiovascular system before injury, resulting cardiovascular consequences after SCI such as OH, and the clinical assessment tools for evaluating autonomic dysfunction after SCI. In addition, current approaches for clinically managing OH are outlined, and new promising interventions are described for managing this condition.

Introduction

Spinal cord injury (SCI) is a life-changing condition that results not only in motor and sensory consequences but also in autonomic dysfunction [1]. As a result of disrupted autonomic pathways after SCI, individuals with SCI (especially those with high thoracic and cervical injuries) develop cardiovascular dysfunction characterized by an extremely low resting blood pressure and difficulty in maintaining stable and appropriate blood pressure levels [2]. In addition to low resting blood pressure, people with SCI often experience orthostatic hypotension (OH), a sudden decrease in blood pressure when moving to an upright position [3]. In contrast, those with SCI also develop autonomic dysreflexia, which is an unregulated and extreme increase in blood pressure, occurring in response to painful or nonpainful afferent stimuli below the injury level [4]. The restoration of autonomic issues is often ranked higher in priority than walking again by individuals with SCI [5], and those with SCI are accordingly subject to a 3- to 4-fold increased risk for stroke and 3-fold increased odds for heart disease compared with uninjured individuals [6,7]. A recent systematic review and combined meta-analysis yielded a global incidence estimate of 763,473 new cases of traumatic SCI worldwide per year [8], and current trends also suggest an increasing time-related prevalence of traumatic SCI [9]. Approximate worldwide incidence for nontraumatic SCI currently is 12 to 76 cases per million population per year [10]. As such, it is imperative to target and prevent cardiovascular complications after SCI to improve the quality of life in this population and lower the incidence of heart disease and stroke. In this review, we provide an overview of the autonomic nervous system, discuss progress with the assessment of autonomic dysfunction after SCI, and specifically detail how the neuroanatomic changes occurring with SCI result in OH. Furthermore, we discuss the recommended guidelines for managing OH and the potential for neuroprosthetics to provide an efficacious therapy for this devastating secondary consequence of SCI.

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The Intact Autonomic Nervous System

The autonomic nervous system is composed of the sympathetic, parasympathetic, and enteric divisions, which are responsible for regulating unconscious systems [11]. The sympathetic and parasympathetic systems play a large role in the regulation of cardiovascular functions. In autonomic regulation, most of the vasculature is almost solely controlled by the sympathetic nervous system, which is the primary factor responsible for blood pressure regulation [12]. The sympathetic nervous system also plays a role in regulating heart rate [13] and contractility [14]. Conversely, the parasympathetic nervous system serves to regulate heart rate [13], cardiac contractility [15], and vascular tone in specific regions such as the genitals, gastrointestinal and salivary glands, and perhaps cerebral vasculature [16-18]. In general, activation of the sympathetic nervous system elevates vascular tone and cardiac contractility, and activations of the parasympathetic nervous system have the opposite effects [19].

The central autonomic circuitry, which is composed of the hypothalamus, cortex, brainstem, and spinal cord, interacts with the peripheral circuitry (autonomic ganglia and receptors) to regulate the sympathetic and parasympathetic nervous systems and blood pressure control [1]. Within the brainstem, the medullary neurons of the rostral ventral lateral medulla form a major cardiovascular area and provide descending sympathoexcitatory control over sympathetic structures, strongly influencing vascular tone and blood pressure [20-22]. These descending neurons project through the dorsolateral funiculus of the spinal cord to synapse on sympathetic preganglionic neurons (SPNs), most of which are located in the lateral horns of the spinal cord gray matter. The SPNs emanate primarily from thoracic and lumbar areas (T1 to L2), exit the spinal cord through the ventral root, and synapse with ganglionic neurons, which are located in the paravertebral (sympathetic chain ganglia) or prevertebral ganglia (celiac, superior, and inferior ganglia) [23]. Ultimately, this leads to innervation of target organs, such as the heart, blood vessels, sweat glands, and piloerectors [19]. Parasympathetic regulation of cardiovascular function is supraspinal and acts through the vagal nerve to innervate target organs. It has been widely accepted that sacral preganglionic cell bodies also are of parasympathetic origin; however, recent progressive evidence has countered this view by drawing a parallel between certain phenotypic and ontogenetic properties of sacral and thoracolumbar neurons and identifying the sacral autonomic outflow as sympathetic [24].

The baroreflex is a key cardiovascular reflex involved in the regulation of blood pressure, which modulates output of the autonomic nervous system to maintain blood pressure stability, such as during orthostatic challenges [25]. Two interdependent systems are known to regulate this reflex: a low-pressure system of cardiopulmonary stretch receptors that detect blood pressure decreases in central venous pressure and volume [26] and a high-pressure system composed of stretch receptors in the tunica adventitia of the aortic arch and carotid bulb [27]. Information regarding stretch (and, hence, pressure) from these afferent receptors is transmitted to supraspinal centers through the glossopharyngeal and vagal nerves to the nucleus tractus solitarius in the medulla oblongata, where it is integrated to modulate sympathetic and parasympathetic nervous system activity to maintain blood pressure stability. Baroreflex sensitivity determines the rate and magnitude with which efferent cardiovascular outputs can respond to afferent changes in vascular tone and blood pressure. Thus, greater sensitivity of the baroreflex may be more effective in modulating blood pressure, allowing more rapid and larger responses to an afferent stimulus [25].

Assessment of Autonomic Dysfunction after SCI

Evaluation of autonomic dysfunctions after SCI presents a challenging clinical issue: most currently available assessments are time consuming and require special equipment, and only limited evaluations can be done at the bedside. Recently, a team of international experts in autonomic dysfunction and SCI developed and proposed a structured bedside evaluation currently known as the International Standards to document remaining Autonomic Function after Spinal Cord Injury (ISAFSCI) [28]. It is recommended that this evaluation be conducted as an adjunct with the International Standards for Neurological Classification of Spinal Cord Injury [29] to document autonomic dysfunctions at different stages of recovery after SCI and during rehabilitation of individuals with SCI. The ISAFSCI has already been implemented in numerous centers and demonstrates moderate to strong inter-rater reliability, especially in the bladder, bowel, and sexual function components of the assessment [30].

Traditionally, assessments of autonomic dysfunction in SCI are accomplished through the detection of changes in blood pressure and heart rate. These cardiovascular parameters can be evaluated by manual or automated blood pressure methods or continuously with heart rate Holter and 24-hour blood pressure monitoring [31]. To appreciate the severity of cardiovascular dysfunctions after SCI, these parameters can be measured at rest, during and after exercise, or during provocative tests (ie, orthostatic tilt table; urodynamics, etc) [32-34]. We provide a brief description of the most frequently used tests in clinical practice and research and novel assessments in Table 1.

In clinical settings, OH is usually assessed by a combination of obtaining a detailed medical history and performing a physical examination and orthostatic