ORIGINAL ARTICLE

Effect of Different Sympathetic Stimuli–Autonomic Dysreflexia and Head-up Tilt–on Leg Vascular Resistance in Spinal Cord Injury

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ABSTRACT. Groothuis JT, Rongen GA, Geurts AC, Smits P, Hopman MT. Effect of different sympathetic stimuli–autonomic dysreflexia and head-up tilt–on leg vascular resistance in spinal cord injury. Arch Phys Med Rehabil 20102010;91:1930-5.

Objective: To compare the effect of different sympathetic stimuli, that is, exaggerated sympathetic activity and orthostatic challenges, on the increase in leg vascular resistance in persons with spinal cord injury (SCI) without and controls with supraspinal sympathetic control.

Design: Case-control intervention study.

Setting: Physiology research laboratory.

Participants: Persons with SCI (N=9; motor and sensory complete spinal cord lesion above the sixth thoracic spinal segment) and able-bodied controls (N=9).

Interventions: In persons with SCI, exaggerated sympathetic activity was evoked by autonomic dysreflexia, and in controls, by using a cold pressor test (CPT). A 30° head-up tilt (HUT) was performed in both groups.

Main Outcome Measure: Leg blood flow was measured by using venous occlusion plethysmography during the different sympathetic stimuli. Leg vascular resistance was calculated as the arterial-venous pressure gradient divided by blood flow.

Results: In persons with SCI, leg vascular resistance significantly increased during autonomic dysreflexia and 30° HUT (25±20 and 24±13 arbitrary units [AU], respectively), with no difference (P=.87) between stimuli. In controls, leg vascular resistance significantly increased during CPT and 30° HUT (15±13 and 29±12AU, respectively) with no difference (P=.03) between stimuli. There were no differences (P=.22) in increase in leg vascular resistance during the different sympathetic stimuli between persons with SCI and controls.

Conclusions: The increase in leg vascular resistance during autonomic dysreflexia in persons with SCI is not different from that during 30° HUT, which might be caused by a limited vasoconstrictor reserve. Despite the lack of supraspinal sympathetic control in persons with SCI, the increase in leg vascular resistance during exaggerated sympathetic activity was not different from controls.

Key Words: Autonomic dysreflexia; Head-up tilt; Leg vascular resistance; Spinal cord injury; Sympathetic nervous system; Rehabilitation.

DESPITE INCREASED BASAL leg vascular resistance,[1-5] persons with SCI show an increase in leg vascular resistance during orthostatic challenges similar to controls.[1,4,5] In controls, this increase in leg vascular resistance is caused by central sympathetic vasoconstrictor mechanisms in conjunction with local vasoconstrictor mechanisms, such as the venoarteriolar axon reflex[6] and myogenic response.[7] Because persons with SCI have a sympathetic disruption caused by their spinal cord lesion and α-adrenergic blockade does not influence the increase in leg vascular resistance during orthostatic challenges in persons with SCI or controls, the leg vasoconstriction in persons with SCI most likely is caused by the myogenic response.[4]

In persons with SCI, an increase in leg vascular resistance also can be caused by a sympathetic-mediated phenomenon called autonomic dysreflexia.[8] This is potentially life-threatening episodic hypertension that develops in 80% to 90% of persons with SCI with a spinal cord lesion at or above T6.[9] Autonomic dysreflexia occurs in these persons with SCI because a large part of the sympathetic nervous system is without central inhibitory pathways.[10,11] An arterial pressure increase is induced by visceral, noxious, or nociceptive stimuli entering the spinal cord below the lesion level and can be initiated by catheterization, bladder distension, and bowel evacuation.[9-12] Autonomic dysreflexia is accompanied by sweating, flushing, and a pounding headache[9,12] and can lead to severe morbidity and even death.[13-16] The vasoconstriction and consequent increase in leg vascular resistance during autonomic dysreflexia is induced by exaggerated sympathetic activity.[2 10,11] However, the quantity of this sympathetic-mediated vasoconstriction compared with non–sympathetic-mediated vasoconstriction during orthostatic challenges (the myogenic response) in persons with SCI is unknown.

In controls, a qualitatively similar strong sympathetic stimulus is available, namely CPT. Although CPT is not directly comparable to autonomic dysreflexia, both are strong sympathetic stimuli, notwithstanding the physiologic and neurologic

List of Abbreviations

ANOVA	analysis of variance
CPT	cold pressor test
HUT	head-up tilt
MAP	mean arterial blood pressure
SCI	spinal cord injury

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Table 1: Subject Characteristics, Including Specific Characteristics of persons with SCI

Subject No. (SCI)	SCI Level	DOI (y)	Age (y)	Height (cm)	Weight (kg)	MAP (mmHg)	Smoking	Medication
1	C5	17	46	181	105	99	−	Bisacodyl
2	T5	28	46	198	65	88	+	
3	C7	45	69	179	81	105	−	
4	C6	23	53	180	92	103	−	Penicillin-G-benzathine
5	C6	18	46	165	80	76	−	Baclofen
6	T5	10	39	178	70	77	+	Laxative
7	C7	34	52	182	92	82	−	Furosemide tolterodine
8	C7	25	46	190	110	95	+	
9	C5	12	36	183	58	72	+	
SCI		n=9	48±10	182±9	84±18	89±13	−	
Control		n=9	35±12*	186±7	84±17	93±7	−	

NOTE. Values represent mean±SD.
Abbreviations: DOI, duration of injury; +, smoking; −, no smoking.
*Significantly different from SCI persons.

differences, especially the presence versus absence of supraspinal sympathetic control.[10,11] This could lead to a difference in the effect of exaggerated sympathetic activity on the increase in leg vascular resistance between controls and persons with SCI caused by central inhibitory pathways.

The aim of this study was to determine and compare the level of leg vascular resistance evoked during different sympathetic stimuli, that is, exaggerated sympathetic activity and an orthostatic challenge, in persons with SCI without and controls with supraspinal sympathetic control. We hypothesized that the increase in leg vascular resistance during exaggerated sympathetic activity in persons with SCI, evoked by autonomic dysreflexia, would be larger than during an orthostatic challenge in persons with SCI and exaggerated sympathetic activity in controls, evoked by means of CPT.

METHODS

Participants

Persons with SCI (9 men) and healthy able-bodied controls (9 men) participated in this study (table 1). All subjects were normotensive (blood pressure <140/90mmHg; auscultatory blood pressure measurement), free of overt cardiovascular diseases, and did not report orthostatic intolerance. Four persons with SCI and 2 controls smoked, and 5 persons with SCI used medication, none of which are known to substantially interfere with vascular reactivity (see table 1). All persons with SCI had long-standing traumatic spinal cord injury with a motor and sensory complete spinal cord lesion above T6 (American Spinal Injury Association impairment scale grade A, zone of partial preservation above T6[17]) (see table 1). SCI level was assessed by means of clinical examination. The study was carried out in accordance with the Declaration of Helsinki and was approved by the medical ethical committee of our institution. All subjects gave written informed consent.

Experimental Procedures and Protocol

All subjects refrained from caffeine-containing food and beverages, vitamin C supplements, nicotine, and alcohol for more than 12 hours and from heavy physical activity for more than 24 hours before the experiment. Subjects had been fasting for more than 12 hours and had emptied their bladders in the hour before the experiment. All experiments were performed in a quiet temperature-controlled (23°C±1°C) room.

Subjects were positioned comfortably on a manually driven tilt table and supported by a chest belt to prevent them from sliding down during the experiment. The experiment started after a supine resting period of 30 minutes or longer. First, baseline leg blood flow was measured for 10 minutes in the supine position by using venous occlusion plethysmography. Subsequently, subjects were tilted manually within 5 seconds to a 10-minute passive 30° HUT, during which leg blood flow was measured. After a supine resting period of 20 minutes, baseline leg blood flow was measured for another 10 minutes in the supine position, and subsequently, autonomic dysreflexia was provoked in persons with SCI for 5 minutes, and in controls, CPT was applied for 3 minutes, during which leg blood flow was measured.

A 30° HUT results in significant cardiovascular effects,[1,4,18] with a significant increase in peroneal muscle sympathetic nerve activity.[19] In addition, the most profound cardiovascular effects are observed from supine to 30° HUT and do not change further with higher tilt angles.[20] Autonomic dysreflexia in persons with SCI was evoked by inflating a blood pressure cuff to 220mmHg on the contralateral upper leg, which gives a nociceptive stimulus,[10,11] as described previously.[2] According to the literature, autonomic dysreflexia was achieved when there was a systolic blood pressure increase to the stimulus of at least 20mmHg[11,21,22] or a 20% increase in blood pressure with visualized vasoconstriction.[12] To increase sympathetic activity in controls, CPT was applied.[23] CPT consisted of immersion of the right hand in ice water (4°C) for 3 minutes.[23]

Measurements

Blood pressure was measured continuously by using a noninvasive blood pressure device.[a] A finger cuff was attached to the middle phalanx of the left third finger to measure finger arterial blood pressure, which accurately reflects intra-arterial blood pressure changes.[24] A built-in heart reference system was in operation to correct for hydrostatic influences. Systolic and diastolic blood pressure and MAP values were derived beat to beat, and heart rate was the inverse of the interbeat interval.

Leg blood flow was measured by means of electrocardiogram-triggered venous occlusion plethysmography using electrically calibrated[25] mercury-in-Silastic strain gauges.[b] In the supine position, the right leg was positioned approximately 5cm above heart level to facilitate venous outflow between venous occlusions.[26] A strain gauge was placed 10cm above the patella, and a 12-cm wide occlusion cuff, placed on the