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Autonomic symptoms in hypertensive patients with post-acute minor ischemic stroke

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ABSTRACT

Background: Most studies regarding autonomic dysfunction in ischemic stroke are limited to heart rate and blood pressure changes during the acute phase. However, there are few data on quantitative assessment of autonomic symptoms. We sought to assess autonomic symptoms in hypertensive ischemic stroke patients.
Methods: In 100 hypertensive patients (45 with symptomatic ischemic stroke (6 months after stroke onset) and 55 without stroke), we assessed autonomic symptoms using the Scale for Outcomes in Parkinson disease-Autonomic (SCOPA-AUT).
Results: The age (mean ± standard deviation) for the stroke group was 66 ± 12 and 63 ± 15 for the without stroke group ($P = 0.8$). Orthostatic hypotension occurred in 3.6% of the stroke group and 4.4% in the group without stroke. The total SCOPA-AUT score was higher in the stroke group compared with the group without stroke ($P = 0.001$). Domain scores for gastrointestinal ($P = 0.001$), urinary ($P = 0.005$) and cardiovascular ($P = 0.001$) were higher in the stroke group. No differences were found when comparing the total SCOPA-AUT scores for stroke subtypes ($P = 0.168$) and for lateralization ($P = 0.6$). SCOPA AUT scores were correlated with depression scores ($P = 0.001$) but not with stroke severity ($P = 0.2$).
Conclusion: Autonomic symptoms, especially, gastrointestinal, urinary and cardiovascular function, were significantly increased in hypertensive patients with minor ischemic stroke. Symptoms were associated with depression but not with the characteristic of the stroke.

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1. Introduction

Autonomic function is frequently altered in patients with ischemic stroke during acute and chronic stages. Cardiac arrhythmias and sudden death during acute stroke are related to autonomic function imbalance [1–3]. Non-invasive tests have suggested sympathetic hyperactivity and cardiovagal dysfunction in acute stroke [1,2,4–7] with diverse results when considering the influence of lateralization, site and sub-type of ischemic stroke [1–3,8]. Autonomic cardiovascular dysfunction is associated with stroke severity [8]. Diminished heart rate variability (HRV) and baroreflex sensitivity (BRS) are related with worse prognosis [2,9]. Gastrointestinal, urinary, sudomotor and sexual dysfunction due to multiple factors, including autonomic dysfunction, also occur in stroke patients [10–18]. Despite clear evidence of objective dysfunction in various autonomic domains there is less information about the assessment of autonomic symptoms in minor stroke patients. We sought to assess autonomic symptoms in hypertensive patients with minor ischemic stroke in comparison with hypertensive patients without symptomatic ischemic stroke.

2. Patients and methods

2.1. Patients

Consecutive ischemic stroke patients (age ≥18 years old) and hypertensive patients without history of symptomatic stroke were recruited from an Outpatient clinic. Stroke patients fulfilled the following inclusion criteria; clinical evidence and neuroimaging study (computed tomography (CT) or magnetic resonance imaging (MRI)) showing a single ischemic lesion based upon AHA/ASA Expert Consensus [19]. Presumed etiology of stroke was based on criteria from the Acute Stroke Treatment (TOAST) study [20]. Stroke severity was evaluated by means of the National Institutes of Health

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Stroke Scale NIHSS (range 0–42 points) and for global disability the modified Rankin scale was used (range 0–6 points) [21]. Clinical classification of the sub-type of cerebral infarction was based on the Oxfordshire Community Stroke Project (OCSP) criteria; posterior circulation infarct (POCI), lacunar infarct (LACI), total anterior circulation infarct (TACI) and partial anterior circulation infarct (PACI) [22]. According to the TOAST classification, patients with strokes due to cardioembolism, strokes due to other causes (e.g., vasculitis, coagulation disorder), and strokes due to unknown or concurrent origin were not included. Patients were assessed between 3 and 12 months after their first symptomatic stroke. For patients without stroke, the following criteria were used; absence of clinical and neuroimaging evidence of ischemic lesion(s). Hypertension was defined as a diastolic blood pressure (supine or sitting) of at least 90 mmHg or a systolic blood pressure (supine or sitting) of at least 140 mmHg.

For both patient groups a patient with mild global disability (Rankin <3) and any neurological disease affecting the autonomic nervous system, like Parkinson's disease, multiple system atrophy, pure autonomic failure, autoimmune neuropathies, were excluded. 45 stroke patients (17 women, 28 men) and 55 hypertensive patients without stroke (36 women, 19 men) fulfilled the inclusion criteria. 45 age-matched (mean age 64.6 ± 9.8 years, 25 women, 20 men) healthy individuals were recruited as a control group for a comparison of SCOPA scores. They were screened to have not clinical history of hypertension, stroke or other neurological disease, diabetes mellitus, systemic disease affecting autonomic nervous system. They were not using medication known to affect autonomic function.

All patients and healthy gave their written informed consent, approved by the Ethical Committee of the Hospital and the University of Valparaiso.

2.2. Autonomic nervous system evaluation

2.2.1. Orthostatic stress testing

Orthostatic blood pressure (BP) testing was performed in the morning between 10 and 12 h. Patients were requested to eat a light breakfast no later than 2 h prior to the test and abstain from caffeine and alcohol during the previous 12 h. Patients laid in the supine position in a quiet room, for 10 min. Patients then assumed the upright posture and stood for 10 min. BP and heart rate were measured intermittently (DINAMAP monitor, Critikon, Tampa, FL), while the subject was lying down and again at 1, 5 and 10 min after standing up. The maximum difference in systolic BP from supine to standing was taken as the orthostatic BP change [13]. A systolic BP fall ≥20 mmHg was considered as indicative of orthostatic hypotension [23].

2.2.2. Autonomic symptoms evaluation

AUT-symptoms were examined using the Scale for Outcomes in Parkinson's disease for Autonomic Symptoms (SCOPA-AUT), a questionnaire divided into six domains, gastrointestinal (7 items), urinary (6 items), cardiovascular (3 items), sudomotor (4 items), pupillomotor (1 item) and sexual in men (2 items). The four response options for each item ranged from 0 (never) to 3 (often) with higher total scores reflecting worse autonomic functioning [24]. We evaluated symptoms related to five domains: gastrointestinal (Gastro), urinary (Uri), cardiovascular (Cardio), sudomotor (Sudo) and sexual (in men) (Sex) dysfunction. All questions referred to symptoms within the past month. In patients with aphasia the answers were obtained from caregivers. We did not explore the Pupillomotor domain. This scale has been demonstrated to be reliable and valid [24]. Patients were screened for depressive symptoms with the Hamilton depression rating scale (HAM-D); a validated method for measuring depression [25].

2.2.3. Statistics

Comparisons were made between groups using Student's independent *t* tests, Fisher's exact tests or Wilcoxon tests, as appropriate. Analysis of variance (ANOVA) and post hoc Tukey–Kramer HSD tests were used to compare SCOPA scores between groups. Kruskall Wallis tests were used to compare sex scores between males. Correlations between SCOPA AUT scores and stroke parameters were assessed with Spearman's rank correlations. Significance was set at 0.05. All data were analyzed (STATA).

3. Results

3.1. Baseline characteristics

There were no differences in age, body mass index, hyperlipidemia and current drug use, between patients with and without stroke (all $P > 0.05$). Stroke patients had a mean NIHSS score of 1.5 ± 2.5 and a mean Rankin score of 0 in 2 and 1–2 in 43 patients. Half of the stroke patients had a lacunar stroke, according to the OCSP classification: LACI = 51.1%, PACI = 31.1%, POCI = 17.8%, TACI 0%. Stroke patients showed male predominance, more smokers and diabetics. The MMES and HAM-D scores showed worse outcomes in stroke patients (Table 1).

3.2. Autonomic evaluation

The number of stroke patients that reported autonomic symptoms was significantly higher than those patients without stroke. Nocturia (37.8%), orthostatic intolerance (31.1%), subjective dysphagia (28.9%), increased urinary day time frequency (24.4%) and urinary incontinence (24.4%) were among the principal symptoms in stroke patients (Table 2). There was no difference in supine BP between groups. Orthostatic hypotension occurred in 2 patients with stroke and in 2 patients without stroke (Table 2).

3.2.1. SCOPA-AUT scores

ANOVA analysis indicated significant differences in total SCOPA-AUT, gastrointestinal, urinary and cardiovascular scores between groups (with stroke and without stroke hypertensive patient

Table 1
Demographic data and clinical characteristic of hypertensive patients without and with symptomatic ischemic stroke.

	Without stroke ($n = 55$)	With stroke ($n = 45$)	*P*
Age (mean ± SD)	65.2 ± 15.1	65.8 ± 11.7	0.811[a]
Sex, male (%)	19 (34.5)	28 (62.2)	0.009[b]
BMI (mean ± SD)	27.2 (3.1)	26.7 (3.2)	0.44[a]
Hyperlipidemia (%)	13 (23.6)	9 (20)	0.809[b]
Diabetes mellitus (%)	8 (14.6)	14 (31.1)	0.055[b]
Depression *n* (%)	7 (12.7)	16 (35.6)	0.009[b]
Smokers[d] *n* (%)	14 (25.5)	23 (51.1)	0.012[b]
MMSE (mean ± SD)	27.9 ± 2.6	25.8 ± 4.2	0.0025[a]
NIHSS (mean ± SD)	0	1.54 ± 2.5	
HAM-D median (IQR)	4 (2–6)	6 (3–9)	0.0004[c]
B blockers *n* (%)	7 (12.7)	6 (13.3)	0.579[b]
ACE inhibitor *n* (%)	17 (30.9)	16 (35.5)	0.389[b]
CCB *n* (%)	7 (12.7)	6 (13.3)	0.5[b]
Diuretic *n* (%)	6 (10.9)	7 (15.6)	0.347[b]
Antidepressant *n* (%)	3 (6.7)	5 (9.1)	0.8[b]

ACE, angiotensin-converting enzyme inhibitor; CCB, calcium channel blocker.
[a] Student *t* test.
[b] Fisher exact test.
[c] Wilcoxon.
[d] Includes ex- and current smoker (≥1 cigarette per day).

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