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Age-Dependent Clinical Characteristics of Micturition Syncope

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***Background*:** Clinical features of micturition syncope (MS) seem to be differ according to age and the present study sought to clarify this.

***Methods and Results*:** The 37 consecutive patients (mean age: 52.2±16.8 years, 26 men) with MS were divided into 2 groups by median age of 55: younger group (YG) consisting of 18 patients <55 years (average 38.2) and an older group (OG) consisting of 19 patients ≥55 years (average 65.5). Alcohol-related MS was significantly more frequent in the YG than in the OG (78% vs 42%, P=0.027). Daily distribution of MS was significantly different (P=0.0009): 85% of the MS in the YG occurred before midnight (PM), whereas 75% of the MS in the OG occurred after midnight (AM). Although overall positive responses of head-up tilt testing were more common in the OG (P=0.046), gender, number of syncope, and association with vasovagal syncope or cardiovascular disease were not different between both groups.

***Conclusions*:** In the YG, MS tended to occur in the evening or nighttime before midnight, whereas MS in the OG tended to occur after midnight or early in the morning. Alcohol intake may be an important precipitating factor for MS in young subjects. (*Circ J* 2009; **73:** 1651 – 1654)

Key Words: Age; Alcohol; Daily distribution; Micturition; Syncope

Micturition syncope (MS) is a type of situational syncope in the neurally mediated syncopal syndrome.[1] MS has been described classically as a stereotype occurring in healthy men after recumbency or sleep.[2,3] Kapoor et al have proposed that the clinical features of MS may differ according to on age,[4] but information about MS is so far very limited. The purpose of this study was to clarify the age-dependent clinical characteristics of MS.

Methods

The study population consisted of 37 consecutive patients with MS referred to 3 institutions (Juntendo University Hospital, Juntendo University Shizuoka Hospital, and University Hospital of Occupational and Environmental Health) for syncope during the period August 1995 and December 2006. The mean age of the patients was 52.2± 16.8 years (range 19–76 years, median 55; 26 men, 11 women). According to the median age of the study population, we divided them into 2 groups: a younger group (YG) consisting of 18 patients aged <55 years (range 19–54 years, average 38.2 years) and an older group (OG) consisting of 19 patients aged ≥55 years (range 55–76 years, average 65.5 years). Clinical characteristics including gender, number of syncope episodes, association with other types of neurally mediated syncope and cardiovascular disease, predisposing factors, time of MS occurrence, and response to head-up tilt testing (HUT) were compared between the YG and OG. All patients underwent a standardized, basic evaluation consisting of the following: complete medical history, physical and neurologic examinations, baseline laboratory examinations, 12-lead electrocardiogram (ECG), ambulatory ECG monitoring of at least 24 h, and an echocardiographic examination. HUT was performed if informed consent was given. Other cardiac or neurologic investigations, including exercise stress test, electrophysiologic study, cardiac catheterization, coronary angiography, a computed tomographic brain scan, and electroencephalography, were performed only when clinically indicated. In all patients other causes of syncope or presyncope were excluded before performing a tilt test. Clinical information was collected retrospectively from medical records. None of the patients was administered any medication or underwent cardiac pacemaker implantation for MS.

After written informed consent was given, HUT was performed in a quiet room after at least a 5-h fast. A peripheral intravenous catheter was inserted 30 min before the tilt test, and a saline solution of 4.3% glucose was started at a rate of 60 ml/h. The ECG was monitored continuously during the test, and arterial blood pressure was monitored noninvasively by a tonometry system (BP-508, Colin Electronics, Komaki, Japan). After at least 15 min resting in the supine position, each patient was positioned upright at an 80-degree angle for a maximum of 30 min on the tilt table equipped with a footboard for weight bearing (passive tilt).

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Table. Clinical Characteristics of the Younger and Older Groups

	Younger group (<55 years)	Older group (≥55 years)	P value
No. of patients	18	19	
Age (years)			
Range	19–54	55–76	
Average	38.2	65.5	
Gender (M/F)	14/4	12/7	NS
Male (%)	78	63	
No. of syncopal episodes			
1	12 (67%)	11 (58%)	NS
2	4	3	
3–5	2	4	
Presyncope	0	1	
Association with other NMS			
Vasovagal syncope	5 (28%)	9 (47%)	NS
Defecation syncope	1	1	
Vomiting syncope	1	0	
Underlying cardiovascular disease			
Yes	5 (28%)	10 (53%)	NS
No	13 (72%)	9 (47%)	
Predisposing factors			
Alcohol intake	14 (78%)	8 (42%)	0.027
Vasodilator	2 (11%)	5 (26%)	NS
Alcohol and/or vasodilator	15 (83%)	11 (58%)	0.091
Daily distribution of the episodes (N=33 episodes)			
After midnight (AM)	3	12	0.0009
Before midnight (PM)	14	4	
Head-up tilt results			
Passive tilt positive	2 (11%)	1 (5.3%)	NS
ISP/NTG tilt positive	1	8	
Overall positive	3 (17%)	9 (47%)	0.046
Type of positive response			
Vasodepressor	2	3	NS
Cardio-inhibitory	0	0	
Mixed	1	6	

NMS, neurally mediated syncope; ISP, isoproterenol; NTG, nitroglycerin.

If the passive tilt ended as negative, the patient was returned to the supine position and HUT with isoproterenol (ISP) or nitroglycerin (NTG) provocation was performed. In the ISP provocation, intravenous ISP was infused at 0.01 μg/kg body weight per minute for 10 min. The tilt test was then repeated for a maximum of 10 min. If the initial ISP tilt ended as negative and the maximum heart rate did not exceed 120 beats/min, the patient was returned to the supine position and intravenous ISP was increased to 0.02 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 10 min. The tilt test was repeated for a maximum of 10 min. For NTG provocation, sublingual tablet at a dose of 0.3 mg was administered after the passive tilt ended as negative. The tilt test was then repeated for a maximum of 15 min. If syncope or presyncope developed during the test, the tilt table was rapidly lowered to the supine position and the study ended.

Syncope is defined as a sudden transient loss of consciousness, associated with the inability to maintain postural tone. Presyncope is defined as experiencing the premonitory signs of syncope or imminent syncope (eg, severe weakness or lightheadedness). MS was defined as an episode of syncope occurring at the beginning of, during, at the termination of, or immediately after urination. A positive HUT response was defined as the development of syncope or presyncope associated with hypotension (systolic blood pressure <90 mmHg), bradycardia (heart rate <50 beats/min), or asystole ≥3 s. Three types of positive responses were noted during the HUT: vasodepressor, cardio-inhibitory, and mixed type.[5]

Continuous variables are presented as mean±SD and were compared by the unpaired Student's t-test. Categorical variables were compared by chi-square test or Fisher's exact test. A P value <0.05 was considered statistically significant.

Results

Gender was not different between the YG and the OG (**Table**). **Figure 1** shows the age and gender distribution of the study patients. MS occurred more in the young and middle-aged men. More than half of the patients in both groups had experienced only 1 episode of MS (**Table**). An association with typical vasovagal syncope was not different between the YG and the OG. Another 3 patients had experienced other types of situational syncope, including 2 with defecation syncope in each group and 1 with vomiting syncope in the YG (**Table**). Underlying cardiovascular disease was found in 15 patients (41%), including hypertension (n=12), coronary artery disease (n=2), heart block with DDD pacemaker (n=2), and diabetes mellitus (n=2), paroxysmal atrial fibrillation (n=1), sick sinus syndrome (n=1), and Wolff-Parkinson-White syndrome (n=1). Underlying cardiovascular disease was not statistically different (**Table**). In addition, prostate hypertrophy was diagnosed in only 1 OG patient.

The occurrence of MS was significantly more related to alcohol intake in the YG than in the OG (14/18: 78% vs 8/19: 42%, P=0.027). Seven patients, 2 in the YG and 5 in the OG, were taking vasodilators for MS, including calcium-channel blocker (n=6: 1 with an angiotensin-converting enzyme inhibitor) and an α-blocker with an angiotensin II

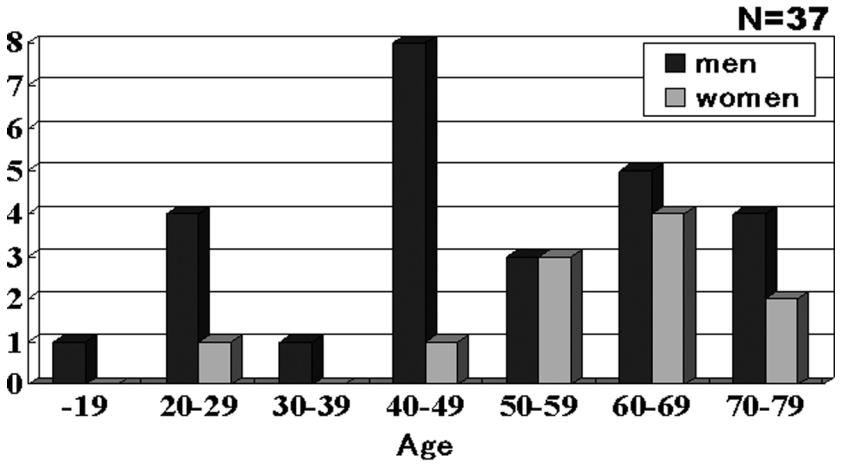

Figure 1. Age and gender distribution of the patients with micturition synocope (MS). MS occurred more in young and middle-aged men.

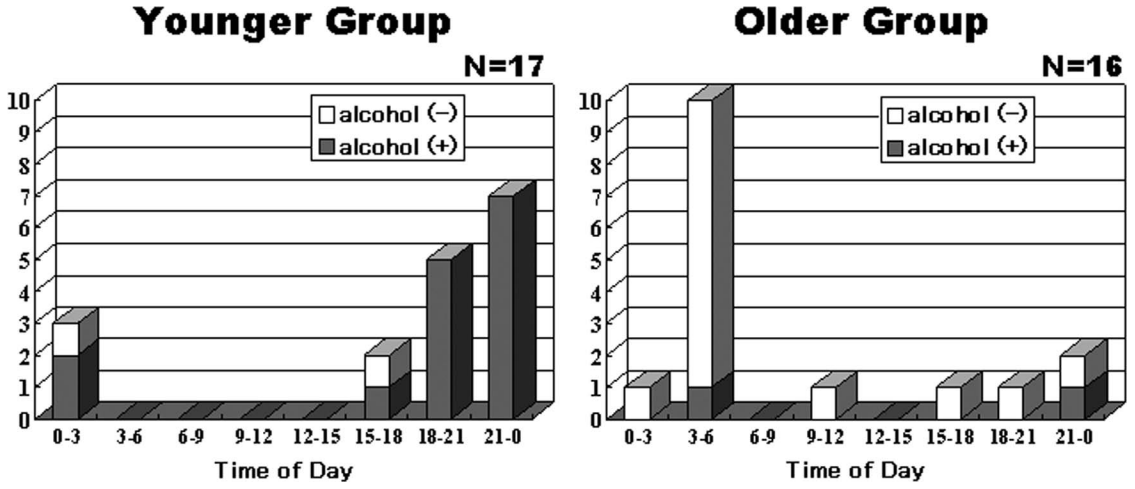

Figure 2. Daily distribution of micturition syncope (MS) in the younger group (YG) and older group (OG). In the YG, 82% of the 17 MS episodes occurred before midnight (PM). In contrast, 75% of the 16 MS episodes in the OG occurred after midnight (AM).

receptor blocker (n=1). No patient was taking diuretics at the time of MS. Overall, 15 patients (83%) in the YG and 11 patients (58%) in the OG were taking alcohol or a vasodilator when the MS occurred, but the difference was not statistically significant (P=0.091) (**Table**).

The daily distribution of MS in both groups is shown in **Figure 2**. The time of MS occurrence was identified in 33 episodes in 24 patients. The diurnal distribution of MS was significantly different (P=0.0009): 82% of the MS in the YG occurred before midnight (PM), whereas 75% of the MS in the OG occurred after midnight (AM) (**Table**). In the YG, all of these evening or nighttime episodes, occurring between 6 PM and 12 AM, were related to alcohol intake (**Figure 2**).

HUT was performed in 35 of the 37 patients; 2 patients in the OG, did not give informed consent. During the passive HUT, the positive rate was not different between the YG and the OG (**Table**). The test was discontinued in 2 patients: 1 in the YG because of hyperventilation and another in the OG because of orthostatic hypotension. The HUT with drug provocation was preformed in 26 patients (22 with ISP and 4 with NTG); 1 patient in the YG (with ISP) and 8 patients in the OG (6 with ISP and 2 with NTG) ended as positive during the provocation HUT. Finally, the overall positive response rate (including the 2 refusal patients in the OG) was greater in the OG (47%) than in the YG (17%) (P=0.046). All positive responses were vasodepressor (n=5) or mixed type (n=7): a cardio-inhibitory response was not observed. The type of positive responses was not different between the 2 groups: 2 vasodepressor and 1 mixed type in the YG and 3 vasodepressor and 6 mixed types in the OG. In 14 patients who had MS associated with vasovagal syncope, 5 patients ended as positive including 1 (20%) of the 5 patients in the YG and 4 (44%) of the 9 patients (1 patient refused HUT) in the OG. There was no difference between the 2 groups.

Discussion

Our study has demonstrated that MS in the YG tended to occur in the evening or nighttime before midnight, whereas MS in the OG tended to occur after midnight or early in the morning. MS was significantly more related to alcohol intake in the YG than in the OG. Alcohol intake may be an important precipitating factor for MS in young people.

Kapoor et al[4] proposed 2 age-dependent types of MS. One group consisted of young healthy men, aged 18–34 years (average, 25 years), which has been well described

classically.[2,3] Another group consisted of older patients, aged 39–88 years (average, 60 years), which included more often women with multiple illnesses and the majority having orthostatic hypotension. However, Kapoor et al did not mention the influence of alcohol. In this study, we have shown that alcohol intake was more related to MS in the young population compared with the elderly.

The daily distribution of the occurrence of neurally mediated syncopal syndrome has been reported.[6,7] We reported a morning peak in the frequency of vasovagal syncope,[7] and that MS tends to occur at night.[6] In the present study, although 88% of the episodes of MS occurred between 6 PM and 6 AM, we have shown that the daily distribution of MS was different between the 2 age groups: most episodes occurred between 6 PM and 12 AM in the YG, whereas the majority of episodes occurred between 12 AM and 6 AM in the OG. We suppose that, in the younger population, MS may occur during or just after drinking in the evening or night. This type of MS has not been reported previously. A change in daily lifestyle, more chances to drink alcohol at a restaurant or bar after work, may precipitate the occurrence of MS. On the other hand, in the older population MS may occur after midnight or early in the morning after sleeping: this is a classic pattern of MS.

Alcohol intake may be a predisposing factor. Lyle et al reported that 14 of 25 patients (56%) with MS had moderate alcohol intake,[3] and we have demonstrated that alcohol was more related to MS in the YG compared with the OG. Alcohol dilates arterial and venous vessels, which leads to diminished venous return and activates the sympathetic nerve system.[8–10] In addition, prolonged sitting while drinking may precipitate the pooling of blood in the lower extremities. Predisposing factors that lower peripheral arterial resistance, such as sleeping or recumbency in a warm bed and taking vasodilators, may promote circulatory collapse.[4] The Valsalva maneuver,[2] diminishing the venous return to the heart, and the neurally mediated reflex during urinary evacuation[11] could be triggers causing a fall in arterial pressure with a decrease in heart rate in MS.

Poor positive responses to HUT, specifically passive HUT, have been identified in patients with situational syncope, including MS.[12] This may be explained by the fact that the afferent pathways of the neurally mediated reflex are different from tilt-induced vasovagal syncope.[1,12] In this study, although the positive rates of passive HUT were similar between the YG and the OG, the percentage of overall positive responses was greater in the OG (47% vs 17%, P=0.046). Grubb et al[13] have reported the usefulness of HUT in elderly patients (≥65 years) with recurrent unexplained syncope, using a similar protocol to ours: passive HUT (80 degrees) for 30 min and HUT with ISP provocation. They have shown a sensitivity of 64% and specificity of 100%. Usually, young patients are more likely to have a positive response to HUT compared with elderly patients.[14,15] Although not statistically significant, this discrepancy in our results might be explained by the fact that more patients susceptible to vasovagal syncope were included in the OG than in the YG: the rate of association with vasovagal syncope was 47% in the OG and 28% in the YG. Genetic factors might also influence the HUT results.[16]

Study Limitations

First, we examined only 37 patients with MS. Although MS is the most common situational syncope, situational syncope itself is a relatively rare type of neurally mediated reflex syncope. From this point of view, our study population may not be small compared with previous studies.[2–4,11] Second, we investigated the clinical data retrospectively from medical records. We could not obtain all of the clinical information from the study patients: the timing of MS episodes was obtained from 65% of the study patients. This may be an important limitation.

Conclusions

MS in young people (<55 years) tends to occur in the evening or nighttime before midnight, whereas MS in the older person tends to occur after midnight or early in the morning. Alcohol intake may be an important precipitating factor for MS in the young population.

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