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Case Study

Effect of cold oral stimulation on orthostatic hypotension in multiple system atrophy: a case study

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Abstract. [Purpose] The aim of this case study is to reconsider the method for preventing orthostatic hypotension in multiple system atrophy. [Participant and Methods] The case was that of a 70-year-old female with multiple system atrophy who experienced frequent falls and orthostatic hypotension. An orthostatic test was performed, and the effect of cold oral stimulation before standing was compared with no stimulation. Outcome measures were blood pressure, heart rate variability and autonomic variables. [Results] In the control test, blood pressure decreased from 150/72 mmHg in the supine position to 98/58 mmHg in the standing position. Heart rate increased from 71 bpm to 82 bpm, high frequency declined from 16.48 msec^2 to 14.07 msec^2, and low/high frequency increased from 2.56 to 5.13. Cold stimulation in the standing position induced changes in blood pressure from 168/82 mmHg to 104/72 mmHg, heart rate from 73 bpm to 83 bpm, high frequency from 61.29 msec^2 to 24.56 msec^2, and low/high frequency from 1.45 to 6.33 msec^2. [Conclusion] Standing after cold stimulation affected autonomic variables, but did not affect the heart rate or blood pressure, possibly because of damaged peripheral blood vessels. Further research is required to demonstrate the effect of cold stimulation on orthostatic hypotension.

Key words: Multiple system atrophy, Orthostatic hypotension, Cold stimulation

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INTRODUCTION

Multiple system atrophy (MSA) is a degenerative nerve disease that exhibits various symptoms such as progressive autonomic dysfunction, parkinsonism, cerebellar features and pyramidal signs[1)]. The onset of the disease tends to occur in middle age or later in life[1)], and the incidence of MSA in a population older than 40 years is 1.6 cases per 100,000 person-years[2)]. The rate of falls in patients with MSA is 83%[3)]. A retrospective study reveals that the differences between fallers and non-fallers include limb rigidity, speech disorder, dysphagia, and pyramidal signs[4)]. However, that research study[4)] did not report a significant relationship between autonomic dysfunction and falls, which could be the reason that the definition of autonomic dysfunctions includes erectile dysfunction and sweating abnormalities, which do not seem to influence the rate of falls directly. Orthostatic hypotension (OH), one of the autonomic failures, is defined as "a sustained reduction of systolic blood pressure of at least 20 mmHg or diastolic blood pressure of 10 mmHg within 3 min of standing or head-up tilt to at least 60° on a tilt table"[5)]. Eighty one percent of the patients with MSA show OH[6)], and 57% of the patients experience falls due to OH[7)]. Therefore, OH seems to be a cause of falls in patients with MSA.

Although a diverse range of non-pharmacological treatments for OH have been reported, such as water and sodium intake, smaller meal size, nocturnal head-up tilt, physical countermaneuvers, abdominal belts, and compression stockings, those

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methods, except for abdominal belts, are based on a weak level of evidence and thus not highly recommended[8]. For instance, drinking water (e.g. 500 mL) as quickly as possible in sitting position may cause an elevation of 30 mmHg of systolic blood pressure and an increase of 15 mmHg in diastolic blood pressure, and this effect can persist for one hour[9]. However, the orthostatic test with drinking water was also performed in a previous study that did not find a significant increase of blood pressure occurred[10]. In addition, there could be an increased risk of supine hypertension due to water intake[9]. Furthermore, considering that 20–30% of patients with MSA suffer from dysphagia[3, 11] and that 80% of them present urinary incontinence and/or insufficient bladder emptying[12], rapid water drinking could not prevent them from OH.

Given the above, this case study aimed to examine an effect of cold oral stimulation on autonomic and circulatory systems to prevent OH in patients with MSA. The reason for the selection of cold oral stimulation was that it could induce peripheral vasocontraction and an elevation of blood pressure. According to Heindl et al.[13], although there was no significant difference, ice cube intake showed an increase of systolic and diastolic blood pressure and sympathetic tone in healthy subjects. The mechanism of this phenomenon is that cold oral stimulation decreases core body temperature and leads to vasoconstriction to avoid further loss of body temperature[14]. To our knowledge, ice cube intake is not examined in patients with MSA. Although they cannot regulate their blood pressure because of deficits of the rostral ventrolateral medulla[15], which normally controls blood pressure when standing[16], the lateral parabrachial nucleus, the center of cool sensation[17], has possibility of leading to vasoconstriction and elevate blood pressure. The hypothesis is that cold oral stimulation increases sympathetic tone and decreases parasympathetic tone, leading to an elevation of blood pressure and heart rate.

PARTICIPANT AND METHODS

The case was a 70-year-old Japanese female with a weight of 45 kg and a height of 150 cm (BMI 20 kg/m^2) and had retired from employment. Her chief complaint was “falls with dizziness when standing”. In May 2018, after repeated falls with lightheadedness and blurred vision, her neurologist diagnosed her with probable MSA with predominant parkinsonism. She started taking medication of levodopa and vasopressor, and was recommended salt and water intake. In May 2019, as falls increased approximately 1–3 times per week, physical therapy was initiated through home visits. Her symptoms were OH, supine hypertension, parkinsonism (right upper and lower limb rigidity, postural instability, and tremor), urinary incontinence, constipation, sweating abnormality, and speech disturbance. Blood pressure strongly declined from 140–180/70–80 mmHg in supine position to 90–110/60–70 mmHg in standing position. She did not present any cognitive or mental illness. Before the patient participated in this study, she received a verbal and written explanation of the possible benefits, risks, and discomforts regarding her participation. The patient was informed of her right to withdraw at any time, and she signed an informed consent.

Two orthostatic tests were performed after 5 minutes of resting in the supine position, and while standing for 3 minutes. In the experimental condition, the patient was asked to hold an ice cube in her mouth while standing, and in the control condition, no stimulation was administered. The outcomes were blood pressure measured every minute using a sphygmomanometer (Kenzmedico Co. Ltd., Saitama, Japan), and heart rate variability was recorded using a heart rate monitor (myBeat WHS-2, Union Tool Co., Tokyo, Japan) during all of the experimental period. The data of heart rate variability was analyzed by MemCalc (GMS Co. Ltd., Tokyo, Japan) and was calculated as heart rate, low frequency (LF), high frequency (HF), and LF/HF. HF and LF/HF refer to the parasympathetic and sympathetic tone respectively[18]. The differences of the outcome measures between before and after standing were compared in the two conditions.

RESULTS

When standing without any stimulation, blood pressure declined from 150/72 mmHg in the supine position to 98/58 mmHg in standing position. Heart beat increased from 71 bpm to 82 bpm. HF revealed a non-significant change from 16.48 msec^2 in the supine position to 14.07 msec^2 in standing position. LF/HF increased from 2.56 to 5.13. On the contrary, standing while holding an ice cube in the mouth decreased blood pressure from 168/82 mmHg in the supine position to 104/72 mmHg in standing position. Heart rate rose from 73 bpm to 83 bpm. HF in supine position at 61.29 msec^2 decreased to 24.56 msec^2 in standing position. LF/HF showed an increase from 1.45 to 6.33 (Table 1).

DISCUSSION

This case study aimed to examine an effect of cold oral stimulation on autonomic and circulatory systems to prevent OH in patients with MSA. In support to our hypothesis, the sympathetic tone increased, and parasympathetic tone decreased due to cold oral stimulation, but heart rate and blood pressure did not show a difference between the condition of cold oral stimulation with an ice cube and the control condition with no stimulation.

In the orthostatic test, the HF of healthy subjects declined from 30.7 ± 6.24 msec^2 to 20.6 ± 3.70 msec^2, and their LF/HF rose from 0.53 ± 0.13 to 1.33 ± 0.19[19]. The study[19] also examined autonomic variables in patients with MSA, and found that HF and LF/HF changed from 14.22 ± 2.59 msec^2 and 0.48 ± 0.10 to 7.58 ± 1.64 msec^2 and 0.99 ± 0.26, respectively. As the experimental condition of this case study showed a decrease of HF from 61.29 msec^2 to 24.56 msec^2 and an increase of

Table 1. Blood pressure, heart rate and autonomic variables in orthostatic test

With an ice cube	Before standing	After standing
Blood pressure (mmHg)	150/72	98/58
Heart rate (bpm)	71	82
HF ($msec^2$)	16.48	14.07
LF/HF	2.56	5.13
Without an ice cube	**Before standing**	**After standing**
Blood pressure (mmHg)	168/82	104/72
Heart rate (bpm)	73	83
HF ($msec^2$)	61.29	24.56
LF/HF	1.45	6.33

HF: high frequency; LF: low frequency.

LF/HF from 1.45 to 6.33, the changes of autonomic variables seem to be larger in the case than in healthy subjects[19]. This suggests that cold oral stimulation reinforces the change of autonomic variables compared with no stimulation.

However, as noted above, the change of autonomic nervous system activity was not accompanied by an increase in heart rate or blood pressure when standing. According to Low et al.[16], the reasons of OH are a baroreflex dysfunction and impaired venomotor tone. The case in this study could have a deficit of baroreflexes because of the presence of OH and supine hypertension[16]. Cold stimulation induced changes HF and LF/HF, which could indicate intact autonomic pathways, and that OH in this case possibly resulted from impaired venomotor tone. In fact, some patients with MSA show lowered peripheral resistance[20]. The limitation of this case study is that only one person was evaluated, and therefore, the result of this study cannot be generalized. More cases are needed to prove the hypothesis of this study.

In conclusion, this case study examined the effect of cold oral stimulation on OH. Although cold stimulation with an ice cube induced changes in autonomic variables, heart rate and blood pressure were not altered. Further research with more cases is required to examine whether cold oral stimulation prevents OH in patients with MSA.

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Conflict of interest

The authors have no conflicts of interest to declare for this study.

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