Syncope Induced by Tobacco Smoking in the Head-up Position

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A 26-year-old man had a loss consciousness for a few minutes while smoking in the standing position, and was referred to hospital. No abnormalities were found in a computed tomography examination of his head, in a 24-h electrocardiogram or in an exercise tolerance test. The head-up tilt test (HUT) while tobacco smoking elicited a positive response in the tilted position, but the HUT without tobacco smoking was negative. The most noteworthy effect of tobacco smoking during the HUT was the high level of plasma epinephrine compared to the levels seen during supine smoking or the HUT alone. Syncope induced by tobacco smoking in the standing position is rare and the mechanism may be the same as that underlying neurally mediated syncope. (Jpn Circ J 2001; 65: 1001 – 1003)

Key Words: Tobacco; Neurally mediated syncope; Epinephrine; Norepinephrine

The main cardiovascular effects of nicotine result from sympathetic neural stimulation. Fukuda et al reported a case of repeated episodes of syncope associated with tobacco smoking in which the syncope was induced by cerebral hypoperfusion! We report a case of suspected neurally mediated syncope (NMS) that was induced by tobacco smoking, but only when standing.

Case Report

A 26-year-old man had suffered from syncope in psychologically stressful situations while in the standing position for the past 3 years, and the episodes has occurred several times in 1 year with palpitation, nausea and/or darkness. He had also noticed that he often felt sick and experienced palpitations while smoking in the standing position. In October 1999, he had a loss consciousness for a few minutes while smoking in this position, and was referred to a hospital. No abnormalities were found in a computed tomography examination of his head, in a 24-h electrocardiogram (ECG) or in an exercise tolerance test, and he was transferred to us for further examination.

His past history revealed that he had suffered from asthma until the age of 11 years. His family history revealed no remarkable findings. Physical examination at the time of admission revealed no abnormal findings, and orthostatic hypotension was not detected. A chest X-ray revealed a cardiothoracic ratio of 39%. An ECG showed no abnormal findings.

A head-up tilt test (HUT) was performed using a tilt table with a foot board. The patient rested in the supine position for 30 min before the test in which he was tilted to an angle of 70° from the horizontal for 20 min; there was not a positive response (data are not shown). However, the HUT with either tobacco smoking while in the tilted position (Fig 1) or isoproterenol provocation (0.5–1.0 μg/min) (Fig 2) elicited a positive response. There was an initial increase in heart rate (HR) and it then fell from 160 beats/min to 100 beats/min without asystole (Figs 1, 2). Blood pressure fell to a hypotensive level (<80 mmHg systole) at the onset of the rapid fall in HR (Figs 1, 2). Based on the classification for tilt-induced vasovagal syncope2 this patient’s syncope was a mixed type. During the HUT, he complained of palpitation and sickness with either smoking or isoproterenol provocation, and finally lost consciousness. These symptoms were identical to those that occurred while smoking in the standing position.

During the HUT, we measured the plasma concentrations of epinephrine (ER) and norepinephrine (NE), and performed echocardiography. The HUT with or without smoking was performed on a separate occasion. The patient rested in each position for 5 min before the blood test or echocardiography. During supine smoking, the blood specimen and echocardiogram data were collected when the symptoms occurred. The plasma concentration of ER increased with HUT alone and with supine smoking, and was markedly increased by smoking during HUT; the plasma concentration of NE was also markedly elevated with both HUT alone and supine smoking, but did not increase during smoking plus HUT (Table 1). Thus, the most noteworthy effect of tobacco smoking during the HUT was the high level of plasma ER compared with the levels detected during supine smoking or HUT alone. The left ventricular end-diastolic dimension (LVEDd) was decreased during the HUT alone and with smoking during HUT; the fractional shortening of the left ventricle (%FS) was increased during the HUT alone, but the increase was more marked when HUT was combined with smoking (Table 1).
In the present case, the HUT combined with tobacco smoking or isoproterenol provocation induced an initial increase in HR followed by a marked and abrupt decrease in both blood pressure (BP) and HR, together with syncope. Generally, the mechanisms underlying NMS are as follows. In the upright posture, the blood volume resides

**Table 1** Plasma Concentrations of Epinephrine and Norepinephrine, and Echocardiographic Data

<table>
<thead>
<tr>
<th></th>
<th>Smoking (−)</th>
<th>Smoking (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supine</td>
<td>HUT</td>
</tr>
<tr>
<td>Epinephrine (pg/ml)</td>
<td>4</td>
<td>64</td>
</tr>
<tr>
<td>Norepinephrine (pg/ml)</td>
<td>276</td>
<td>992</td>
</tr>
<tr>
<td>LVEDd (mm)</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td>FS (%)</td>
<td>22</td>
<td>43</td>
</tr>
</tbody>
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LVEDd, left ventricular end-diastolic dimension; FS, fractional shortening.

**Discussion**

In the present case, the HUT combined with tobacco smoking or isoproterenol provocation induced an initial increase in HR followed by a marked and abrupt decrease in both blood pressure (BP) and HR, together with syncope. Generally, the mechanisms underlying NMS are as follows. In the upright posture, the blood volume resides
mainly in the lower half of the body. As venous return decreases, the right ventricular pressure and left ventricular volume both decrease. The sympathetic supply to the heart is excited and the parasympathetic supply depressed through the baroreceptor reflex, and myocardial contractility and HR are both elevated. An increase in left ventricular contractility at a reduced volume stimulates mechanoreceptors in the left ventricle, which causes a decrease in HR, because of excitation of cardiac vagal efferents, and a fall in BP from both the reduced HR and the peripheral vasodilatation. The main cardiovascular effects of nicotine occur via sympathetic nerve stimulation, which increases both HR and myocardial contractility.

In the present case, the syncope induced by tobacco smoking in the standing position can be explained as follows: nicotine causes sympathetic nerve stimulation leading an elevation of both myocardial contractility and HR at a reduced stroke volume (caused by a decrease in venous return while standing and by a dilatation of peripheral vascular beds). As described earlier, this would lead to abrupt falls in both HR and BP, followed on at least some occasions by syncope. The high levels of plasma ER seen in the present case during the HUT plus smoking would make a major contribution to peripheral vasodilatation by dilating resistance vessels in skeletal muscle in addition to the cardiac effects induced by smoking. This hypothesis is supported by the similarities between the effects induced by smoking during the HUT (Fig 1) and those induced by isoproterenol provocation during the HUT (Fig 2).

A limitation in this case is that we did not measure cerebral blood flow when syncope was induced by smoking in the standing position or during the HUT. The simultaneous decrease in BP and HR would be expected to cause cerebral hypoperfusion (if the cerebral perfusion pressure falls below the range of autoregulation). Consequently, measurement of cerebral blood flow would be of great interest. Moreover, measurement of the serum concentration of nicotine and/or the HUT with placebo smoking would be of great importance to exclude the effect of stress caused by smoking itself, and to identify the direct effects of nicotine on NMS.

References