Autonomic nervous system function in myotonic dystrophy

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Symptoms suggestive of dysautonomia are often reported in Myotonic Dystrophy (MD) patients. 12 patients with MD underwent cardiovascular function testing with assay of plasma noradrenaline (NA) and adrenaline (A) in supine rest condition and after orthostatic and cold stimulus. Statistical analysis showed no differences between MD patients and an age and sex matched control group.

Key Words: Myotonic dystrophy — cardiovascular reflex — autonomic nervous system — catecholamines

Introduction

Myotonic Dystrophy (MD) is a multisystem disease transmitted in autosomal dominant fashion, marked by myotonia, muscular weakness, atrophy and characteristic electromyographic abnormalities [10, 11]. Clinical features known to be associated with autonomic nervous system (ANS) dysfunction such as orthostatic hypotension, gastrointestinal motility disorders, cardiac arrhythmias, ventilatory, bladder and sexual disturbances are common in MD [9, 12]. ANS activity in MD patients has been investigated by studying pupillary function, cardiovascular reflexes and plasma catecholamine levels [1, 4, 7, 13-15]. The results of these studies have been contradictory; some authors suggested a primary involvement of ANS in MD and others a defective function of the target organs.

This study aimed to assess whether signs of subclinical ANS dysfunction in MD patients can be revealed by means of cardiovascular reflexes and the evaluation of NA and A plasma levels.

Subjects and methods

We studied 12 patients, 6 males and 6 females, with mild to moderate MD. The severity of the disease was classified on the basis of the patient’s ability to perform everyday activities. 5 cases were sporadic, the other 7 came from 3 families. The mean age of patients was 36±15 years (range 15-62). Clinical diagnosis was confirmed by EMG studies. Clinical history and physical examination were negative for signs of autonomic dysfunction.

None of the patients had diabetes, hypertension, renal or endocrine disease.

Patients were compared with 23 age (36±15 years, range 14-67) and sex (12 males and 11 females) matched controls. All subjects had normal glucose tolerance test and sodium and potassium plasma levels.

Studies were performed in a temperature-controlled (23±1°C) clinical investigation room. We monitored: systemic blood pressure (automatic sphygmomanometer), heart rate (pectoral elec-
trogdyes), thoracic breathing (strain-gauge), oronasal breathing (thermistor). Blood sample were drawn from an indwelling intravenous cannula in a forearm vein for measurement of plasma NA and A by means of high pressure liquid chromatography with electrochemical detection [2].

Autonomic function studies:
1) Beat to beat heart rate variability: recording 150 R-R intervals in basal conditions. We considered: mean and standard deviation (SD) of 150 successive R-R intervals, the SD of the differences between one R-R interval and the next (Mean-square successive difference; MSSD) and the maximum change with respect to the mean of R-R intervals expressed as a percentage (N%).
2) Head-up tilt test: After 30 min of resting supine the patients were moved by means of a tilting table with footrest from the supine to the erect position (65°) for 10 min. Blood pressure and heart rate were measured every minute. Venous blood was sampled for the determination of plasma NA and A levels 5 and 1 min before the test and at the 2nd min during the test. The variations from the basal value of systolic and diastolic blood pressure, heart rate, NA and A plasma levels were measured.
3) Valsalva manoeuvre: the patients were asked to blow into a mouthpiece attached to a mercury manometer to maintain a pressure of 40 mmHg for 12 sec. We calculated the ratio of the longest R-R interval after the manoeuvre (within about 20 beats) to the shortest R-R interval during the manoeuvre (Valsalva ratio; VR).
4) Deep breathing: the heart rate variation was recorded during deep breathing (6 breaths/min for 2 min). The following parameters were considered: the heart rate variation (ΔHR) calculated using the 10 longest R-R intervals during expiration and the 10 shortest R-R intervals during inspiration, and the ratio of the mean R-R interval during inspiration to the mean R-R interval during expiration (I/E).
5) Cold pressor test: patients were requested to immerse a hand in water at 4°C for 2 min. Blood pressure and heart rate were measured every minute. Venous blood was sampled for the determination of plasma NA and A levels 5 and 1 min before the test and at the 2nd min during the test. The variations from the basal value of systolic and diastolic blood pressure, heart rate, NA and A plasma levels were measured.
6) Lying down: the patients were requested to maintain the erect position for 20 sec and then quickly lie down and stay supine breathing regularly. We calculated the ratio of the longest R-R interval during the beats before lying down to the shortest R-R interval during the 10 beats after lying down (standing to lying ratio; S/L).

Statistics

Results are presented as mean ±SD. The differences between MD patients and controls were compared by a Mann Whitney test. Variables were considered to be significant if p < 0.05.

Table I. Cardiovascular and catecholamine responses to tilt test and to cold pressor test (Mean ±SD)

<table>
<thead>
<tr>
<th>TILT TEST</th>
<th>SBP (mmHg)</th>
<th>DBP (mmHg)</th>
<th>HR (bts/min)</th>
<th>NA (pg/ml)</th>
<th>A (pg/ml)</th>
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<tbody>
<tr>
<td>Basal Tilt Basal Tilt Basal Tilt Basal Tilt Basal Tilt Basal Tilt</td>
<td></td>
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<tr>
<td>MD n=11 36±16 yrs</td>
<td>110±13 108±13 66±11 68±10 67±12 81±10</td>
<td>181±87 398±89</td>
<td>28±17 64±65</td>
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</tr>
<tr>
<td>CONTROLS n=23 36±15 yrs</td>
<td>114±14 117±8 69±7 73±8 68±8 83±9</td>
<td>185±89 378±138</td>
<td>20±10 36±18</td>
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</tbody>
</table>

| COLD PRESSOR TEST | Basal Cold P. Basal Cold P. Basal Cold P. Basal Cold P. Basal Cold P. Basal Cold P. |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| MD n=12 36±16 yrs | 110±13 136±12 66±10 87±14 66±9 75±10 | 157±34 204±58 | 30±24 34±20 |
| CONTROLS n=23 36±15 yrs | 113±7 125±12 68±7 79±6 65±6 71±6 | 123±56 164±34 | 19±11 31±23 |

SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate; NA = noradrenaline; A = adrenalin.