Assessment of cardiac autonomic neuropathy in young diabetics with postural orthostatic tachycardia syndrome

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Abstract

Background: One of the serious complications of diabetes mellitus is cardiac autonomic neuropathy (CAN) which may lead to life-threatening complications such as silent myocardial infarction. Autonomic neuropathy is one of the established causes of postural orthostatic tachycardia syndrome (POTS).

Aim: In this study, we performed various autonomic function tests in young diabetics who were diagnosed with POTS. Our aim was to assess the severity of CAN in them.

Methods: 20 young diabetics mean age 16.5 years (SD 2.66) diagnosed with POTS were assessed for this study. Autonomic function tests such as deep breathing test (DBT), Valsalva ratio (VR), 30:15 ratio, lying to standing test (LST) and cold pressor test (CPT) were performed in all the subjects. Degree of CAN was assessed in them and categorized as per the severity.

Result: In these subjects, we found that the symptoms of orthostatic intolerance such as a headache, sweating, palpitations etc were present in all the subjects. Autonomic function tests that were deranged are DBT (5%), VR (1%), 30:15 ratios (1%), LST (50%) and CPT (15%). In these subjects 10% subjects had “Early CAN”, 30% had “Definite CAN” and 60% had “Severe CAN”.

Conclusion: Clinical assessment revealed that all the subjects had orthostatic intolerance and some degree of CAN. Further studies need to be carried out to assess the autonomic functions and severity of CAN in young diabetics with POTS for proper management which may help in improving quality of life in them. TCM-GMJ April 2018; 3 (I):P13-P16

Keywords: POTS, cardiac autonomic neuropathy, type1 diabetes mellitus, adolescents.

Introduction

Postural orthostatic tachycardia syndrome (POTS) is a form of dysautonomia associated with symptoms of orthostatic intolerance such as nausea, blurring of vision, light headedness and near syncope upon acquiring upright position1. These symptoms are immediately relieved by a recumbent posture1. The main characteristic feature of POTS in adults is a resting heart rate of ≥ 120 beats per minute (bpm) or an increase in the heart rate of ≥ 30 bpm upon standing within 10 minutes of head-up tilt test or lying to standing test2. In young people such as adolescents, POTS is defined as a resting heart rate of ≥ 130 bpm or an increase in heart rate of ≥ 40 bpm upon acquiring an upright posture within 10 minutes of standing3. Adolescence is a period of rapid growth and development which may lead to temporary impairment in the flexibility of autonomic nervous system thus leading to a physiological phenomena called as “developmental POTS” which usually peaks at around 14 years of age and fades away at around 19 years of age4. However, in young people, POTS may also occur as a result of autonomic neuropathy due to diabetes mellitus5. It must be noted that not all the patients with POTS exhibit peripheral or autonomic neuropathy5. Thus normally cardiac autonomic neuropathy (CAN) can’t be proposed as a mechanism underlying POTS6. Yet it is not uncommon to find some degree of CAN in patients diagnosed with POTS preferentially impairment of sympathetic innervation of the lower limbs7. Nearly half of the patients with POTS exhibit some signs of autonomic neuropathy8.

Materials and methods

Study design and population

After obtaining clearance from the institutional ethical committee we recruited 20 adolescents with type 1 diabetes mellitus (T1DM) who were diagnosed with POTS from the outpatient department of Endocrinology, GMC Srinagar and SMHS hospital, J&K, India for this descriptive study. Prior to the commencement of study all the subjects or their caretakers were consulted. They have explained the significance of this study. Once they agreed to participate in this study informed written consent was taken from the subjects or their caretakers. Later they were invited to the autonomic function testing laboratory in the Department of Physiology for assessment of CAN. Subjects on drugs that tend to alter heart rate such as β adreno-mimetics / blockers were excluded from this study.

Data collection

Symptoms related to autonomic nervous system functioning were assessed in all the subjects. All the subjects completed a self-reported questionnaire to assess the severity of orthostatic intolerance. The questionnaire contained various symptoms of orthostatic intolerance such as a headache, sweating, palpitations etc. Later subjects were made to rest for at least
15 minutes in a recumbent position before the beginning of autonomic function tests for the assessment of CAN. Resting blood pressure and heart rate were measured. Various autonomic function tests such deep breathing test (DBT); E/I ratio, Valsalva ratio (VR), 30:15 ratio, cold pressor test (CPT) and lying to standing test (LST) were performed. The severity of CAN was assessed and divided on the basis of Ewing's classification of autonomic failure.

Analysis of data

The data obtained have been presented in terms of percentages wherever applicable.

Result

The inclusion of patients and their characteristics

Overall 20 adolescents with T1 DM who were diagnosed with POTS were selected for this study. Mean age of the patients was 16.5 ± 2.66 years. All the patients were assessed for the symptoms of orthostatic intolerance and CAN.

Findings

As shown in Table 1 most of the patients complained of weakness (85%), palpitations (80%) and headache (70%). Least common symptom reported by the subjects was hyperventilation (5%). Table 2 shows the various autonomic function tests that were performed. We observed that LST was abnormal in 10 patients (50%). DBT was abnormal in 5 patients (25%), CPT was abnormal in 3 patients (15%) and both VR and 30:15 ratio were abnormal in 1 patient each (5%) as shown in Table 2. Ewing’s criteria were used to assess the severity of CAN as shown in Table 3. As shown in Table 3 we observed that none of the patients had normal findings (0%), 2 patients (10%) had “Early CAN”, 6 patients (30%) had “Definite CAN” and 12 patients (60%) had “Severe CAN”.

Discussion

In adolescents, POTS is defined as an increase in heart rate of ≥ 40 bpm upon acquiring upright posture within 10 minutes or a sustained resting heart rate of ≥ 130 bpm. Diabetes mellitus is regarded as one of the important causes of POTS. As already mentioned nearly half of the patients with POTS exhibit CAN at some stage.

Symptoms of orthostatic intolerance

In our study, we observed that all the subjects had symptoms of orthostatic intolerance. The most common symptom of orthostatic intolerance was a weakness (85%) which was described as tiredness by the subjects not related to the amount of work done followed by palpitations (80%). Both these symptoms were reported upon standing up from a recumbent position. Similar findings were reported by Kanjwal et al (10) who studied 9 patients diagnosed with POTS. They found that all the patients 9/9 (100%) developed fatigue and palpitations upon acquiring upright posture. Presyncope/Syncope was found in 6 patients (30%) of patients which were defined as lightheadedness, chest tightness, blurring of vision or transient loss of consciousness upon acquiring upright posture. All these symptoms faded away upon acquiring a recumbent posture. Kanjwal K et al11 reported findings similar to our study. They recruited 300 subjects diagnosed with POTS and found that 18 of them developed syncope upon head-up tilt test (HUTT).

Autonomic function tests and CAN

All the subjects were made to rest in a recumbent position before beginning the procedure. Standard autonomic function tests like DBT, VR and 30:15 ratio (to assess parasympathetic activity) were performed in all subjects12. LST and CPT (to assess sympathetic activity) were also done (13). A rest of 5 minutes was given in between all the tests. We observed that all patients had impaired parasympathetic and sympathetic activity which suggests the presence of CAN in them. Autonomic neuropathy in patients with POTS was also reported by Jacob G et al17 who compared the autonomic function tests of 10 patients diagnosed with POTS with age and sex-matched healthy controls. They found that the autonomic function tests of POTS group were significantly reduced (p< 0.05) as compared to the controls. They concluded that patients with POTS had developed CAN. In another study Oner T et al14 studied 125 patients with symptoms of POTS. They found that patients with POTS had deranged sympathetic functions and they concluded that these patients had autonomic neuropathy. In contrast to our findings, Qi Fu et al15 in their study of 19 patients with POTS did not find autonomic neuropathy in them when compared to controls. Findings in our preliminary study suggest autonomic neuropathy in young diabetics with POTS. We observed that LST and CPT which are used to assess the sympathetic activity were abnormal in 50% and 3% patients respectively. This means that sympathetic activity was impaired in most of the patients with POTS. Other tests to assess parasympathetic activity such as DBT, VR and 30:15 ratio were deranged in 25%, 5%, and 5% patients respectively which means that parasympathetic activity was also impaired in these patients. It may be concluded that CAN was present in young diabetics with POTS and most of them had abnormal sympathetic activity.

Assessment of severity of CAN in young diabetics with POTS

CAN in these patients was assessed and graded according to Ewing’s classification of autonomic failure. Normal: normal tests or one parasympathetic test borderline. Early CAN: 1 abnormal parasympathetic test or 2 tests borderline. Definite CAN: ≥ 2 abnormal parasympathetic tests. Severe CAN: ≥2 abnormal parasympathetic tests + 1 abnormal sympathetic test/2 borderline sympathetic tests.

In our study, we found that CAN was present in all the subjects 20/20 (100%). Most of the patients had “Severe CAN” which means that both parasympathetic and sympathetic activity was impaired in them with a sympathetic preponderance. As already mentioned autonomic failure with a sympathetic preponderance in patients diagnosed with POTS was also reported by Raj SR6 and Jacob G et al7 in their studies. We also observed, “Early CAN” and “Definite CAN” in 10% and 30% of patients respectively which means that there is an excessive abnormality of parasympathetic activity in them. Thus we found CAN in all the young diabetics with POTS.

This study has limitations. We obtained the information regarding symptoms of POTS from all the subjects but we did
not perform HUTT in them to confirm POTS as the patients were already diagnosed. We did not perform heart rate variability analysis of these patients which would otherwise have been beneficial. In our case sample size was small as it is very difficult to find young diabetics with POTS. One of the major limitations is that we could not ascertain whether POTS in these patients resulted due a rapid spurt of growth in adolescence which is purely a physiological process or it was a result of diabetes mellitus that these young patients were suffering from. Further studies with a large sample size are needed to confirm our findings and biochemical parameters such as fasting glucose and glycaemic control (HbA1c) must be recorded to ensure a proper analysis.

In conclusion, all the young diabetic patients diagnosed with POTS had symptoms of orthostatic intolerance that affected the quality of their life. Furthermore, all the patients had underlying autonomic dysfunction which was graded accordingly. Our thinking is that the loss of flexibility of autonomic nervous system has led to POTS in them. Appropriate treatment and counseling may be beneficial for them as it can improve their quality of life.

**Acknowledgments**

We are extremely grateful to Dr. Riyaz Ahmad Lone for his contribution.

There is no conflict of interest.

No funding or financial support was received.

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**Table 1. Symptoms of orthostatic intolerance in young diabetics with POTS.**

<table>
<thead>
<tr>
<th>Symptoms of Orthostatic Intolerance (OI)</th>
<th>Percentage of subjects with symptoms of OI</th>
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<tbody>
<tr>
<td>Headache</td>
<td>70%</td>
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<tr>
<td>Fatigue</td>
<td>50%</td>
</tr>
<tr>
<td>Sweating</td>
<td>55%</td>
</tr>
<tr>
<td>Palpitations</td>
<td>80%</td>
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<tr>
<td>Weakness</td>
<td>85%</td>
</tr>
<tr>
<td>Sleep disorder</td>
<td>25%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>20%</td>
</tr>
<tr>
<td>Tremors</td>
<td>10%</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>5%</td>
</tr>
<tr>
<td>Dizziness/Vertigo</td>
<td>35%</td>
</tr>
<tr>
<td>Presyncope/ Syncope</td>
<td>30%</td>
</tr>
</tbody>
</table>

**Table 2. Autonomic function tests in young diabetics with POTS.**

<table>
<thead>
<tr>
<th>Autonomic function tests</th>
<th>Percentage (%) of subjects with abnormal tests.</th>
</tr>
</thead>
<tbody>
<tr>
<td>DBT</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>VR</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>30:15 ratio</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>LST</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>CPT</td>
<td>3 (15%)</td>
</tr>
</tbody>
</table>

DBT - deep breathing test; VR - Valsalva ratio; 30:15 ratio - ratio of maximum R-R interval at around 30th beat to the minimum R-R interval at around 15th beat; LST - lying to standing test; CPT - cold pressor test

**Table 3. Assessment of CAN in young diabetics with POTS as per Ewing’s classification of autonomic failure.**

<table>
<thead>
<tr>
<th>Severity of CAN</th>
<th>Young diabetics with POTS (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Early CAN</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Definite CAN</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Severe CAN</td>
<td>12 (60%)</td>
</tr>
</tbody>
</table>
References