Postural ortostatik taşıkardi sendromunda piridostigminin tedavisi

Pyridostigmine treatment in postural orthostatic tachycardia syndrome

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**Summary** - A 34-year-old female patient was admitted with the complaints of inability to stand upright, palpitations, dizziness, and fatigue in the upright posture for the last one year. She was found to stand upright for less than one minute without symptoms. Tilt table testing showed that, compared to baseline her heart rate increased 55 beats/min in the fifth minute of the test with the symptoms of palpitations, fatigue and sweating without any significant change in her blood pressure. Postural orthostatic tachycardia syndrome was diagnosed, and pyridostigmine treatment was started. Four months after treatment her symptoms were relieved so that she was able to function as a nurse.

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**Abbreviation:**

POTS Postural orthostatic tachycardia syndrome

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Postural orthostatic tachycardia syndrome (POTS) generally affects women in their reproductive age, and it is characterized by complaints of palpitations, distress on the chest, dizziness, and blackout when standing upright. Typically these complaints resolve after assuming seated or supine positions. The most typical characteristics of this syndrome is especially extreme increase in heart rate without any change in the blood pressure when the patient assumes standing position. Fludrocortisone which increases intravascular volume, midodrine which increases peripheral vasoconstriction or beta blockers which suppress increase in heart rates have been tried for the pharmacological treatment of these patients. A few studies also demonstrated the effectiveness of pyridostigmine in patients with POTS which is an acetylcholine esterase inhibitor used in the treatment of myasthenia gravis. We also initiated pyridostigmine treatment for our patient, and received excellent responses within the subsequent four months. Our patient who had been a disabled nurse before the treatment, practiced her profession again after the treatment.

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Medical treatment with pyridostigmine was initiated at twice daily doses of 15mg. In addition, ivabradine treatment was started to control her sinus rate. However eye problems related to ivabradine therapy developed which necessitated discontinuation of this drug, and only pyridostigmine therapy was maintained. Even though intravenous fluid therapy was not maintained during subsequent days, the patient was able to remain at standing position for longer periods day by day, and at the end of the 5. day this standing period neared to half an hour. The patient was discharged with recommendations of wearing compression stockings, increasing her daily water, and salt intake, and taking 30 mg pyridostigmine tablets three times a day. One month later, her complaints markedly regressed. She was again performing her daily routine, and returned to practise her profession of nursing which requires long hours of standing.

**DISCUSSION**

Under normal conditions standing upright causes pooling of nearly 500 ml of blood from the thorax down to lower extremities, and lower abdominal quadrants  This decrease in the cardiac preload also decreases filling pressure of the heart, and blood pressure. Decrease in the compressive forces on baroreceptors leads to decrease in parasympathetic tonus, and sympathetic activation. Systemic vasoconstriction, and increase in heart rate occurs. In conclusion net hemodynamic effect of standing upright include an increase of 10-20 bpm in heart rate, insignificant changes in systolic blood pressure, and nearly 5 mm Hg increase in diastolic blood pressure. When these changes occurring against gravity do not develop properly, the patient presents with symptoms of orthostatic hypotension (autonomic nervous system insufficiency) or orthostatic tachycardia (POTS). In POTS patient’s blood pressure do not drop when he/she stands up, on the contrary it can increase. The most important characteristic feature of this syndrome is that excessive increase in heart rate when assuming standing position is accompanied by many symptoms which are relieved when the patient lies down.[5]

Diagnostic criteria of POTS include symptoms of chronic orthostatic intolerance recurring for at least 6 months, increase in heart rate of ≥ 30 bpm within 10 minutes of assuming upright posture that develops without orthostatic hypotension. Other causes of orthostatic symptoms or tachycardia (incl. prolonged bed rest, bleeding, dehydration and drugs) should be ruled out. [5]

Nearly 80% of the patients are female age between 13, and 50 years. [6] Patient symptoms start usually after a viral disease, pregnancy or major surgery. Patients have both cardiac (palpitations, dizziness, chest distress, and shortness of breath), and non-cardiac complaints (headache, vomiting, nausea, shivering, blackout, sleep disorders, fatigue, and intolerance to exercise).

A single treatment modality is not successful per se. Correctable causes should be investigated (complaints of the patients which develop following a prolonged bed rest will be resolved a short time after he stands up). The patient should be counseled, and he/she should avoid dehydration, and exposure to very warm environments which might exacerbate his/her complaints. The patient should increase his/her fluid, and salt intake (daily intake of 8-10 glasses of water, and 8-10 gr sodium). Compression stockings (up to the waist with a compressive pressure of 30-40 mmHg) which decrease peripheral venous congestion should be recommended. [5] The first required step in pharmacological therapy is discouraging the patient from using tachycardia inducing drugs (diuretics, vasodilators, and tricyclic antidepressants which are noradrenaline transport blockers) if possible. Volume expanders (fludrocortisone, desmopressin) can be recommended for hypovolemic patients. With its peripheral α-1 receptor agonist properties, midodrine can induce vasoconstriction, and alleviate orthostatic tachycardia. Beta blockers can be used in low doses (10-20 mg propranolol t.i.d).[5]
Pyridostigmine is currently used in the treatment of neurogenic orthostatic hypotension.\(^7\) In recent years, some publications have indicated its marked symptomatic beneficial effects in patients with POTS.\(^3,4\) Pyridostigmine through inhibition of acetylcholine esterase at synaptic level, increases acetylcholine levels with resultant stimulation of preganglionic (sympathetic, and parasympathetic) and postganglionic parasympathetic receptors. Possibly the most predominant effect of pyridostigmine in patients with POTS is its suppressive impact on heart rate through increase in parasympathetic tonus. In turn, increase in sympathetic tonus via its α-1 stimulatory effect also increases peripheral vascular resistance particularly detected in lower extremities.\(^4\) Raj et al.\(^4\) measured heart rates, and blood pressures of the patients with POTS, 2, and 4 hours after administration of pyridistigmine therapy. They demonstrated that pyridostigmine therapy achieved significant drop in heart rates relative to placebo without significant alterations in blood pressure.

Pyridostigmine has known adverse effects predominantly involving gastrointestinal system (nausea, vomiting, diarrhea, and abdominal pain), then less frequently on neuromuscular (muscle cramps), and genitourinary (frequency in urination) systems. For that reason, initially twice daily doses of 30 mg are recommended, and if it doesn’t demonstrate any therapeutic response, and the patient can tolerate higher doses then one week later the dose can be increased to thrice daily doses of 60 mg. After a treatment period lasting one or two weeks, if any response can not be elicited, and the patient can still tolerate higher doses, then increasing the daily doses to 90 mg tid or switching to once daily 180 mg doses of sustained-release tablets is recommended.\(^3\) In our patient, initially lower doses of pyridostigmine (15 mg bid) were prescribed to refrain from its adverse effects, and in parallel with the treatment response dose was gradually, and successfully increased to thrice daily doses of 30 mg.

Since expert concensus opinion cited in the literature also recommends serotonin reuptake inhibitor (SSRI) therapy for patients with POTS, we maintained patient’s previous SSRI therapy.\(^8\)

**Conflict of Interest:** None declared

**REFERENCES**


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