

# Comparison of Health Education, Oral Rehydration Solution, Metoprolol and Midodrine Intervention in Children with POTS

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## ABSTRACT

**Introduction:** The postural orthostatic tachycardia syndrome is heterogeneous group of disorder. When a healthy individual stands up, gravity causes about 10%-15% of his or her blood to settle in the abdomen or limbs. This pooling of blood means that less blood reaches the brain, the result of which can be a feeling of lightheadedness, darkening of vision, or even fainting. Hence, the aim of the present study was to evaluate the clinical features and the effectiveness of non-pharmacological and pharmacological treatment in patients with POTS.

**Material and Methods:** A retrospective medical record analysis of the patients referred to pediatric cardiology unit of our Second Xiangya Hospital of Central South University since June 2003 to February 2010 was done. This study included 33 children patients aged 6 to 16 years old among 17 male (mean 10.62±2.88 years) and 16 female (mean 11.81±1.64 years) after medication within 14 days to 6 months with follow up record.

**Results:** The most common presenting symptoms of POTS were found to be dizziness or light-headedness (66.66%) followed by chest tightness (30.30%), syncope (27.27%), headache (24.24%) and pallor (24.24%) respectively. About 75.5% of children patients met diagnostic criteria for POTS during 5 to 10 minute of HUTT. There was significant statistic difference in heart rate between before and after treatment of total patients during 5 and 10 minute of HUTT (P<0.05). The overall improvement found in 24(72.72%) patients whereas 9(27.27%) patients not respond to the given treatment regimen.

**Conclusion:** The most common presenting symptom of POTS was dizziness or light-headedness. Most of the patients meet diagnostic criteria for POTS during 5 to 10 minute duration of HUTT. Health education, ORS, propranolol and midodrine were effective in treatment of POTS and helpful to diminish the upright tachycardia. Whereas health education and health education with midodrine hydrochloride treatment method were more likely effective than health education with ORS and health education with metoprolol method.

**Keywords:** Postural Orthostatic Tachycardia Syndrome, Health Education, Oral Rehydration Solution, Midodrine, Propranolol

hypotension within 10 minutes of orthostatic. Usually POTS develops in childhood or early adult life and is more predominantly seen in females.<sup>1</sup>

The frequent symptoms associated with POTS are light-headedness or dizziness, syncope, weakness, palpitation, tremulousness, shortness of breath, chest pain, bloating nausea, vomiting, abdominal pain, constipation, diarrhea, bladder dysfunction, papillary dysfunction, fatigue, sleep disturbance, migraine headache, myofascial pain, and neuropathic pain. These symptoms are life altering. Such patients have to use 3 times more energy to stand than a healthy person; activities such as house work, and even mean bathing can exacerbate symptoms. Quality of life in the POTS patients is similar to those with congestive heart failure and chronic obstructive pulmonary disease.<sup>2</sup>

The cardinal clinical sign in POTS is an abnormal tachycardia on during upright position, less common or rare physical sign include the development of acrocyanosis in 40%-50% of the patients during prolong standing. Currently, the key method for treatment of POTS are non-pharmacological treatment (health education) supplemented with pharmacological treatment.

Educate children with POTS and their parents a simple description of physiological mechanism regarding the nature of this disorder and guide the patients and their parents to

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## INTRODUCTION

The term “postural orthostatic tachycardia syndrome” (POTS) is a clinical syndrome of orthostatic intolerance characterized by increased heart rate of more than 30 beats per minute (>40 beats per minute children aged 12-19 years of age) associated with symptoms of orthostatic intolerance (for ex. brain fog, pre-syncope) in the absence of orthostatic

avoid aggravating factors such as dehydration, prolonged standing, warm confining environments and crowded places etc.<sup>3</sup>

Daily life increased water and salt intake in patients with POTS can moderately reduce orthostatic tachycardia, experts recommend to drink at least 2 litre of water daily and salt supplement may helpful in POTS for those patients with low blood volume. It can stimulate baroreceptors, and decrease the heart rate by increasing parasympathetic tone. Schroeder et al demonstrated that water drinking improves orthostatic tolerance, whereas Claydon et al studied among adult patients and concluded that salt supplementation improved orthostatic symptoms such as postural syncope.<sup>4,5</sup>

Beta blockers such as propranolol are frequently used, primarily to blunt heart rate acceleration. It is reported that propranolol prevent the abnormal relaxation of blood vessels and allow more time for left ventricular filling and particularly effective in patients with POTS. In a study done by Raj et al it was found that low dose beta blockers can decrease tachycardia and improve symptoms in patients with POTS.<sup>6</sup>

Midodrine hydrochloride can increase peripheral vascular resistance by inducing vasoconstriction. It is reported that it can improves orthostatic tolerance and potentially suppress the inappropriate tachycardia.<sup>7</sup> The aim of the present study was to assess the clinical features, outcome of the treatment and also to compare the efficacy of health education, ORS, metoprolol and midodrine hydrochloride in children with POTS so that the relative efficacy and impact of these drug therapies on the functioning and quality of life in pediatric patients diagnosed with POTS can also be evaluated.

## MATERIAL AND METHODS

The present study was a retrospective study with follow up record within 15 days to 6 months of the patients referred to pediatric cardiology unit of our Second Xiangya Hospital of Central South University since June 2003 to February 2010. This study included 33 children patients aged 6 to 16 years old among 17 male (mean 10.62±2.88 years) and 16 female (mean 11.81±1.64 years). The written informed consent was taken with the parents of all the children, which was approved by ethics committee of Second Xiangya Hospital of Central South University.

An absolute increase in HR of >30 beats per minute or sustained HR of >120 beats per minute within 10 minute of initiation of the tilt with associated symptoms of orthostatic intolerance like light-headedness or dizziness, weakness, palpitation tremulousness, chest pain, chest discomfort, sweating and even syncope etc. in absence of drop in systolic blood pressure of >20 mmHg and/or diastolic blood pressure of >10 mmHg (1 mmHg=0.133 kPa) were considered as an inclusion criteria for HUTT.

The patients were selected with POTS on the basis of preexisting head-up tilt table test (HUTT) diagnosis including normal supine heart rate without any organic heart disease. History of each patient was recorded in detail with complete physical examination done very carefully. A

series of examinations such as 12-lead electrocardiography (ECG), echocardiography, chest X-ray, electrocardiography, electroencephalography (EEG), CT scan or MRI of head routine blood including fasting blood glucose and cardiac troponin, was done to exclude organic heart disease and other diseases then HUTT.

Total 33 patients meets the inclusion criteria and were randomly divided into 4 treatment method groups, health education group (n=6), health education with ORS (n=16), health education with metoprolol (n=6), health education with midodrine hydrochloride (n=5). Instruments used were computed radiography imaging system, direct view CR 850, Kodak Corporation, USA. Ultrasound, SEQUIOA-512 MODEL, Siemens Corporation, Germany, Single-spiral CT scanner Hispeed, GE Corporation, USA, dual-gradient magnetic resonance imaging, Singna 1.5T, GE Corporation, USA, Nervous system digital EEG machine, Nation 9128-05, NCC Corporation, Shanghai, China and multi-functional automatic ECG analyzer with multi-functional ECG monitor, DASH 2000, GE MARQUEETE Corporation, USA.

Children and their parents were informed about the occurrence and prognosis of POTS and were educated regarding necessary guidelines such as raising the lower limbs, squatting or leg crossing etc. which can improve quality of life in patients. Elastic support was also advised which can help to minimize the degree of peripheral venous pooling and enhance venous return. Aerobic and resistance training was also advised which can improve orthostatic symptoms etc. About 1 pack of ORS (14.75g) per day with 500 ml of water was given. Metoprolol was provided to children and was prescribed 1 mg per kilogram per twice a day of metoprolol. About 1.25gm midodrine hydrochloride twice a day was given at 8 o'clock in the morning and at 4 o'clock evening.

Patient who meets the POTS positive criteria (n=33) were divided into 4 treatment method groups i.e. health education group (n=6), health education with ORS (n=16), health education with metoprolol (n=6) followed by health education with midodrine hydrochloride (n=5). In 1<sup>st</sup> group health education method was recommended. In 2<sup>nd</sup> group, 1 pack (14.75g) per day of ORS with 500 ml of water added with health education was recommended. In 3<sup>rd</sup> group 1mg per kilogram twice a day of metoprolol added with health education were prescribed. In 4<sup>th</sup> group were prescribed 1.25 mg of midodrine hydrochloride twice a day once at 8 o'clock morning and once at 4 o'clock evening added with health education were prescribed.

## STATISTICAL ANALYSIS

The data was entered into the excel sheet and statistical analysis was carried out using SPSS 16.0 package Quantitative data was performed using t-test and qualitative data were compared with chi square ( $\chi^2$ ) test or fisher exact test. P<0.05 was considered to be statistically significant.

## RESULTS

The main symptoms among 33 patients aged between

Group	Male	Female
Age	10.70±2.80	11.81±1.64
t value	-1.373	
p value	>0.05	

**Table-1:** Shows the mean age difference between male and female

Symptoms among the patients	Percentage
Dizziness	22 (66.6%)
Chest tightness	10 (30.30%)
Syncope	9 (27.27%)
Headache	8 (24.24%)
Pallor	8 (24.24%)
Sudden visual disturbance	8 (24.24%)
Chest discomfort	5 (15.15%)
Abdominal Pain	3 (9.09%)
Hot extremities	3 (9.09%)
Chest pain	2 (6.06%)
Tremulousness	1 (3.03%)
Nausea	1 (3.03%)

**Table-2:** Shows the symptoms among patients with POTS

Time	Before Treatment	After Treatment	t value	p value
Supine Position	81.69±16.10	81.75±3.62	-.027	>0.05
During Tilt starts	101.09±15.44	99.15±14.43	.736	>0.05
During 5 minutes of HUTT	112.03±14.32	105.39±15.88	2.074	<0.05
During 10 minutes of HUTT	116.76±15.29	106.94±15.55	2.896	<0.05

**Table-3:** Shows the before and after treatment heart rate of children with POTS in supine position, during tilt starts, 5 minutes and 10 minutes of HUTT

Group	Before Treatment	After Treatment	t value	p value
Health Education	78.83±5.87	76.733±2.85	.531	>0.05
Health Education with ORS	83.12±4.34	83.62±2.74	.902	>0.05
Health Education with metoprolol	86.16±8.05	88.50±9.84	-.449	>0.05
Health Education with midodrine hydrochloride	75.20±9.73	74.20±6.76	.443	>0.05

**Table-4:** Shows the comparison of heart rate in children with POTS treated with four different methods in supine position

Group	Before Treatment	After Treatment	t value	p value
Health Education	98.83±6.63	93.83±5.78	.548	>0.05
Health Education with ORS	103.56±13.07	102.88±9.65	.189	>0.05
Health Education with metoprolol	97.20±10.58	90.40±7.74	1.468	>0.05
Health Education with midodrine hydrochloride	95.00±11.64	93.80±8.81	.209	>0.05

**Table-5:** shows the comparison of heart rate in children with POTS treated with four different methods during tilt start

Group	n	Improved and also functionally normal	No response with treatment
Health Education	6	5(83.3%)	1(16.7%)
Health Education with ORS	16	11(68.8%)	5(31.2%)

**Table-6:** Shows the comparison in treatment outcome of health education group and health education with ORS group after 14 days to 6 month of medication

Group	n	Improved and also functionally normal	No response with treatment
Health Education	6	5(83.3%)	1(16.7%)
Health Education with Metoprolol	6	4 (66.7%)	2(33.3%)

**Table-7:** Shows the comparison in treatment outcome of health education group and health education and metoprolol group after 14 days to 6 month of medication

6 to 16 years old (mean age), 17(51.5%) male of mean age (10.70±2.80) and 16 (48.5%) female of mean age (11.81±1.64) were included in this study (Table no. 1). The most common symptom seen was dizziness, chest tightness and syncope followed by headache, pallor, chest discomfort and visual disturbances (Table no. 2). When heart rate of total 33 patients was compared with POTS after 14 days to 6 months of medication in supine position, during tilt starts, 5 minutes of HUTT and 10 minutes of HUTT, heart rate in supine position and during tilt starts was found to be statistically not significant ( $p>0.05$ ) but heart rate during 5 and 10 minutes of HUTT was statistically significant ( $p<0.05$ ) (Table no. 3).

In present study, it was found that when comparison of heart rate in children treated with POTS was done with four different methods in supine position, the majority of the patients showed reduction in mean scores in health education group followed by health education with midodrine hydrochloride but this was not found to be statistically significant at  $p$  value  $>0.05$  (Table no. 4). It was found that during tilt start, health education with metoprolol showed maximum reduction in

Group	n	Improved and also functionally normal	No response with treatment
Health Education	6	5(83.3%)	1(16.7%)
Health Education with midodrine hydrochloride	5	4 (80%)	1 (20%)

**Table-8:** Shows the comparison in treatment outcome of health education group and health education and midodrine hydrochloride group after 14 days to 6 month of medication

mean scores which was again not found to be statistically significant at p value >0.05 (Table no. 5).

When comparison in treatment outcome of health education group and health education with ORS group after 14 days to 6 month of medication was done it was found that with health education only 1 patient did not showed any improvement whereas with health education and ORS, 5 patients did not showed any response (Table no. 6). With health education and metoprolol, 2 patients did not show any response with treatment whereas health education with midodrine hydrochloride, only 1 patient did not responded and 4 patients improved functionally normal (Table no. 7 and 8).

## DISCUSSION

The concept of poor orthostatic tolerance was a questionnaire by researchers since 19<sup>th</sup> century, firstly reported by an American physician “Decosta” were on American civil war soldiers and termed as Irritable heart syndrome. Later on in 1919 Sir Thomson Lewis termed these conditions as “The effort syndrome” and termed “Postural tachycardia syndrome” (POTS) by McClean identical symptom appeared caused by venous pooling of blood in lower extremities in his study.<sup>8</sup>

In patients with POTS may manifest some abnormality in physiological compensatory mechanism, typically in the body’s ability to recover from the initial hemodynamic shift. Thus with postural changes to an upright position, venous return is not adequately augmented and the patient’s heart rate continues to increase, to compensate for this lack of venous return to the central circulatory system. Change in blood pressure is characteristically blunted in patients with POTS. Many signs and symptoms of POTS in particular, likely result from abnormalities in appropriate fluid shifting in response to triggers.<sup>9</sup>

All the patients have wide variety of symptoms that were exacerbated by postural changes. In a study conducted by Sandroni et al it was found that in their large series study more than 75% of their patient’s chief complaints was dizziness or light headedness, lower extremity or diffuse weakness, disequilibrium.<sup>10</sup>

In a study done by Pandian et al reported that the common presenting symptoms were light-headedness in 100% of patients in their study followed by pallor (90%), weakness (80%) and clammy skin (80%), both of above study was on adult patients. In this study, total 33 patients aged between 6 to 16 years old, male 17(51.2%) with mean age of 10.70±2.80 years and female 16 (48.8%) with mean age of 11.81±1.64. Thieben et al reported that patients with POTS were predominantly female (86.8%) and relatively young 30.8±13.3 years and male 20(13.2%) with the mean age of

26.3±13.3 years.<sup>11,12</sup>

In a study done by Claydon et al reported that the salt intake has no effect on resting heart rate or blood pressure but orthostatic intolerance symptoms can be improved and decrease in heart rate by cerebrovascular and peripheral vascular control without affecting blood pressure.<sup>5</sup>

These studies done by various authors have suggested that drinking water can improve sympathetic activity caused by autonomic system dysfunction hence water presser could be applied to the patients with POTS caused by autonomic system dysfunction. The present study results also showed that treatment outcome with oral rehydration solution, there is decrease in postural heart rate suggestive that it is an effective treatment for patients with POTS.<sup>13,14</sup>

In a study done by Hoeldtke et al demonstrated potency of midodrine hydrochloride in the treatment of patients with POTS and orthostatic intolerance and described that the standing heart rate in POTS, 114±0.7 beats per minute suppressed to 92.8±0.7 (P<0.001) after midodrine hydrochloride therapy and thus concluded it suppress tachycardia in POTS and improve standing time in orthostatic intolerance in adult patients.<sup>15</sup>

There are several important limitation of this study, first is the relatively small sample of the patients, after treatment the effect on hemodynamic index are different in comparing total patients and by dividing them into 4 groups. Secondly, short duration of medication s as some patients had follow up after 14 days and also there are a lot of patients who came to follow up after several months. Nonetheless, this study suggested that these patients can overall improve by these 4 methods of treatment. Non-pharmacologic and pharmacologic therapies had greater efficiency in some patients but as POTS is a heterogeneous disorder so which patients will benefit from which medication needs further exploration of research.

## CONCLUSION

POTS are heterogeneous group of disorders with peripheral autonomic dysfunction. The causes of POTS are remaining uncertain. The treatment of POTS requires a multidisciplinary approach entailing pharmacologic and dietary strategies correlating the prevailing clinical deficits. Health education and health education with midodrine hydrochloride treatment method were more likely effective than health education with ORS and health education with metoprolol method.

## REFERENCES

1. Grubb BP, Kanjwal Y, Kosinski DJ. The postural tachycardia syndrome: a concise guide to diagnosis and management. *J Cardiovasc Electrophysiol*, 2006; 17:108-112.
2. Stewart JM. Chronic orthostatic intolerance and the

- postural tachycardia syndrome (POTS). *J Pediatr.* 2004; 145:725-730.
3. Raj SR. The postural tachycardia syndrome (POTS): pathophysiology, diagnosis and management *J. Indian Pacing Electrophysiol.* 2006; 6: 84-99.
  4. Benarud-Larson LM, Dewar MS, Sandroni P, et al. Quality of life in patients with postural tachycardia syndrome. *Mayo Clinical proceedings.* 2002; 77:531-537.
  5. UM Ango, MO Oche, IS Abubakar, KJ Awosan, Kaoje AU, MO Raji. Effect of health education intervention on knowledge and utilization of health facility delivery services by pregnant women in Sokoto State, Nigeria. *International Journal of Contemporary Medical Research* 2018; 5:F4-F9.
  6. Schroeder C, Bush VE, Norcliffe LJ, et al. Water drinking acutely improves orthostatic tolerance in healthy subjects. *Circulation.* 2002; 106:2806-2811.
  7. Yashaswi P, Kudachi, Madhav Prabhu, Mubashir Bashir Angolkar. Impact of health education on knowledge of new-born care among expectant women in urban area of Belagavi, India: pre and post study. *International Journal of Contemporary Medical Research* 2017; 4:305-308.
  8. Abe H, Kohshi K, Nakashima Y. Efficacy of orthostatic self-training in medically refractory neurocardiogenic syncope. *Clinical and experimental hypertension.* 2003; 25:487-493.
  9. Shannon JR, Diedrich A, Biaggioni I, et al. Water drinking as a treatment for orthostatic syndromes. *Am J Med* 2002; 112: 355-360.
  10. Sandroni P, Opfer- Gehrking TL, McPhee BR, et al. Postural tachycardia syndrome: clinical features and follow up study. *Mayo Clin Proc.* 1999; 74:1106-1110.
  11. Pandian JD, Dalton K, Hendreson RD, et al. Postural orthostatic tachycardia syndrome: an under-recognized disorder. *Intern Med J.* 2007; 37:529-535.
  12. Tanaka H, Matsushima R, Yamaguchi H, et al. effects of midodrine on circulatory responses to standing in children with instantaneous orthostatic hypotension and those postural tachycardia syndrome. *Autonomic Nervous system.* 2001; 38:299-305.
  13. Thieben MJ, Sandroni P, Sletten DM, et al. Postural orthostatic tachycardia syndrome: the Mayo clinic experience. *Mayo Clin Proc.* 2007; 82:308-313.
  14. Bush VE, Wight VL, Brown CM, et al. Vascular responses to orthostatic stress in patients with postural tachycardia syndrome (POTS), in patients with low orthostatic tolerance, and in asymptomatic controls. *Clin Auton Res.* 2000; 10:279-284.
  15. Hoeldtke RD, Bryner KD, Hoeldtke ME, et al. Treatment of postural tachycardia syndrome: a comparison of octreotide and midodrine. *Clin Auton Res,* 2006; 16:390-395.

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