Online Supplement

Exercise Training versus Propranolol in the Treatment of the Postural Orthostatic Tachycardia Syndrome

[1,2]Qi Fu, [1]Tiffany B. VanGundy, [1,2]Shigeki Shibata,
[2]Richard J. Auchus, [3]Gordon H. Williams, [1,2]Benjamin D. Levine

[1]Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital Dallas
[2]The University of Texas Southwestern Medical Center at Dallas, Dallas, Texas
[3]Brigham & Women's Hospital, Harvard Medical School, Boston, Massachusetts

Running title: Drug vs. Nondrug Therapy in POTS

DISCUSSION

Studies regarding the effectiveness of β-blockers in POTS have been limited and the results are inconsistent. Table S1 summaries the current literature on β-blockers in POTS patients. Data on chronic β-blockade treatment in POTS are lacking. Future research is needed in this regard.

REFERENCES

1. Sumiyoshi M, Nakata Y, Mineda Y, Yasuda M, Nakazato Y, Yamaguchi H. Analysis of heart rate variability during head-up tilt testing in a patient with idiopathic postural orthostatic tachycardia syndrome (POTS). *Jpn Circ J.* 1999;63:496-498.
2. Abe H, Nagatomo T, Kohshi K, Numata T, Kikuchi K, Sonoda S, Mizuki T, Kuroiwa A, Nakashima Y. Heart rate and plasma cyclic AMP responses to isoproterenol infusion and effect of beta-adrenergic blockade in patients with postural orthostatic tachycardia syndrome. *J Cardiovasc Pharmacol.* 2000;36:S79-S82.
3. Gordon VM, Opfer-Gehrking TL, Novak V, Low PA. Hemodynamic and symptomatic effects of acute interventions on tilt in patients with postural tachycardia syndrome. *Clin Auton Res.* 2000;10:29-33.
4. Freitas J, Santos R, Azevedo E, Costa O, Carvalho M, de Freitas AF. Reversible sympathetic vasomotor dysfunction in POTS patients. *Rev Port Cardiol.* 2000;19:1163-1170.
5. Raj SR, Black BK, Biaggioni I, Paranjape SY, Ramirez M, Dupont WD, Robertson D. Propranolol decreases tachycardia and improves symptoms in the postural tachycardia syndrome: less is more. *Circulation.* 2009;120:725-734.
6. Stewart JM, Munoz J, Weldon A. Clinical and physiological effects of an acute alpha-1 adrenergic agonist and a beta-1 adrenergic antagonist in chronic orthostatic intolerance. *Circulation.* 2002;106:2946-2954.
7. Seeck M, Blanke O, Zaim S. Temporal lobe epilepsy and postural orthostatic tachycardia syndrome (POTS). *Epilepsy Behav.* 2002;3:285-288.
8. Chen L, Du JB, Zhang QY, Wang C, Du ZD, Wang HW, Tian H, Chen JJ, Wang YL, Hu XF, Li WZ, Han L. [A multicenter study on treatment of autonomous nerve-mediated syncope in children with beta-receptor blocker]. *Zhonghua Er Ke Za Zhi.* 2007;45:885-888.
9. Lai CC, Fischer PR, Brands CK, Fisher JL, Porter CB, Driscoll SW, Graner KK. Outcomes in adolescents with postural orthostatic tachycardia syndrome treated with midodrine and beta-blockers. *Pacing Clin Electrophysiol.* 2009;32:234-238.

T**able S1**. The Effectiveness of β-Blockers in POTS

Types	Authors, Year, Reference	Agents	Patient Characteristics	Study Design	Measured Variables	Effectiveness
Non-selective β-blockers	Sumiyoshi et al, 1999[1]	Propranolol (oral, 10 mg daily)	1 male POTS patient (age 16 y)	Case report, treatment duration not reported	Heart rate variability, clinical symptoms	Effective, symptoms abolished, orthostatic tolerance improved
	Abe et al, 2000[2]	Propranolol (oral, 30 mg)	POTS patients (8 women, 2 men, age 15-28 y)	Acute case-control study	Heart rate, clinical symptoms	Symptoms abolished in ~70% of patients
	Gordon et al, 2000[3]	Propranolol (oral, 40 mg)	POTS patients (20 women, 1 man, age 14-39 y)	Acute, randomized crossover design	Heart rate, blood pressure, symptom scores	Tachycardia improved, symptom tended to be improved
	Freitas et al, 2000[4]	Bisoprolol	POTS patients (n = 11, all women)	Acute case-control study	Heart rate, blood pressure, baroreflex, orthostatic tolerance	Improved greatly
	Raj et al, 2009[5]	Propranolol (oral, low-dose 20 mg or high-dose 80 mg)	POTS patients (~90% women, mean age 34 y)	Acute, randomized crossover design	Heart rate, blood pressure, symptoms	Effective, low-dose was better than high-dose
Selective β_1-blockers	Stewart et al, 2002[6]	Esmolol (rapid infusion 300 μg/kg for 3 min, then at 200 μg/kg/min to attain a ~20% decrease in heart rate	POTS patients (11 girls, 3 boys, age 13-19 y)	Acute case-control study	Heart rate, blood pressure variability, peripheral blood flow, orthostatic tolerance	Did not improve orthostatic tolerance or hemodynamics
	Seeck et al, 2002[7]	Bisoprolol (oral, 5 mg/day for 10 wks)	1 female POTS patient with partial epilepsy (age 20 y)	Case report	Heart rate, blood pressure	Effective, tachycardia and associated anxiety disappeared
	Chen et al, 2007[8]	Metoprolol (oral)	POTS patients (n = 27, 50% women, age 5-19 y)	Randomized design	Clinical symptoms	Improved in ~69% of patients
	Lai et al, 2009[9]	Metoprolol or atenolol (treated for >6 mo in 64% of patients)	POTS patients (11 women, 3 men, age 11-17 y)	Retrospective study, single center, chart review, survey	Heart rate, clinical symptoms	Symptom improved in 57% of patients