

# Orthostatic intolerance syndromes –medical treatment

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# Orthostatic intolerance – medical treatment

- There is little evidence that any treatment helps children with vasovagal syncope or POTS...

**2015 Heart Rhythm Society Expert Consensus Statement  
on the Diagnosis and Treatment of Postural Tachycardia  
Syndrome, Inappropriate Sinus Tachycardia, and  
Vasovagal Syncope**

Sheldon et al. Heart Rhythm 2015;12:e41-e63

- and physicians rely on insights from adult medical literature.





# Orthostatic intolerance in children – medical treatment

## Recommendations—POTS and Vasovagal Syncope in the Young

|   | Class | Level |
|---|-------|-------|
| Pediatric patients presenting with suspected vasovagal syncope or POTS should undergo a detailed medical history review and physical examination and undergo a 12-lead ECG. | I     | E     |
| Pediatric patients with suspected POTS should undergo orthostatic testing.  | I     | E     |
| Tilt-table testing is reasonable for highly selected pediatric patients with suspected vasovagal syncope.   | IIa   | C     |
| It seems reasonable to treat selected pediatric patients with vasovagal syncope with midodrine.   | IIb   | B-R   |
| It seems reasonable to treat pediatric patients with vasovagal syncope or POTS with interventions that are recommended for adults with these disorders.                     | IIb   | E     |



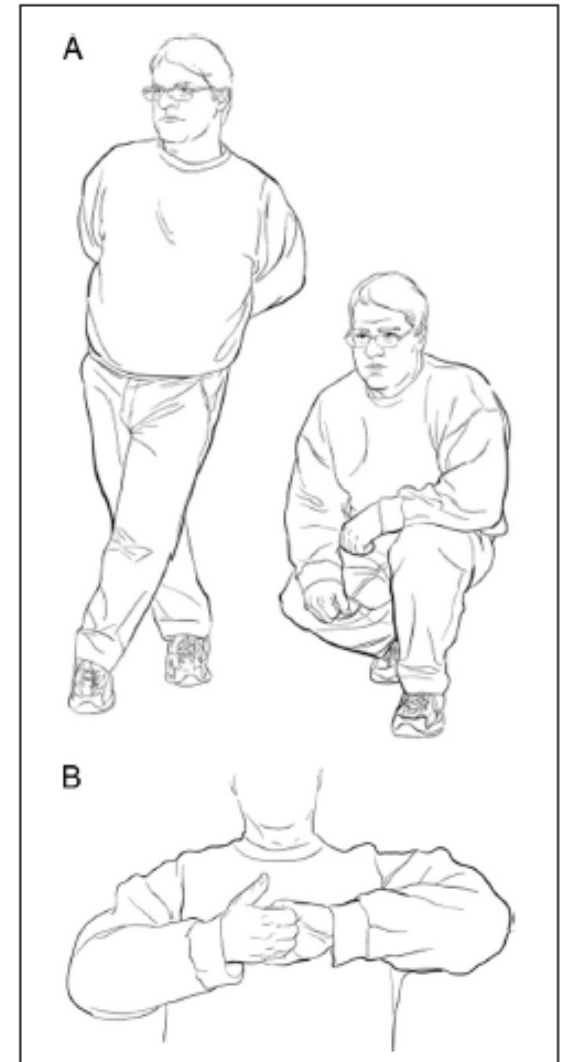
# Orthostatic intolerance – medical treatment

- Education and reassurance
- Promoting fluid and salt intake
- Physical counterpressure maneuvers
  - Fludrocortisone
  - Pyridostigmine
  - Ivabradine
  - Beta blockers
  - SSRI inhibitors
  - Clonidine, methyldopa
  - Midodrine



# Physical counterpressure

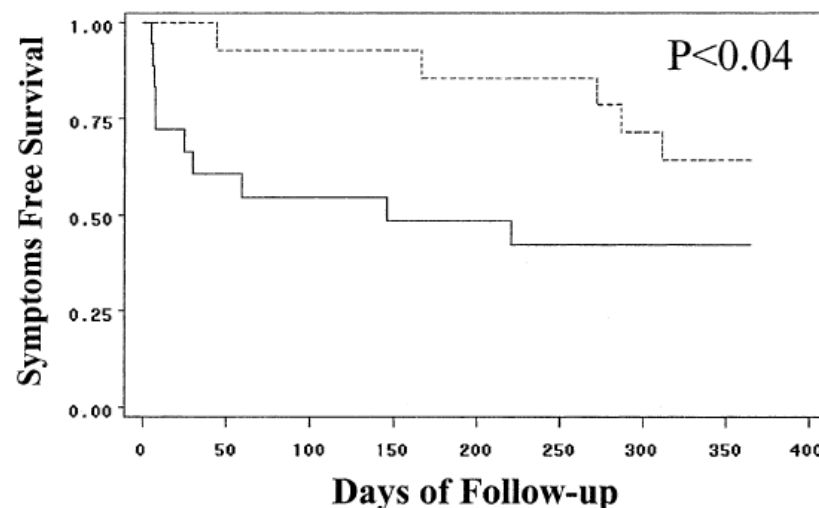
- Maneuvers to delay an imminent vasovagal or orthostatic faint
  - Boosting blood pressure enough to delay symptoms
- A) leg-crossing with lower body muscle tensing or squatting
- B) Arm-tensing





# Fludrocortisone

- Corticosteroid with mainly mineralocorticoid activity
  - Na and water retention, K excretion
  - Open label studies showing efficacy in children
  - One randomized, double-blind, placebo controlled study
- Use reasonable (IIb)
  - POTS (LOE E)
  - Syncope (LOE C)



**Figure 1.** Symptom-free survival. Dashed line = placebo; solid line = salt and fludrocortisone.



# Pyridostigmine

- Parasympatomimetic agent
  - Acetylcholinesterase inhibitor
  - Blunts orthostatic tachycardia
  - Many adverse effects
    - Diarrhea, abdominal pain, nausea
- IIb (LOE C) for POTS



# Ivabradine

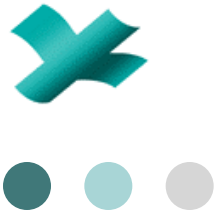
- Developed for treatment of stable angina and heart failure
  - Specific slowing effect on sinus node (25-40 bpm)
  - No effect on atrial, AV or intraventricular conduction
  - No decrease in BP
- One study reports symptom improvement in 60% of POTS patients
- No recommendation for POTS
- IIa (LOE B-R) for ITS





# Beta blockers

- Low dose propranolol lowers heart rate and improves symptoms in POTS
  - Higher doses less tolerated
- Not effective in IST: side effects
- Not effective in vasovagal syncope
  - III (ESC 2009)
  - IIb (LOE B-R) in persons > 40 years



# Selective serotonin uptake inhibitors

- Fluoxetine, paroxetine
- Serotonin is involved in the midbrain regulation of HR and BP
- Contradictory evidence
- Uncertainty on the use of SSRIs in preventing syncope



# Alpha-2-agonists

- Clonidine
- Methyldopa
- Act centrally to decrease sympathetic tone
- IIb (LOE E) in POTS with prominent hyperadrenergic features



# Midodrine

- Pro-drug
  - Desglymidodrine, alpha-1-agonist
  - Constricts veins and arteries
  - Short acting, T1/2 3 hours
  - Administered tid, daytime only
- Significant reduction of orthostatic tachycardia
- Mean risk reduction of 62% in syncope
- IIb (LOE B-R) syncope and POTS



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# POTS – treatment recommendations

## Recommendations—Treatment for POTS

|  | Class | Level |
|--|-------|-------|
| A regular, structured, and progressive exercise program for patients with POTS can be effective.   | IIa   | B-R   |
| It is reasonable to treat patients with POTS who have short-term clinical decompensations with an acute intravenous infusion of up to 2 L of saline.   | IIa   | C     |
| Patients with POTS might be best managed with a multidisciplinary approach.  | IIb   | E     |
| The consumption of up to 2–3 L of water and 10–12 g of NaCl daily by patients with POTS may be considered.   | IIb   | E     |
| It seems reasonable to treat patients with POTS with fludrocortisone or pyridostigmine.  | IIb   | C     |
| Treatment of patients with POTS with midodrine or low-dose propranolol may be considered.  | IIb   | B-R   |
| It seems reasonable to treat patients with POTS who have prominent hyperadrenergic features with clonidine or alpha-methyl dopa.   | IIb   | E     |
| Drugs that block the norepinephrine reuptake transporter can worsen symptoms in patients with POTS and should not be administered.   | III   | B-R   |
| Regular intravenous infusions of saline in patients with POTS are not recommended in the absence of evidence, and chronic or repeated intravenous cannulation is potentially harmful.  | III   | E     |
| Radiofrequency sinus node modification, surgical correction of a Chiari malformation type I, and balloon dilation or stenting of the jugular vein are not recommended for routine use in patients with POTS and are potentially harmful. | III   | B-NR  |



# Idiopathic sinus tachycardia – treatment recommendations

## Recommendations—Treatment for IST

|  | Class | Level |
|--|-------|-------|
| Reversible causes of sinus tachycardia should be sought and treated.   | I     | E     |
| Ivabradine can be useful for treating patients with IST.   | IIa   | B-R   |
| Sinus node modification, surgical ablation, and sympathetic denervation are not recommended as a part of routine care for patients with IST. | III   | E     |



# Vasovagal syncope – treatment recommendations

## Recommendations—Lifestyle and Medical Treatment for Vasovagal Syncope

|  | Class | Level |
|--|-------|-------|
| Education, reassurance, and promoting salt and fluid intake are indicated for patients with vasovagal syncope, unless contraindicated. | I     | E     |
| Reducing or withdrawing medications that can cause hypotension can be beneficial for patients with vasovagal syncope.                  | IIa   | E     |
| Physical counterpressure maneuvers can be useful for patients with vasovagal syncope who have a sufficiently long prodromal period.    | IIa   | B-R   |
| The use of fludrocortisone seems reasonable for patients with frequent vasovagal syncope who lack contraindications for its use.       | IIb   | E     |
| Beta-blockers may be considered for patients older than 40 years with frequent vasovagal syncope.                                      | IIb   | B-R   |
| The use of midodrine seems reasonable for patients with frequent vasovagal syncope and no hypertension or urinary retention.           | IIb   | B-R   |



# Conclusions

- Ortostatic intolerance syndromes remain difficult to manage
  - Evidence for different modalities is quite vague
- Increased fluid and sodium intake are recommended
- Midodrin seems promising in treating vasovagal syncope
- Ivabradine seems promising in treating IST