June 8, 2018, London UK

TREATMENT OF VASOVAGAL SYNCOPE
Where to go for help

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

2017 ACC/AHA/HRS Guideline for the Evaluation and Management of Patients With Syncope: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

2018 ESC Guidelines for the diagnosis and management of syncope

The Task Force for the diagnosis and management of syncope of the European Society of Cardiology (ESC)
Syncope: HRS Definition

- Syncope is defined as:
  - a transient loss of consciousness,
  - associated with an inability to maintain postural tone,
  - rapid and spontaneous recovery,
  - and the absence of clinical features specific for another form of transient loss of consciousness such as epileptic seizure.
Syncope

- Vasovagal
- Cardiac
- Orthostatic
- Carotid sinus
Vasovagal syncope is defined as a syncope syndrome that usually:

1. occurs with upright posture held for more than 30 seconds or with exposure to emotional stress, pain, or medical settings;
2. features diaphoresis, warmth, nausea, and pallor;
3. is associated with hypotension and relative bradycardia, when known; and
4. is followed by fatigue.
Physiology of Symptoms and Signs

Decreased cardiac output

Hypotension
- Weakness
- Lightheadness

Retinal hypoperfusion
- Blurred vision, grey vision, coning down
Physiology of Symptoms and Signs

Decreased cardiac output

Reflex cutaneous vasoconstriction

• Maintains core blood volume

• Pallor, looks grey or very white
Vasovagal reflex

Worsened hypotension
- More weakness
- More lightheadness

Vagal
- Nausea and vomiting
- Diarrhea
- Abdominal discomfort
Increase arterial conductance

Rapid transit of core blood to skin
- Hot flash
- Warmth and discomfort
- Lasts seconds
- Pink skin

Physiology of Symptoms and Signs
Physiology of Symptoms and Signs

Collapse

- Preload restored
- Reflexes end
- Skin colour recovers
- Exhausted
Why do we need to treat people?

- Impact on life
- Work, school, driving
- Quality of life
- Injury
- Anxiety

- Everyone is different
STRATEGY

First: Listen
Second: Teach
Third: Drugs
Fourth: Pace, rarely
Prognosis depends on previous year

7% recurrence

46% recurrence
VVS Treatment Strategy

- **Occasional episode**
  - reassure, fluid/salt, counterpressure maneuvers

- **No episode in previous year**
  - no Rx

- **Recurrent VVS**
  - conservative Rx, eliminate drugs causing hypotension

- **Recurrent VVS**
  - fludrocortisone,
  - midodrine or
  - β-blockers (over age 40)
Placebo vs no pill control

Meta analysis of recurrences without treatment
Orthostatic stress almost always involved
Many patients avoid salt actively
Intravenous saline prevents positive tilt tests and vasovagal syncope
Simple, safe, inexpensive
Probably need 6 gm salt per day
PHYSICAL MANOEUVRES

- Shuffling and leg crossing
- Lying down
- Squatting
- Isometric leg crossing
PC-TRIAL

Log rank p=0.018
HR 0.59 (0.38-0.92).
Active treatments to consider

- Fludrocortisone
- Midodrine
- Beta blockers
POST2: Fludrocortisone in VVS

Syncope Free Survival (ITT)

- Fludrocortisone (F) - 43.6%
- Placebo (P) - 60.0%

P = 0.066 (Logrank)

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Fludrocortisone</th>
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<tbody>
<tr>
<td>Total</td>
<td>105</td>
<td>105</td>
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<tr>
<td>Months since randomization</td>
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<tr>
<td>0</td>
<td>62</td>
<td>68</td>
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<td>3</td>
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Graph showing the proportion of patients free from syncope over time with Placebo and Fludrocortisone treatment groups.
Post Hoc Analysis Outcome Results

After 2 weeks

0.2 mg treatment

Syncope Event Rate

Months since Dose Stabilization

Number at risk
Placebo 103 65 45 34 17
Fludrocortisone 101 69 54 44 25

Number at risk
Placebo 62 42 29 21 9
Fludrocortisone 63 49 41 34 20
Prevention of Syncope Trial (POST)

β-Blockers for VVS

R Sheldon et al., Circulation. 2006;113(9):1164-70.
POST: Treatment by Age Group

POST 5

R Sheldon et al., Circulation. 2006;113(9):1164-70.
Age < 42
- Cohort
- POST
- Pooled

Age >= 42
- Cohort
- POST
- Pooled

Hazard Ratio
MIDODRINE EFFECTS

- Prodrug for alpha₁ adrenergic agonist
- Does not penetrate blood brain barrier
- Metabolite half life 2.5 hours
- Increases venoconstriction and arteriolar constriction
- Increases preload and peripheral resistance
- Start at 5 mg po tid q4h
- Piloerection, paresthesias, hypertension, urinary retention
<table>
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<tr>
<th>Study or subgroup</th>
<th>Midodrine Events</th>
<th>Midodrine Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Weight</th>
<th>Risk ratio M-H. random, 95% CI</th>
<th>Risk ratio M-H. random, 95% CI</th>
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<td>Recurrent reflex syncope</td>
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<td>8</td>
<td>9</td>
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<td>0.23 (0.06, 0.79)</td>
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<tr>
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<td>33</td>
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<tr>
<td>Total</td>
<td>27</td>
<td>94</td>
<td>15</td>
<td>112</td>
<td>100.00%</td>
<td>0.43 (0.27, 0.68)</td>
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</table>

Total events 27 73

Heterogeneity: Tau²=0.09; Chi²=6.27, df=4 (p=0.18); I²=36%
Test for overall effect: Z=3.64 (p=0.0003)
Non-invasive treatment of vasovagal syncope

- Treat patients who have fainted in the previous year
- Teach increased salt and fluid intake in patients with normal blood pressure
- Teach patients to use physical manoeuvres
- Start with clinical trial of florinef in normotensive patients
- Use metoprolol in patients >40 years, especially with co-morbidities such as hypertension
- Midodrine in normotensive patients with frequent syncope
STRATEGY

1. We as physicians are the best treatment
2. Reduce hypotensive drugs
3. Teach, teach, teach
4. Commit to seeing again if unsure
5. Florinef or midodrine
6. Beta blockers
7. Rarely pacemakers