What is POTS? Diagnosis, treatment and management options

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Overview

- Pathophysiology
- Diagnostic criteria & classification
- Symptoms
- Investigation
- Treatment
Autonomic disturbance

- Described in studies as early as 1940
- First named and identified in 1993 (Schondorf and Low)
- Hypertension associated with POTS previously described as the "hyperadrenergic syndrome" (Streeten)
- Described as "idiopathic hypovolemia" by Fouad
- Hypotension associated with POTS has been previously described as the "neurally mediated hypotension" form of POTS.

Pathophysiology

- Upright posture $\rightarrow$ instantaneous descent of $\sim 500$ ml of blood from the thorax to the lower body $+10$-$25\%$ shift of plasma volume extravascularly
- $\downarrow$ venous return $\rightarrow$ $\downarrow$ arterial pressure/cardiac filling
- $\downarrow$ baroreceptor pressure $\rightarrow$ sympathetic activation $\rightarrow$ $\uparrow$ heart rate/systemic vasoconstriction
- Upright posture $\uparrow$ 10-20 bpm HR/negligible SBP/$\sim 5$ mmHg $\uparrow$ DBP
Pathophysiology

- Dysautonomia
- Impaired peripheral vasoconstriction
- NET abnormalities
- Autonomic nerve disruption
- Abnormalities of RAAS
Diagnostic criteria

• Heart rate increase ≥30 beats per minute (or > 120) from supine to standing (10 min) (5-30)

• Symptoms get worse with standing and better with recumbence

• Symptoms lasting ≥6 months

• Standing plasma norepinephrine ≥600 pg/ml (≥3.5 nM)

• Absence of other overt cause of orthostatic symptoms or tachycardia (e.g. active bleeding, acute dehydration, medications).
Diagnostic criteria
Symptoms

- Tachycardia
- Exercise intolerance
- Lightheadedness
- Extreme fatigue
- Headache
- Mental clouding
- Many others associated with autonomic disturbance
Classification

- Primary POTS
- Partial dysautonomic/neuropathic POTS
- Hypovolaemic POTS
- Central Hyperadrenergic POTS
- Deconditioning POTS
- Developmental POTS
- POTS secondary to other causes
Classification

- Partial dysautonomic/neuropathic POTS (peripheral adrenergic failure)
- Peripheral autonomic neuropathy
- Venous pooling and compensatory tachycardia
- 4:1 ♀:♂
- Abrupt symptom onset (post viral, other event)
- ? autoimmune
Classification

- Hypovolaemic POTS
- Sensitive to salt/plasma volume changes
Classification

• Central Hyperadrenergic POTS
• Excessive sympathetic discharge
• Single NET point mutation
• High levels of upright NA
• Orthostatic hypertension
• Gradual/progressive symptoms
• Family history
• Migraines
Classification

• Deconditioning POTS
• Fatigue symptoms prominent
• ? Initial illness/event with orthostatic symptoms
• ↓ Physical activity/deconditioning
Classification

- Developmental POTS
- Younger onset/growth spurt
- Mainly ♀
- Severe disability
- Good prognosis
Classification

- POTS secondary to other causes
- Joint hypermobility syndrome (JHS)
- Earlier symptoms
- ↑ syncope/migraine
Investigations

- ECG
- Blood tests (U&E’s/FBC/Ferritin/Vitamin B12/folate/TFTs/Short synacthen testing & ATCH
- Echocardiography
- 24 hr Holter monitor/event recorder
- 24hr urinary catecholamines and free metanephrines.
- 24hr urinary sodium
Investigations

- Head up tilt table test (HUTT) and Active Stand Test (30 bpm threshold - an active stand has a specificity of 79% compared to a tilt test of 23%)

- Supine noradrenaline is often high normal in subjects whilst supine but on standing can be elevated (>600pg/ml)

- Further autonomic function tests (thermoregulatory sweat test typically, preserved vagal function and often a vigorous pressor response to the Valsalva manoeuvre)
Acral cyanosis
Treatment

• Identify and treat reversible causes/remove potentially causative drugs

• Ensure patient sufficient fluid/sodium intake (1,500–2,500 ml and sodium excretion of 170 mmol/24 hours)

• Compression stockings

• Countermanoeuvres

• Exercise (aerobic/resistance)
Treatment

- Pharmacological treatments
- Beta Blockers
- Hyperadrenergic PoTS (labetalol/carvedilol)
- Not usually used with POTS/reflex syncope overlap
Treatment

- Pharmacological treatments
- Clonidine
  - 0.1-0.4 mg twice daily
  - Alpha 2 agonist inhibits sympathetic outflow (hyperadrenergic form)
- Side effects: dry mouth, low resting HR/BP, constipation, blurred vision
Treatment

- Pharmacological treatments
- Fludrocortisone
- 50-200 mcg once daily Max dose can be up to 400 mcg daily
- partial dysautonomic POTS/hypovoleamia
- Expand plasma volume by enhancing sodium retention
- Sensitise peripheral alpha adrenergic receptors
- Does not work immediately/effects last after stopping
Treatment

- Pharmacological treatments
- Fludrocortisone
- Can deplete potassium and magnesium - monitoring required
- Side effects: worsening headaches, depression, hypokalaemia, hypomagnesemia, acne and fluid retention
- Symptoms of sympathetic over activity can be enhanced
Treatment

- Pharmacological treatments
- Ivabradine
- 2.5 – 5 mg twice daily (may be more)
- Side effects: muscle cramps
Treatment

- Pharmacological treatments
- Midodrine
  - 2.5-10mg 3-4 times a day (Each dose 3-4 hours apart; last dose no later than 3 hrs before bedtime)
- Alpha 1 agonist (neuropathic PoTS)
- Midodrine needs to be taken with an increased salt and water intake.
- Side effects: Piloerection, dilation of pupils, goose bumps, tingling, itching especially of the scalp, supine hypertension, nausea
Treatment

• Pharmacological treatments

• Octreotide

• 25 mcg bd or tds by subcutaneous injection (can be increased if necessary to 100-200 mcg tds)/depot

• Potent vasoconstrictor

• Side effects: nausea, abdominal pain, muscle cramps, hypertension
Treatment

- Pharmacological treatments
- Slow sodium
- 600mg once daily (10mg sodium)
- Aim: 24 hr urinary sodium 150-170 mmol/24hrs
Treatment

- Pharmacological treatments
- Selective Serotonin Reuptake inhibitors (SSRI’s) or Serotonin Noradrenaline Reuptake Inhibitors
- Sertraline starting at 25mg od (other SSRIS may be used)
- Venlafaxine and duloxetine (SNRI)
- SSRIs particularly useful in reflex syncope
- May help chest pain
- Side effects: GI upset, tremor, sleep disturbance, agitation and sexual dysfunction.
Treatment

- Pharmacological treatments
- Pyridostigmine
- Start dose of 30mg BD and titrate to 60-90mg tds if necessary
- Acetylcholinesterase inhibitor facilitates ganglionic neural transmission (postviral POTS/ POTS secondary to an autoimmune disorder (e.g. lupus/Sjögren).
- Side effects – Nausea, constipation, weakness
Summary

• Autonomic nervous system disorder
• Many/variety of symptoms
• Heart rate increase of ≥30 bpm/ >120 bpm standing 10 minutes
• High levels upright plasma norepinephrine/low blood volume
• Various subtypes
• Correct hypovolemia/non pharmacological measures
• ‘Pharmacological ladder’
Any Questions