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Clinical Protocol: Postural Orthostatic Tachycardia Syndrome (POTS)

Preamble

- POTS is diagnosed by the following criteria
  - Increased HR ≥30 bpm, or HR > 120 within 10 minutes of assuming an upright posture
  - No or minimal postural hypotension (a decrease in BP <20/10 mm Hg)
    - Some patients become hypertensive on standing
  - These criteria are more specific than tilt-table testing (i.e., tilt-table testing NOT required to make a diagnosis)
  - Symptoms worsen with standing and improved with recumbence
  - Symptoms last ≥6 months
  - Absence of other overt cause of orthostatic symptoms or tachycardia
    - E.g., volume depletion, medications, etc.
- Testing most sensitive when done in the morning
- Patients may have other cardiac and non-cardiac symptoms
  - Overlap with ME/CFS and related disorders
- Some patients may need a more extensive cardiac workup
- Up to 30% may faint
- Up to 50% may have dependent acrocyanosis
- Patients may be misdiagnosed with anxiety as a result of a misinterpretation of their physical symptoms
- POTS is a syndrome, not a disease
  - Blood Volume dysregulation
    - Seen in many, but not all patients
    - Patients have plasma volume deficits of almost 13%
    - Also, have inappropriately low levels of standing plasma renin activity and aldosterone (should be high when volume depleted) contributing to hypovolemia and impaired sodium retention
  - Neuropathic POTS:
    - Some patients have a form of dysautonomia, with preferential denervation of sympathetic nerves from the lower limbs
  - Central adrenergic POTS:
    - Most commonly secondary to a partial dysautonomia or hypovolemia
    - In a small subgroup of patients, the primary underlying problem seems to be excessive sympathetic discharge
      - Elevated norepinephrine levels
      - Sometimes have large increases in BP on standing
  - Other: genetic, epigenetic, mast cell activation
    - This subgroup sometimes has large increases in BP on standing
- Various mechanisms and phenotypes are described
  - Impaired sympathetically mediated vasoconstriction
  - Excessive sympathetic drive
  - Volume dysregulation
  - Deconditioning
- Non-pharmacological approaches should be tried first

- Switch patients off OCP with drospirenone (e.g., Yaz®, Yasmin®, Zarah®, Zamine®, Mya®)
  - Drospirenone is a spironolactone analog that could worsen hypovolemia
- Withdraw medications that might be predisposing to tachycardia
  - E.g., diuretics, vasodilators, TCAs,
- SNRIs can be helpful in some patients but worsen tachycardia in others
- The tachycardia in POTS patients should originate from the sinus node
- POTS patients often have preserved vagal function
- Much of the evidence is anecdotal or lower levels of evidence
- The treatments described below may occur one-on-one or in a group setting depending on resources
- Provide patient with information/dose adjustment handout
- It is expected that physicians would educate themselves about these drugs beyond the outline provided below

1. Patient Education

- Improves compliance and reduces symptoms activity
  - Avoiding aggravating factors (e.g., dehydration and extreme heat)
  - Waist-high compression stockings (30 – 40 mm Hg)
  - Increased salt and fluid intake (see Diet)
- Exacerbating factors
  - Symptoms tend to be worse in the morning
  - Rapid postural change
  - Raised temperature
  - Dehydration
  - Food ingestion
  - Alcoholic drinks
  - Physical exertion
  - Menstrual period
  - Prolonged bed rest or deconditioning
- Physical counter maneuvers may be helpful
  - Leg crossing
  - Bending forward and placing a foot on a chair
  - Making a fist, or active contraction of abdominal or buttock muscles
- Patients should keep a log/diary of symptom severity, associated disability, and response to treatments
- Incorporated into multiple offerings (e.g., handouts, web-based resources)
  - POTS Patient Resources
- Incorporated into core group: Living with Complex Chronic Diseases
- "Family and Friends" evening session
  - To register for the next event contact infoccdp@cw.bc.ca

2. Physical Activity

- Primarily aerobic with some leg-based resistance exercises
- Initially avoid upright exercises and focus on rowing machines, swimming, and recumbent cycles

- Other forms of exercise that focus on core such as Pilates, may be beneficial
- An exercise plan needs to be followed for those who have been inactive for a period of time
- May be difficult for patients with ME/CFS due to post-exertional malaise
- Offered in group setting and individual sessions with PT and OT
- Tai-Chi and mild Yoga
    - Suggested
    - Offerings in community rather than CCDP

3. Sleep

- See Sleep Protocol for details

4. Diet

- Increase water intake: 8 – 10 cups per day
- Increase salt intake: 9 g per day = 1 heaping tsp
    - Usually taken as ¼ tsp QID in liquid
    - Note: this is 9 g of NaCl, not 9 g of Na
    - Remember: normal saline is 0.9 % NaCl
        - That is 0.9 g per 100 mL (or 9 g per L)
        - So, I L of NS is equivalent to 1 heaping tsp of salt
- Occasionally, higher doses of salt may be needed
    - 24 hr urine Na of < 150 mmol per 24 hrs suggests more salt may be helpful
    - Up to 18 g (2 tsp) per day in divided doses
- Symptoms may worsen after eating
    - Eating smaller meals more often, and avoiding large heavy meals, may be helpful
- Stimulants such as coffee, tea, certain fizzy drinks and alcohol may also make symptoms worse, as can refined sugar, carbohydrates and dairy products
- Offered in group setting and individual sessions with dietitian

5. Alterative and Complementary Therapies

- none

6. Psychological and Behavioural Therapies

- Somatic hypervigilance, behavioral arousal, and emotional conditioning are important contributors in the maintenance to symptoms
- Incorporated in core group: Living with Complex Chronic Diseases
    - Combines Education, Pacing, CBT &, Mindfulness
    - 10 weekly sessions
- One-on-one counselling
- Incorporated into other groups

7. Interventions

- none

8. Medications

8.1 Propranolol

- Only added if persistent postural tachycardia remains despite 9 g of salt and water
  - The use of beta blockers in the presence of low intravascular volume can lead to hypotension and the blunting of a tachycardic response
  - Use low doses
    - Higher doses can worsen symptoms due to postural hypotension
- Doses:
  - Start with a 10 mg test dose to make sure patient can tolerate propranolol
  - 10 – 20 mg orally 3 – 4 times a day
  - Increase to 10 mg TID – QID, then 20 mg TID – QID if needed
  - Occasionally, higher doses are needed
- In patients with co-existing ME/CFS, beta blocker may worsen fatigue
- Watch for: Dizziness, hypotension, bradycardia, depression, diarrhea, rash, photosensitivity
- Beta-1 selective alternatives:
  - Longer acting beta blockers are less well tolerated
  - Metoprolol: 12.5 mg PO daily, increase to 25-50 mg PO BID, may double dose q 2 weeks as required/tolerated: Max 200 mg/day
  - Bisoprolol: 1.25 mg PO daily. May double dose q 2 weeks as required/tolerated: Max 20 mg/day.

8.2 Fludrocortisone

- Potent mineralocorticoid
- 9 g of salt and water is a better option than fludrocortisone
  - Salt is effective with minimal side effects
- Can be added to 9 g of salt and water in patients who do not tolerate propranolol
- Watch for hypokalemia, edema, headaches, and acne
- Dose: Fludrocortisone 0.05 – 0.2 mg once daily
- Watch for: Hypokalemia, edema, headaches, hyperglycemia (polyuria, polydipsia), hypertension and acne

8.3 Midodrine (Orvaten)

- Midodrine is a peripheral α-1 agonist that serves as a vasoconstrictor and reduces venous pooling
- Dose:
  - Titrate: 5 – 10 mg PO q4h during daytime hours
  - Maximum 15 mg/dose
- Watch out for: anxiety, goose bumps, scalp itch, hypertension, worsening of GI symptoms and urinary retention
- Practical considerations
  - Prescribe 5 mg tablets

- This drug causes stimulation. Duration of action ~3 hours. Taking it around bedtime is likely to cause/worsen insomnia

8.4 Pyridostigmine (Mestinon)

- Use: Acetylcholinesterase inhibitor; potentiates sympatho-excitation during orthostatic stress and may contribute to reducing heart rate
- About 50% of patients find it helpful
- Dose:
  - Initial: 30 mg PO BID x 7 days
  - Titrate next step to 60 mg PO TID x 1 – 2 weeks then increase to 90 mg PO TID (or 180 mg SR daily)
- Watch out for: May exacerbate visceral hypermotility (severe cramping, abdo pain, nausea, diarrhea; most common ADRs for stopping drug), hypersalivation, urinary urgency, tremors, twitching, hypotension
  - Be cautious with diarrhea predominant IBS

8.5 Ivabradine

- Selective I_f channel blocker 19 (where f stands for 'funny') of the sinoatrial node which is the main pacemaker of the heart
- Decreases chronotropy but not inotropy (like beta blockers)
- Slows the heart rate without the adverse side that can be seen with beta blockers
- 60% effective in one retrospective case series

8.1 Modafinil

- Modafinil, a stimulant with a mechanism that is not yet clear
- Beneficial in some patients with POTS
- Caution is advised because modafinil may aggravate the orthostatic tachycardia in some patients
- Modafinil is sometimes used for mental alertness/brain fog in patients with ME/CFS but it may also give a false sense of increased energy
- We do not use this medication very often given that many of our patients have anxiety and autonomic dysfunction; modafinil can make these worse
- Also, the false sense of increased energy is at risk of pushing patients with ME/CFS beyond their energy envelope and causing crashes of symptoms (post-exertional malaise)
- Start 100 mg daily
- May increase to 200 mg daily

Watch for anxiety, insomnia, and adrenergic side effects

8.6 Clonidine

- Can be useful in patients with the central hyperadrenergic form of POTS (with hypertension) but may not be as well tolerated in patients with neuropathic POTS
- Clonidine is an α-2 agonist that acts centrally to decrease sympathetic nervous system outflow
- Side effects include: dizziness, lightheadedness, hypotension
- Usual dose: 0.1 mg – 0.2 mg BID or TID

9. Assess and Treat Coexisting Central Sensitivity Syndromes

- Level A evidence for most of these conditions
- May require referral out

- Central Sensitivity Syndromes include:
  - ME/CFS
  - FM
  - IBS
  - Migraine
  - Tension Type Headaches
  - POTS (Postural Orthostatic Tachycardia Syndrome)
  - Multiple Chemical Sensitivities
  - Interstitial Cystitis
  - Pelvic Pain Syndromes
  - Irritable Larynx Syndrome
  - Restless Leg Syndrome
  - Temporomandibular Disorders
  - Myofascial Pain Syndrome
  - PTSD

10. Assess and Treat for Coexisting Anxiety and Mood Disorders

- Level A evidence
- Protocols to be developed
- Referral to psychiatrist for selected patients

Patient Resources

http://www.bcwomens.ca/health-info/living-with-illness/living-with-complex-chronic-disease