Novel Use of Subcutaneous Octreotide via an Insulin Pump for Postural orthostatic Tachycardia Syndrome (PoTS)

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Case History

- A 22 year old female presented in April 2002 with **five episodic bouts** of **self-remitting palpitations**, each lasting thirty seconds, over a period of four months.
- Each episode was associated with **chest discomfort, dyspnoea and dizziness.**
- Patient denied experiencing nausea, diaphoresis or syncope.
- The patient had no significant medical or surgical history.
- The patient was not taking any prescribed or over the counter medications.
- Patient reported no history of such a presentation within the family and no significant family medical conditions.

Clinical Course

- Initial systemic examination revealed **nothing of note** par a **regular resting heart rate** of **99 beats per minute (bpm)**.
- Patient underwent a series of investigations which included full blood count, urea, electrolytes, thyroid function tests, 5 day Holter monitoring, chest X-ray, cardiomemo, electrophysiological studies and an echocardiogram.
- Despite such an exhaustive list of investigations, the only finding of note was **sinus rhythm alternating with sinus tachycardia** on Holter monitoring.
- **Over a period of 3 years** since initial presentation, her symptoms had **escalated** to the point where :
  - She was **forced** to become **wheelchair bound** due to the **severity** of her orthostatic symptoms
  - She was now experiencing **multiple syncopal** episodes resulting in **long bone fractures**
  - She was **forced** to **withdraw** from her **medical training**
  - Her **declining quality of life** left her **clinically depressed**
- In **2005**, after **3 years of inconclusive studies**, the patient underwent **Tilt Table Testing (TTT).**
- TTT revealed **four pre-syncopal episodes** associated with a sinus tachycardia and decrease in BP; **maximum rise in heart rate of 42bpm and minimum BP recorded being 103/92mmHg**.
- **TTT confirmed a diagnosis of PoTS** which was later confirmed using **autonomic testing** (Table 1).

Parameter		Blood Pressure (mmHg)	Heart Rate (beats per minute)
Head Position	Supine	135/90 – 145/91	83 – 90
	60° head rise	148/103 – 149/110	108 – 109
Isometric Exercise	Before	135/90	85
	During	155/102	95
Mental Arithmetic	Before	132/99	88
	During	138/93	87
Cutaneous Cold	Before	138/90	85
	During	141/91	85
Hyperventilation		-	Marked Rise
Deep Breathing		-	84 – 99
Valsalva manoeuvre	Resting	-	78
	Phase II	-	128
	Phase IV	-	56
Bodily Position	**Supine**	**135/90 – 145/91**	**83-90**
	After 3 minutes of standing	**134/102**	**111**
	After 5 minutes of standing	**137/99**	**115**
Venepuncture		Did not provoke symptoms/syncope	

Table 1: Results from autonomic testing. Presence of a high supine resting heart rate which excessively rose on postural challenge satisfied the criteria required for a diagnosis of PoTS[2].

Treatment

- Initial therapies involved trials of:
  - **Fludrocortisone – 300µg OD**
  - **Slow Sodium MR – 600mg up to 10 times a day**
  - **Midodrine – 5mg TDS**
  - **Ivabradine – 7.5mg BD**
- All therapies mentioned above proved either **ineffective or caused intolerable side effects.**
- She was later started on a trial of **SC octreotide** using gradual titration until she reached **300µg/24h – 50µg every 90 minutes, six times a day**
- Despite symptomatic relief from her PoTS, the patient reported **unbearable abdominal cramps and diarrhoea following each injection of octreotide.**
- In October 2011 she was seen by the endocrine team to consider the possibility of **octreotide LAR** but the concept of delivering SC octreotide via an **Animas insulin pump** (Figure 1) was discussed.
- Patient wore the device for **7-12 hours during waking hours** over which she received approximately **100µg per day** at an infusion rate of **10µg/hour.**
- At two week follow up, patient reported being **asymptomatic** and **not experiencing any side effects** associated with the medication.
- **Since then, the patient has been able to walk independently and has been able to return to her medical training**.

Figure 1: Animas Insulin Pump[1]

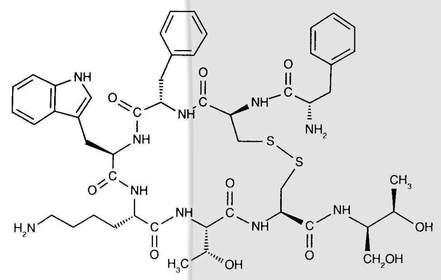

Figure 2: Molecular structure of Octreotide Acetate[6]

Discussion

- PoTS reflects a **dysfunction** of the **autonomic nervous system** leading to several debilitating features.
- Clinically, PoTS is defined by a **sustained rise in heart rate of ≥30bpm or an increase in heart rate to ≥120bpm within 10 minutes on movement from supine to an upright position[2]**.
- Although several pharmaceutical options exist, one therapy includes the use of the **somatostatin analogue octreotide[3]** (Figure 2).
- Octreotide acts as a **somatostatin analogue,** binding with **high affinity** to the **somatostatin receptor subtypes 2 and 5[4]**.
- Its proposed efficacy in PoTS centres on its ability to **stimulate vasoconstriction** in the **systemic** and **splanchnic vasculature,** thereby **increasing venous return[5]**.
- Despite SC and intramuscular long acting release (LAR) preparations being efficacious, the **side effects, cost and inconvenience of frequent injections** makes them far from ideal[5].
- Our case highlights how **delivery of SC octreotide via an Animas insulin pump** provides a **novel mode of delivery of therapy for PoTS**, whereby a **lower dose** can be given with **fewer undesired effects**.

References

1. *Animas.* http://www.childrenwithdiabetes.com/pumps/an_product.htm (Accessed February 2013).
2. Grubb, B. P., Y. Kanjwal, et al. (2006). "The postural tachycardia syndrome: a concise guide to diagnosis and management." J Cardiovasc Electrophysiol 17(1): 108-112.
3. Carew, S., M. O. Connor, et al. (2009). "A review of postural orthostatic tachycardia syndrome." Europace 11(1): 18-25.
4. Johnson JN, Mack KJ, Kuntz NL, Brands CK, Porter CJ, Fischer PR. Postural orthostatic tachycardia syndrome: a clinical review. *Pediatr Neurol* 2010;42(2):77-85.
5. Lamberts SW, van der Lely AJ, de Herder WW, Hofland LJ. Octreotide. *N Engl J Med* 1996;334(4):246-54.
6. *Octreotide Acetate.* http://www.stabilis.org/Monographie.php?IdMolecule=355 (Accessed February 2013).