CASE REPORT

Structural cure for reflex syncope?

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SUMMARY

The ROX Coupler is a device that allows creation of a central arteriovenous anastomosis at the iliac level. The device has been shown to improve exercise capacity in patients with chronic obstructive pulmonary disease and is CE marked for the treatment of resistant and uncontrolled hypertension. Reflex syncope is a challenging clinical condition with limited proven therapeutic options. We describe the resolution of symptoms and tilt table response of a patient who underwent insertion of a ROX Coupler to treat hypertension, and also incidentally had pre-existing vasodepressor syncope.

BACKGROUND

Reflex syncope is a heterogeneous group of conditions in which cardiovascular reflexes become intermittently inappropriate, resulting in vasodilation and/or bradycardia, and a fall in blood pressure (BP) and global cerebral perfusion.[1] The goal of therapy is prevention of recurrence and improvement of quality of life. Management includes: lifestyle measures, education and reassurance, physical countermeasures, tilt training and pharmacological therapy. These have varying degrees of success.

We present a case of a 77-year-old woman with a history of frequent and recurrent tilt test positive, vasodepressor syncope and resistant hypertension. Implantation of a central arterial-venous anastomosis (the ROX Coupler) led to immediate and complete resolution of syncope and near perfect BP control.

We propose that increased venous return occurring with the ROX Coupler leads to a concomitant increase in cardiac output, reversing adverse baroreceptor responses in patients with vasodepressor syncope. In addition, increased venous return impacts the Bainbridge reflex, attenuating neurally-mediated sympathoinhibition, the proposed mechanism of reflex syncope.

CASE PRESENTATION

A 77-year-old woman was referred for specialist management of her resistant hypertension. Despite an antihypertensive regime consisting of atenolol 50 mg once a day (OD), valsartan 160 mg OD, hydrochlorothiazide 12.5 mg OD and lacidipine 4 mg OD, her mean daytime office BP was 150/69 mm Hg and mean 24 h BP was 143/68 mm Hg. The patient could not tolerate further up-titration of her antihypertensive medications and therefore fulfilled the inclusion criteria for the novel device. After thorough screening and baseline investigations, it was agreed she would be an appropriate candidate.

Medical history included ischaemic heart disease (with prior surgical and percutaneous revascularisation), frequent and recurrent reflex syncope in the preceding 4 years and hypercholesterolaemia. Syncope occurred irregularly but frequently (on average, monthly). Careful and precise history-taking suggested reflex syncope secondary to orthostatic stress. The patient underwent tilt table testing to assess the syncope, in a controlled setting.

Tilt test evaluation of her syncope revealed an initial BP of 157/85 mm Hg, which dropped to 109/78 post-GTN administration. Within minutes, her BP decreased to 85/65 mm Hg and she became syncopal. She was placed in the supine position and recovered within 10 s. The reflex nature in which the patient developed hypotension was suggestive of vasodepressor syncope on clinical grounds. The tilt test could also be explained by progressive orthostatic hypotension (figure 1).

The patient was treated with standard therapeutic options including lifestyle measures, education regarding physical countertraction manoeuvres and tilt training. Despite these interventions, her syncope remained a significant inconvenience and affected her quality of life.

The patient went on to have central arterial-venous anastomosis (ROX Coupler) in July 2013.[2] A four French sheath was inserted into the right femoral artery and a six French sheath into the right femoral vein (right sided due to venous stripping on the left). Right heart catheterisation confirmed normal pulmonary artery pressure and pulmonary capillary wedge pressure and therefore the ROX Coupler was inserted. The venous sheath was upgraded to 11 French. An arterial helical wire was used to delineate the artery and puncture the vein. Easy passage and deployment of the coupler device ensued. Following this, angioplasty with a 4 mm balloon to 12 atmospheres for 20 s resulted in an excellent result with good flow from artery to vein (figure 2). There were no immediate complications. The patient's BP immediately improved from 170/90 mm Hg to 130/50 mm Hg. She was asked to wear bilateral full length surgical stockings for 6 weeks, as per standard protocol. Her follow-up 24 h BP average was 123/54 mm Hg, confirming procedure success.

The patient underwent extensive follow-up with a repeat tilt test undertaken a week following the intervention, showing initial BP of 134/74 mm Hg, decreasing to 90/56 mm Hg following GTN and 103/53 mm Hg 10 min post-GTN (figure 1). The patient was asymptomatic throughout this test, with no symptoms of syncope and no presyncope.

In the 12 months following the ROX Coupler insertion, no further syncopal episodes have

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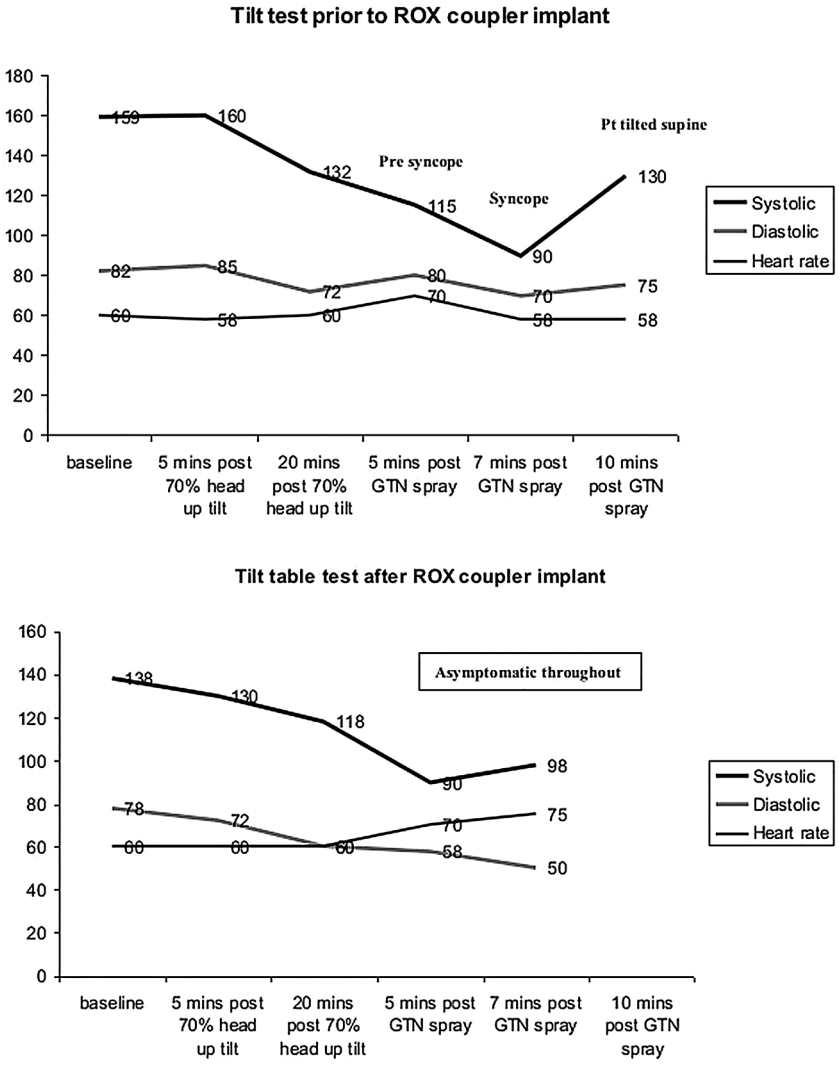

Figure 1 Tilt table test results before and after ROX Coupler insertion.

Figure 2 Femoral angiogram demonstrating ROX Coupler forming an iliac arteriovenous fistula, taken immediately after deployment.

occurred. She achieved target BP with a reduction in her medication (lacidipine was stopped after 3 months, valsartan halved after 6 months). Follow-up right heart catheterisation revealed significant changes neither in pulmonary artery mean pressure nor in pulmonary capillary mean wedge pressure (tables 1 and 2).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of this case would include progressive orthostatic hypotension as the cause of the patient's transient loss of consciousness. However, it is the authors' belief, based on the clinical history and initial clinical assessment, that this was a case of reflex syncope. The rapid onset, short duration and spontaneous complete recovery of the episodes would be in keeping with this diagnosis. In addition, the reflex nature of the syncopal episode during the initial head up tilt test also aligns with this diagnosis.

Table 1 Mean diurnal blood pressure readings (mm Hg)

	Pre-ROX	24 h Post-ROX	3 months	6 months
Office BP	163/56	138/48	163/57	142/67
24 h ABPM	150/69	Not recorded	124/55	127/56

Table 2 Cardiac catheterisation values

mm HG	Right heart pressures at implant	Right heart pressures at 6 months
Pulmonary arterial mean	17 mm Hg	14 mm Hg
Pulmonary capillary wedge pressure mean	3 mm Hg	5 mm Hg

ABPM, ambulatory blood pressure monitoring; BP, blood pressure.

DISCUSSION

Syncope is a transient loss of consciousness due to transient global cerebral hypoperfusion characterised by rapid onset, short duration and spontaneous complete recovery. Cerebral perfusion pressure is largely dependent on systemic arterial pressure, which itself is determined by cardiac output and total peripheral vascular resistance. A fall in either can cause syncope.[3]

Reflex syncope traditionally refers to a heterogeneous group of conditions in which cardiovascular reflexes that normally control the circulation become intermittently inappropriate, in response to a trigger, resulting in vasodilation and/or bradycardia, and thereby a fall in arterial BP and global cerebral hypoperfusion. Reflex syncope is often mediated by emotion or orthostatic stress. It is usually preceded by prodromal symptoms of autonomic activation (sweating, pallor, nausea) and is often triggered by inappropriate activation of sympathetic and parasympathetic reflexes, causing hypotension ('vasodepressor'), bradycardia ('cardioinhibitory') or both ('mixed').[4] Recurrent syncope can seriously impact on quality of life and results in a negative physical, psychological and social impact on the patient.[1]

The cornerstone of non-pharmacological management of patients with reflex syncope is education and reassurance regarding the benign nature of the condition. Initial treatment comprises education regarding awareness and avoidance of triggers (eg, volume depletion), early recognition of prodromal symptoms and performing manoeuvres to abort the episode (eg, physical counterpressure manoeuvres) as recommended in the European Society of Cardiology (ESC) guidelines.[1]

Drug therapies such as midodrine and fludrocortisone have been used in the treatment of reflex syncope, with variable results.[5] These strategies expand blood volume and increase cardiac filling by causing fluid retention or mechanically preventing reflex mediated increases in venous capacitance preventing hypotension due to depressed preload.

The ROX Coupler is Conformité Européenne (CE) marked for the treatment of essential hypertension and a recent trial confirms efficacy.[2] A complex of responses result from creating an iliac arteriovenous anastomosis with this device (figure 2).[6] The device allows a fixed arterial-venous flow rate of 0.8 L/min into the central venous system at iliac level resulting in a significant increase in right heart inflow with associated increased right atrial pressure. A concomitant increase in cardiac output results, which may affect the baroreceptor response in patients with vasodepressor syncope.[6] Increased venous tone also impacts the Bainbridge reflex, thereby attenuating neurally mediated sympathoinhibition.

This is the first documented case of insertion of a ROX Coupler leading to an abolition of reflex syncope. Further research is required and is ongoing to reproduce this initial observation and to better understand the physiological effects of the ROX Coupler in vasodepressor syncope, which may prove to be a useful non-drug treatment for this common and disabling syndrome that has few other proven therapies.

Learning points

- There are few proven therapies in the management of reflex syncope and a potential structural cure demands further attention and research.
- Clinical research, particularly for a novel device such as the ROX Coupler, will often result in incidental or unexpected observed effects. These might be positive or negative and must be diligently documented to enhance our understanding and progression.
- Hypertension affects approximately a billion individuals worldwide. Approximately 20–30% of those will suffer with resistant hypertension. This should be of great concern to the medical community. The novel ROX Coupler appears to be safe and effective in the treatment of resistant hypertension.

Contributors NS is consultant cardiologist at Eastbourne District General Hospital. The case refers to a patient under the care of NS. NS had the primary role in the patient's management. In addition, NS contributed the greatest to the writing and editing of the manuscript. He was a key contributor to the landmark ROX Control HTN Study, published in the Lancet in January 2015. WE is the cardiology research fellow, working under the supervision of NS, and contributed to the writing and editing of the manuscript. SB is the previous cardiology research fellow, under NS's supervision, and contributed to the writing and editing of the manuscript. SF is consultant cardiologist and electrophysiologist at Eastbourne General Hospital, and also one of the key contributors to the landmark ROX Control HTN Study, published in the Lancet in January 2015. His expertise in the physiological effects of the ROX Coupler was greatly appreciated in the writing of this manuscript.

Competing interests None declared.

Patient consent Obtained.

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