CASE REPORT

A hairy fall: syncope resulting from topical application of minoxidil

S W Dubrey,¹ J VanGriethuysen,¹ C M B Edwards²¹Department of Cardiology, Hillingdon Hospital, Uxbridge, Middlesex, UK²Department of Endocrinology, Hillingdon Hospital, Uxbridge, Middlesex, UK

Correspondence to

Dr S W Dubrey,
simon.dubrey@thh.nhs.uk

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SUMMARY

We describe the case of a young man who developed syncope after using a high strength formulation of topical minoxidil as a hair growth restorer. Other potential cardiovascular and endocrine causes were excluded, and his symptoms resolved on discontinuation of the product. While syncope is a recognised side effect of using this powerful systemic antihypertensive agent, few cases are documented in the literature, which we illustrate in our discussion.

BACKGROUND

Minoxidil is a potent oral antihypertensive, developed at the end of the 1980s. The antihypertensive activity of minoxidil (2,4-diamino-6-piperidinopyrimidine-3 oxide) occurs through its sulfate metabolite, minoxidil sulfate, which exerts its effect by opening ATP-sensitive potassium channels in vascular smooth muscle cells. The predominant site of vasodilation is arterial, which means that postural or orthostatic hypotension, both largely due to venous dilation, are unusual with its administration.¹ An unwanted side effect, hypertrichosis, has subsequently been utilised in the treatment of male pattern baldness. We report a case where the systemic cardiovascular effects of minoxidil caused significant hypotension and syncope in a young man.

CASE PRESENTATION

A 29-year-old African-American man presented after having experienced two episodes of syncope and general malaise. These episodes occurred after exercising in the gym, but he also felt pre-syncope on standing up in the train while going to work. He was physically very active, attending a gym four times a week; he was on no medication and had no history of any significance.

On examination, he was of muscular build and demonstrated borderline hypotension for a man in his late 20s, with a value of 104/62 mm Hg. The rest of the clinical examination was unremarkable, with a regular normal volume pulse of 78/min, no postural drop in blood pressure and normal heart sounds.

During a series of cardiovascular and endocrine assessments, he admitted using an over-the-counter topical cream, applied daily, to increase scalp hair growth. Examination showed this to contain 12.5% minoxidil with a 5% excipient component of azelaic acid. His symptoms correlated with starting the use of this hair-restoration medicament 12 weeks earlier. Having stopped using the topical

minoxidil product, his symptoms have now resolved, with a recent resting blood pressure of 115/80 mm Hg.

INVESTIGATIONS

An ECG, 24 h Holter ECG, echocardiogram and exercise treadmill stress test were entirely normal as were a full blood count, blood glucose, urea and electrolytes, thyroid function, basal cortisol level and short synacthen test.

DIFFERENTIAL DIAGNOSIS

Idiopathic hypotension, postural hypotension and adrenal insufficiency were the primary considerations in the differential. However, the full differential in a young patient is very wide and includes neurally mediated syncope (ie, carotid sinus hypersensitivity, situational syncope, vasovagal, micturition, cough and swallowing syncope), cardiac (ie, tachyarrhythmias or bradyarrhythmias of various aetiologies, obstructive valvular lesions and structural heart disease), orthostatic (ie, POTS syndrome) or a primary neurological process (ie, Parkinson's disease) or secondary autonomic failure (ie, amyloidosis, diabetes). Common non-syncopal conditions that may confound the diagnosis include seizures, intoxication, metabolic disorders (ie, hypoglycaemia, hypoxia), psychogenic or drug-induced episodes.²

The clear relationship to use of this topical minoxidil product appeared the most likely culprit.

TREATMENT

The product (topical minoxidil) was discontinued and symptoms resolved.

OUTCOME AND FOLLOW-UP

The patient made a full recovery on discontinuation of using the topical product.

DISCUSSION

Minoxidil became available as a vasodilatory antihypertensive in the late 1980s, with an indication for use in resistant hypertension, usually in combination with a β -blocker and diuretic. It was noted that around 80% of patients taking minoxidil reported an unwanted side effect of excess fine body hair (growing darker or longer) in different parts of the body.³

This side effect led to its development and marketing as a hair growth restorer. It is now also marketed as a topical agent (Regaine in the UK and Rogaine in the USA, among a myriad of other trade names) for androgenetic alopecia (and

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alopecia areata) in men and in women. The license for a 'prescription only' status of the topical formulations was removed in January 1995, opening the door to over-the-counter distribution. In women, the regular strength cutaneous solution contains 2% minoxidil, while in men, an extra strength solution and foam contains 5% minoxidil.

The mechanism of action of minoxidil in inducing hair growth is not fully understood, but is presumably related to increasing blood flow, nutrients and oxygen to hair follicles. Moreover, minoxidil contains a nitric oxide moiety and may act as a nitric oxide agonist.

Recognised side effects (British National Formulary) include headache, local irritation and, *less commonly*, hypotension. It is estimated that around 2–5 mg of applied minoxidil may be absorbed to become systemically available,⁴ which compares to an average effective oral antihypertensive dose of 10–40 mg/day. We have not re-challenged our patient, but it seems highly probable that his use of topical minoxidil solution was responsible for his syncopal episodes.

Despite the potential for hypotension through topical use, the majority of studies have shown little or no effect, aside from a mild increase in heart rate.⁵ Reports to US Poison Centres from 1985 to 1991 conclude that all topical exposures resulted in what are described as 'minor' to 'no effects'.⁶ Reviewing the literature, the most likely cause of significant hypotension and cardiovascular side effects has been through the accidental ingestion of topical minoxidil by children as well as by adults. A web-based review on the use of minoxidil reported that between 1977 and 2015, 2816 people reported side effects from minoxidil (route of administration is not defined), of whom 51 (1.8%) described syncope.⁷ The reliability of such sites is difficult to estimate with the same web-based review site reporting that of 2082 people taking topical minoxidil (Rogaine), 49 (2.35%) reported syncope.⁸ Only one other published full case report describes a similar scenario to our patient, in which a young airline pilot doubled the recommended dose of Rogaine and experienced two episodes of near-syncope while standing and one of syncope while driving.⁹

This case illustrates the potential for hypotension and syncope with the use of topical minoxidil, albeit from a high strength formulation. It also cautions to the use of any freely

available over-the-counter products with potentially serious systemic effects.

Learning points

- ▶ Topical minoxidil may cause symptomatic hypotension.
- ▶ Topical preparations of minoxidil are available over-the-counter under many trade names, including (among others) Rogaine, Regaine, Tugain, Loniten, Mintop, Neocapil, Lipogaine, Avacor and Amexidil.
- ▶ Topical minoxidil can only be obtained as a private prescription, or as an over-the-counter product, and is not available as a prescribed product through the National Health Services.
- ▶ Clinicians should consider the possibility that patients with hair loss might be using over-the-counter formulations of topical minoxidil.

Competing interests None declared.

Patient consent Obtained.

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REFERENCES

- 1 Sica DA. Minoxidil: an underused vasodilator for resistant or severe hypertension. *J Clin Hypertens* 2004;6:283–7.
- 2 Gauer RL. Evaluation of syncope. *Am Fam Physician* 2011;84:640–50.
- 3 Minoxidil-official FDA site. <http://www.drugs.com/pro/minoxidil.html>
- 4 Franz TJ. Percutaneous absorption of minoxidil in man. *Arch Dermatol* 1985;121:203–6.
- 5 Leenen FH, Smith DL, Unger WP. Topical minoxidil: cardiac effects in bald man. *Br J Clin Pharmacol* 1988;26:481–5.
- 6 Rose SR, Tomaszewski C. Evaluation of oral and topical minoxidil exposures reported to US Poison Centres from 1985–1991. *Drug Invest* 1994;8:81–94.
- 7 Review: Could minoxidil cause syncope (fainting)? <http://www.ehealthme.com/ds/minoxidil/syncope> (accessed 2 Jul 2015).
- 8 Review: Could rogaine cause syncope (fainting)? <http://www.ehealthme.com/ds/rogaine/syncope> (accessed Jul 2015).
- 9 Klorig W. Idiopathic syncopal episodes: saving our scalp only to lose your head. *Fed Air Surg Med Bull* 2012;50:10–11.

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