Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Heart block following topical latanoprost treatment

Elisabeth De Smit,¹ Maria Theodorou,² Göran Darius Hildebrand,³ Philip Bloom⁴

¹Eye Unit, Croydon University Hospital, Croydon, UK;

²Eye Unit, Kings College Hospital, London, UK;

³Prince Charles Eye Unit, King Edward VII Hospital, Windsor, UK;

⁴Eye Unit, The Hillingdon Hospital, Uxbridge, UK

Correspondence to Dr Elisabeth De Smit, desmitel@doctors.org.uk

Summary

The authors report a case of second degree heart block associated with topical latanoprost treatment. The authors discuss the possibility of a causative effect as the cessation of this treatment resulted in improvement of the arrhythmia. The authors highlight previous reports and research in humans and animals which demonstrate an association of arrhythmias with prostaglandin analogues. This report draws attention to the possibility that an extremely commonly prescribed topical drug may trigger arrhythmias in susceptible individuals. It is important that prescribers are aware of this possible side-effect.

BACKGROUND

Cardiovascular adverse effects of topical β -blockers are well known, but topical prostaglandin analogues are thought to be relatively safe with few systemic adverse effects. As a result, they are often used as first-line treatment in patients with cardiorespiratory contraindications to a topical β -blocker. Here, we report a case of a cardiac arrhythmia associated with topical latanoprost (prostaglandin analogue) treatment.

Glaucoma is an extremely common condition and makes up a large proportion of an ophthalmologist's work. It is a frequent co-morbidity in patients presenting to other health-care services and therefore being aware of a possible serious side-effect of one of the most commonly prescribed antiglaucoma medication has relevance for most doctors.

CASE PRESENTATION

A 54-year-old Afro-Caribbean midwife with suspected early primary open angle glaucoma was commenced on latanoprost 0.005% eye drops following poor compliance with a twice daily topical β -blocker. At review at 4 months, after starting latanoprost treatment, she complained of feeling increasingly dizzy and fatigued. Her intraocular pressures were found to be well-controlled and she was advised to continue her treatment. However, 1 week later, she presented to the accident and emergency department

with shortness of breath on minimal exertion, lethargy and palpitations. She had taken her own pulse over the previous week and described the pulse to have slowed as the week had progressed. She was previously fit and well without any prior cardiovascular disease, any known cardiovascular risk factors and on no medication other than the latanoprost 0.005% eye drops.

An electrocardiogram on admission demonstrated second degree heart block, Mobitz type 2, with 3:1 atrioventricular conduction (figure 1). Chest radiograph and baseline bloods, including electrolytes, full blood count, thyroid function and troponin T levels, were all within normal limits. An echocardiogram demonstrated only trivial mitral regurgitation. Cardiological review revealed no clear underlying cause.

While in hospital, the latanoprost eye drops were not administered as the patient did not wish to take them. It was noticed that 2 days following the discontinuation of the latanoprost eye drops, the ECG still showed Mobitz type 2 heart block, but the atrioventricular conduction had improved to 2:1 (figure 2 showing the change from 3:1 to 2:1). Although the atrioventricular conduction ratio improved, she remained bradycardic and her symptoms did not improve. A permanent pacemaker was therefore inserted and the patient made an uneventful recovery. The cardiology team advised that it was safe to resume the latanoprost eye

Figure 1 ECG strip taken on arrival in the emergency department, demonstrating 3:1 atrioventricular conduction (second degree heart block, Mobitz type 2).

Figure 2 12-lead ECG printed from the cardiac monitor in the coronary care unit, 2 days after stopping the latanoprost eye drops. It captures the improvement from 3:1 to 2:1 atrioventricular conduction.

drops once the pacemaker was in situ. However, the patient declined any further topical ocular hypotensive treatment. She has been monitored closely in the ophthalmology clinic without signs of progression so far.

DISCUSSION

To our knowledge, this is the first published report of heart block associated with topical latanoprost treatment.

The manufacturer, Pfizer, alerted us to three cases of heart block which may be associated with latanoprost, two cases of first degree heart block and one of second degree heart block. These cases were reported to Pfizer by the Medicines and Healthcare products Regulatory Agency (MHRA).¹ The MHRA have received 49 reports of cardiac disorders associated with latanoprost. Other cardiac disorders possibly caused by latanoprost include palpitations, cardiac myopathies, cardiac failure, ischaemic heart disease, multiple forms of arrhythmias and two fatal cases of cardiac arrest. The association arrhythmias largely involve those with an increase in heart rate however there are reported cases of bradycardias. The case discussed in the article was reported to the MHRA.

Latanoprost is a prostaglandin F₂ α (PGF_{2α}) analogue which has been shown to affect cardiac rate and rhythmicity in both humans and animal models. Three cases of ventricular arrhythmias have been reported previously in young women following intramyometrial injection. Kabutan *et al* reported two young, previously healthy women who developed ventricular arrhythmia following intramyometrial injection of PGF_{2α}.² Shoham *et al* described a young woman with onset of life-threatening ventricular tachycardia after injection of PGF_{2α}.³ Li *et al* found PGF_{2α} to be more potent than PGD₂ or PGE₂ in generating tachyarrhythmias in cultured neonatal rat cardiac myocytes.⁴ Rao *et al* reported ventricular arrhythmias and atrioventricular conduction disturbances in cats following a bolus of intravenous PGF_{2α}.⁵

Although the report of an association between latanoprost treatment and heart block does not prove a causal relationship and may have been coincidental, the improvement in atrioventricular conduction from 3:1 to 2:1 on

cessation of treatment may support a causal link. This case raises the possibility that in some susceptible patients the PGF_{2α} analogue latanoprost may increase the risk of heart block. The reasons for the paucity of previous reports of serious cardiac disease during topical prostaglandin treatment may reflect a safe cardiac safety profile, but under-reporting and attribution to factors other than medication cannot be excluded. More systematic studies are required to investigate any link between cardiac arrhythmias and topical prostaglandin treatment. The prescribing ophthalmologist and treating cardiologist should be aware of such a potential association and report any relevant cases as the potential adverse effects may be life-threatening.

Learning points

- ▶ Topical prostaglandin analogues may have cardiovascular side effects.
- ▶ Topical medications may have significant systemic adverse effects.
- ▶ Do not omit eye drops when taking a drug history.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. Medicines and Healthcare products Regulatory Agency (MHRA). Latanoprost Drug Analysis Print, 7 May 2011. http://www.mhra.gov.uk/home/groups/public/documents/sentineldocuments/dap_1306406731772.pdf (accessed on 7 May 2011).
2. Kabutan K, Satou K, Ono J, *et al*. [Ventricular arrhythmia during cesarean section due to intramyometrically administered prostaglandin F₂ alpha: report of two cases]. *Masui* 1994;**43**:392–4.
3. Shoham Z, Ezri T, Konichevsky S, *et al*. Ventricular tachycardia associated with injection of prostaglandin F₂ alpha into the uterine cervix during anesthesia. *Anesthesiology* 1990;**72**:775–6.
4. Li Y, Kang JX, Leaf A. Differential effects of various eicosanoids on the production or prevention of arrhythmias in cultured neonatal rat cardiac myocytes. *Prostaglandins* 1997;**54**:511–30.
5. Rao TS, Seth SD, Manchanda SC, *et al*. Contrastive effects of prostaglandin F₂ alpha on normal cardiac rhythm and ouabain-induced cardiac arrhythmias in cats: possible neural basis. *Arch Int Pharmacodyn Ther* 1989;**302**:128–44.

This pdf has been created automatically from the final edited text and images.

Copyright 2011 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

De Smit E, Theodorou M, Hildebrand GD, Bloom P. Heart block following topical latanoprost treatment. *BMJ Case Reports* 2011; 10.1136/bcr.08.2011.4607, date of publication

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow