Short communication

Hypertension secondary to treatment with latanoprost*

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ABSTRACT

Case report: An 80 year old woman operated on by trabeculectomy for primary open-angle glaucoma due to increased pressure, who started treatment with latanoprost. Monitoring of blood pressure (BP) showed a statistically significant increase in both systolic and diastolic BP, coinciding with the use of topical hypotensive, which resolved by voluntarily suspending treatment, thus increasing again to reintroduce the prostaglandin.

Discussion: Prostaglandin analogues reduce intraocular pressure to produce vasodilation of the episcleral and ciliary arteries, increasing the outflow of aqueous humour. Cardiovascular effects are rare, but have been described by the vasoconstrictor effect that can trigger the reversible increase in BP, as in this case.

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RESUMEN

Hipertensión arterial secundaria a tratamiento con latanoprost

Caso clínico: Mujer de 80 años intervenida mediante trabeculectomía por glaucoma primario de ángulo abierto en la que, debido al incremento tensional, se inició tratamiento con latanoprost. La monitorización de la tensión arterial (TA) demostró un incremento estadísticamente significativo de la TA tanto sistólica como diastólica coincidiendo con el uso del hipotensor tópico, que se resolvió al suspender voluntariamente el tratamiento, volviendo a elevarse al reintroducir la prostaglandina.

Discusión: Los análogos de las prostaglandinas disminuyen la presión intraocular al producir vasodilatación de las arterias ciliares y epiesclerales, aumentando el drenaje del humor.


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Introduction

Latanoprost is a prostaglandin (PG) F\(_2\) alpha analogue used in patients with glaucoma or ocular hypertension with a mechanism of action based on the vasodilation of the ciliary and episcleral arteries, increasing the drainage of the aqueous humour.

Some of the most outstanding common side effects of this drug include increased iris pigmentation, ocular irritation and changes in eyelashes. Cardiovascular effects are uncommon although angina pectoris, stroke and high blood pressure (HBP) have been described due to the vasoconstrictor effect that may be triggered in certain patients\(^1\)–\(^4\).

Clinical case

An 80-year-old female patient who underwent a trabeculectomy in both eyes for primary open-angle glaucoma who was started on topical latanoprost (Xalatán\textsuperscript{®}, Pfizer, Alcobendas, Madrid, Spain) in both eyes, due to hypertension. Her personal history was notable for HBP under medical treatment, type-2 diabetes mellitus on oral antidiabetic drugs. Additionally, she had an oesophageal neoplasm subject to surgery one year before and operated hip fracture in rehabilitation.

Daily monitoring of patient’s blood pressure (BP), performed three times a day (9:00 a.m., 3:00 p.m. and 9:00 p.m.), showed an increase in both systolic (SBP) and diastolic (DBP) blood pressure when treatment with the PG was initiated. Such increase resolved when the topical treatment was voluntarily discontinued (Figs. 1 and 2), and reappeared after one month when the drug was resumed. Both the decrease and increase in BP values occurred progressively between four and seven days after the drug introduction and discontinuation (Fig. 3).

The data obtained from the three daily measurements for three months were statistically analysed. The Sapiro–Wilk test did not reveal any violation to the assumption of normality in the distribution of all the variables considered. The mean systolic and diastolic blood pressure values were obtained. The mean SBP and mean DBP at the beginning of the study were 140.24 mm Hg (95% confidence interval [CI]: 133.03–147.46) and 69.45 mmHg (95% CI: 67.72–71.19), respectively. The mean SBP and mean DBP in the latanoprost treatment phase were 159.9 mmHg (95% CI: 150.54–167.25) and

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**Fig. 2** – Diastolic blood pressure without and with latanoprost treatment. Diastolic blood pressure: systolic [sic] blood pressure.

**Fig. 3** – Blood pressure curve with three daily checkups for three months. M SBP: morning blood pressure; E SBP: evening blood pressure; A SBP: afternoon blood pressure; ttm: treatment; latano: latanoprost.
Table 1 – Systolic and diastolic blood pressure values with means and confidence intervals.

<table>
<thead>
<tr>
<th></th>
<th>Mean SBP (mmHg)</th>
<th>95% CI</th>
<th>Mean DBP (mmHg)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No latanoprost</td>
<td>140.24</td>
<td>133.03–147.46</td>
<td>69.45</td>
<td>67.72–71.97</td>
</tr>
<tr>
<td>Latanoprost</td>
<td>159.90</td>
<td>150.54–167.25</td>
<td>73.97</td>
<td>71.49–76.45</td>
</tr>
<tr>
<td>Difference</td>
<td>18.66</td>
<td>8.42–28.89</td>
<td>4.51</td>
<td>1.74–7.35</td>
</tr>
</tbody>
</table>

CI: confidence interval; DBP: diastolic blood pressure; SBP: systolic blood pressure.

73.97 mmHg (95% CI: 71.49–76.45), respectively. A statistically significant difference (p < 0.05) was seen between the SBP with and without treatment (mean difference 18.66 mm Hg; 95% CI: 8.42–28.89) and the DBP with and without treatment (mean difference 4.51 mmHg; 95% CI: 1.74–7.35) (Table 1).

Discussion

Latanoprost was approved by the United States Food and Drug Administration (FDA) in June 1996. In less than one year, by May 1997, the FDA had already received 177 reports of adverse side effects, including 14 cases of HBP, 12 cases of peripheral and facial oedema, 6 asthma exacerbations and 5 cases of dyspnoea. Of note, the cardiovascular processes included seven cases of angina pectoris, one myocardial infarction and two strokes.4

PG F2α alpha analogues cause vasodilatation of the ciliary and episcleral arteries, favouring and increasing the drainage of aqueous humour. However, the systemic effect of PG F2α alpha is vasoconstrictor,4 so the systemic absorption of the drug administered via topical route may trigger this effect, thus increasing BP.4–6

The presence of cardiovascular risk factors in elderly patients with multiple conditions, such as vascular atheromatosis, often associated with endothelial dysfunction, in the presence of vasoconstrictor stimuli (such as the administration of latanoprost) may favour local hyperactivity and the occurrence of spasm or contraction of the vascular smooth muscles,4–6 thus triggering HBP.

It has been considered that the systemic vasoconstrictor effect occurred at high doses of the drug.4,5 In our case, however, the HBP was seen between treatment Day 5 and 7 in the two scheduled periods, and HBP normalisation was seen within the first week of drug discontinuation. Thus, in our case, the effect occurred with minimum latanoprost doses, responding to five or seven drops of the drug. The vasoconstrictor effect of latanoprost or cases of HBP secondary to treatment with other PGs have not been described.7,8

In summary, even though it is an uncommon occurrence, the increase in BP should be taken into account in patients on treatment with topical latanoprost, particularly in elderly patients with multiple conditions, concomitant cardiovascular disease, atheromatosis or endothelial dysfunction. This paper also shows the relation between latanoprost and the reversible increase in BP with minimum doses of the drug.

References