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Additive Effect of Bunazosin on Intraocular Pressure When Topically Added to Treatment with Latanoprost in Patients with Glaucoma

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Purpose: To investigate whether an α-1 blocker, bunazosin, has an additive effect on lowering intraocular pressure (IOP) when topically added to latanoprost treatment in patients with glaucoma.

Methods: Bunazosin twice a day was added topically to the treatment for 12 patients with glaucoma who had been instilling latanoprost once a day for more than 1 month. IOP was measured and adverse events were checked 2, 4 and 8 weeks after the addition of bunazosin to their treatment.

Results: One of the 12 patients dropped out in the course of the study. Therefore, 11 patients were included for the analysis of IOP, and 12 for the analysis of adverse events. IOPs were decreased significantly ($P = .008$, Wilcoxon signed rank test) from 18.2 ± 3.4 mm Hg to 16.6 ± 3.5 mm Hg 8 weeks after the addition of bunazosin. Adverse events were seen in 5 of the 12 patients.

Conclusion: Bunazosin has an additive effect on lowering IOP when topically added to latanoprost treatment in glaucoma patients. **Jpn J Ophthalmol 2003;47:526–528** © 2003 Japanese Ophthalmological Society

Key Words: Bunazosin, glaucoma, intraocular pressure, latanoprost.

Introduction

Bunazosin, an α-1 adrenergic antagonist, is an antiglaucomatous eye drop that was launched in 2001 in Japan. Bunazosin increases uveoscleral outflow of aqueous humor and reduces intraocular pressure (IOP) by blocking an α-1 receptor.[1,2] Latanoprost also lowers IOP by increasing uveoscleral outflow of aqueous humor; however, that action is mediated by a prostaglandin F receptor.[3] Although both bunazosin and latanoprost increase uveoscleral outflow of aqueous humor, the effect of each is mediated by a different receptor.

To our knowledge, there have been no reports that investigated the combined effect of latanoprost and bunazosin on lowering IOP in patients with glaucoma. Therefore, in the present study, we investigated whether bunazosin has an additive effect on lowering IOP when topically added to latanoprost treatment in glaucoma patients.

Materials and Methods

The inclusion criteria for this study are as follows: (1) patients with open-angle glaucoma or ocular hypertension; (2) patients who had been under treatment with latanoprost alone for 1 month or more; (3) patients whose IOP under treatment with latanoprost had been ≥18 mm Hg; and (4) patients whose visual field defect worsened in spite of IOP < 18 mm Hg.

The following patients were excluded from the study: (1) those with an allergy to bunazosin or latanoprost; (2) those who had acute ocular disease; (3) those who had undergone glaucoma surgery; and (4) those who had undergone cataract surgery within 3 months.

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Latanoprost instillation (once daily) was continued and bunazosin instillation (twice daily) was added. IOP was measured at 9 AM–10 AM and patients were checked for adverse events 2, 4 and 8 weeks after the addition of bunazosin.

IOP was analyzed in 1 eye per patient. If both eyes were found to be eligible as the study eye, the eye with a higher baseline IOP or, in the case of the same IOP values, the eye with the greater optic nerve disorder was selected as the study eye.

IOP values are shown as mean ± SD, and Wilcoxon signed rank test was used for the statistical analysis.

Informed consent was obtained from all patients.

Results

Of the 12 patients selected, 1 dropped out in the course of the study because of ocular itching. Consequently, 11 patients were accepted for the analysis of IOP, and 12 for the analysis of adverse events.

Table 1 shows the backgrounds of the 11 patients included for the analysis of IOP.

Figure 1 shows the course of IOP after the addition of bunazosin. IOP before the addition of bunazosin was 18.2 ± 3.4 mm Hg. The IOP 2, 4 and 8 weeks after the addition of bunazosin was 17.1 ± 3.6 mm Hg, 16.8 ± 3.3 mm Hg, and 16.6 ± 3.5 mm Hg, respectively. Significant decreases in IOP were observed at 2 weeks ($P = .021$), 4 weeks ($P = .012$), and 8 weeks ($P = .008$) after the addition of bunazosin as compared with the IOP before the addition. The value of the decrease in IOP 8 weeks after the addition was 1.5 ± 0.9 mm Hg.

As for adverse events, hyperemia in 2 patients (17%), an unpleasant feeling in 2 patients (17%), and ocular itching in 1 patient (8%) were observed. The hyperemia in 2 patients and the unpleasant feeling in 2 patients were mild in nature, and it was possible to continue instillation of bunazosin. Ocular itching occurred in the patient who dropped out. The itching itself was mild and transitory in nature, but the patient refused to continue the study.

Table 1. Background of Patients

Sex	
Male	3
Female	8
Age (y)*	70.1 ± 10.9
Disease type	
Primary open-angle glaucoma	10
Ocular hypertension	1
IOP before treatment with latanoprost (mm Hg)*	20.5 ± 3.5
Duration of latanoprost administration (mo)*	11.6 ± 10.7
IOP before addition of bunazosin (mmHg)*	18.2 ± 3.4

IOP: intraocular pressure.
*Mean ± SD.

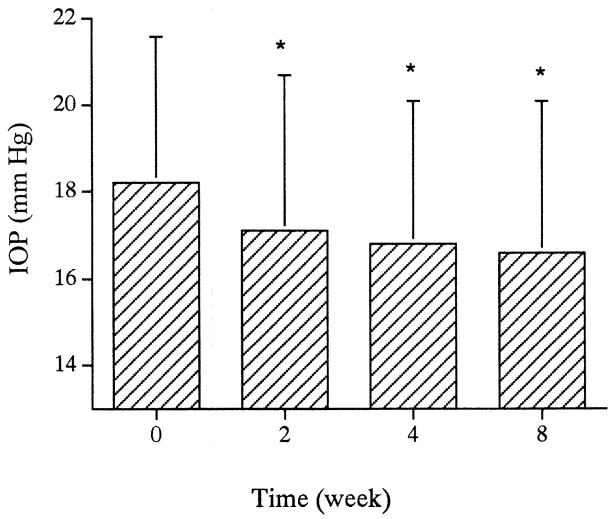

Figure 1. The intraocular pressure (IOP) changes after the addition of bunazosin. *Significant decreases in IOP 2 weeks ($P = .021$), 4 weeks ($P = .012$), and 8 weeks ($P = .008$) after the addition of bunazosin as compared with the IOP before the addition (Wilcoxon signed rank test).

Discussion

Drugs for glaucoma are classified into two types. One type lowers IOP by suppressing the production of aqueous humor, and the other type lowers IOP by increasing the outflow of aqueous humor. The latter type is further classified by mediation route. One is mediated by the trabecular meshwork and the other by the uveoscleral route.

Bunazosin and latanoprost are both considered to lower IOP by increasing the outflow of aqueous humor from the uveoscleral route.[1–3] However, bunazosin and latanoprost act on different receptors. That is to say, bunazosin exhibits its action by blocking the alpha-1 receptor of the sympathetic nerve, while latanoprost displays its action by combining with the prostaglandin receptor.

In the combined use of drugs for glaucoma, it is considered efficient to combine a drug that suppresses the production of aqueous humor with a drug that accelerates the outflow of aqueous humor, and in actual treatment of glaucoma, such a combination is used in many cases. On the other hand, the cause of glaucoma is the inhibition of the outflow of aqueous humor and, therefore, there is an opinion that in the treatment of glaucoma, it is more physiologically sound to accelerate the outflow of aqueous humor.

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As representative drugs for accelerating the outflow of the aqueous humor, prostaglandin-related drugs such as latanoprost, isopropyl unoprostone, bimatoprost, and travoprost are already being used clinically. As regards the combined use of a drug that accelerates the outflow of the aqueous humor, there has been a report that IOP further decreased when latanoprost was added to unoprostone; however, no decrease in IOP was observed when unoprostone was added to latanoprost.[4] Bunazosin is also a drug that accelerates the outflow of the aqueous humor.[1] However, there have been no reports of the combined use of a prostaglandin-related drug and bunazosin.

In the present study, the IOPs before and after the treatment with latanoprost were 20.5 ± 3.5 mm Hg and 18.2 ± 3.4 mm Hg, respectively. The IOP reduction by the latanoprost treatment was 2.4 mm Hg (range: 2–3 mm Hg) and there were no patients who did not respond to latanoprost. Therefore, in this study we evaluated the additive effect of bunazosin in lowering IOP in the latanoprost responders. Bunazosin was added to the treatment for glaucoma patients who had been under treatment with only latanoprost, which resulted in a further decrease in IOP. The value of the decrease in IOP 8 weeks after the addition of bunazosin was 1.5 ± 0.9 mm Hg. Although the sample size of this study was small and the decrease in IOP was not so great, this value was statistically significant. This statistical decrease in IOP does not necessarily have clinical significance.

Nevertheless, the present study is noteworthy as the first report which showed the combined effect of bunazosin and latanoprost in lowering IOP.

As a reason for the need for a further decrease in IOP by the addition of bunazosin to latanoprost, it may be considered that latanoprost alone did not fully accelerate the outflow of aqueous humor from the uveoscleral route. This idea is supported by the fact that the action of bunazosin and latanoprost is mediated by different receptors.

Hyperemia, an unpleasant feeling, and ocular itching were observed as local adverse events attendant upon the use of bunazosin in this study, but systemic adverse events were not observed. Latanoprost has no serious systemic adverse reactions.[5] Therefore, the combined use of latanoprost with bunazosin is considered suitable from the perspective of safety.

The above results of the present study suggest possible advantages in the combined use of latanoprost with bunazosin in the treatment of glaucoma.

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