Abstract. – Aims: To evaluate the ocular hypotensive effects and tolerability of the once daily fixed combination latanoprost-timolol versus twice daily 0.50% timolol associated or not with once daily latanoprost in patients suffering from Primary Open-Angle Glaucoma (POAG).

Methods: We compared the effects of such a combination with those of 0.50% timolol alone twice daily in a group of 24 patients and with the effects of timolol 0.50% twice daily associated with once daily latanoprost in a second group of 20 patients with a follow-up of 24 months.

Results: In the first group of patients after one month the Intraocular Pressure (IOP) was reduced from a mean of 19.93 to a 17.04 mmHg. This reduction remained stable with a mean value of 17.00 mmHg at the third month, of 16.49 mmHg at the sixth month, of 17.04 at the twelfth month, 16.00 at the eighteenth month, and of 15.86 mmHg in the twenty-fourth month. In the second group there was a statistically significant reduction from 19.4 to 16.84 mmHg after one month. This reduction remained constant with mean values of 16.47 at the sixth month, of 16.20 at the twelfth month and of 16.00 mmHg at the twentyfourth month of treatment.

Conclusions: The once daily latanoprost-timolol combination was shown to furtherly reduce the Intraocular Pressure (IOP) \((p=0.001)\) and to maintain under control the intraocular pressure for the observation period (24 months). Both topical and systemic side-effects were scarce and tolerability was good.

Key Words: Primary Open Angle Glaucoma (POAG), Intraocular Pressure (IOP), Latanoprost, timolol.

Introduction

The twice daily administration of beta-blockers, till nowadays considered the first choice treatment to reduce the intraocular pressure (IOP) in the glaucomatous pathology, sometimes is not sufficient to maintain under control the clinical situation in these patients.

Therefore, it is necessary to add an ocular hypotonizing drug with a different mechanism of action such as a carbonic anhydrase inhibitor or an alpha-2 agonist or a prostaglandin. However, the role of human uveoscleral tissue was emphasized by the rich catecholaminergic innervation. A decrease of catecholaminergic nerve fibers and norepinephrine occurs when intraocular pressure is elevated\(^1\).

To improve the patient’s compliance and avoid the instillation of two drugs three or four times a day some fixed combinations have become available, such as timolol-pilocarpine, timolol-dorzolamide and timolol-latanoprost.

Various Authors have already described favourable data in treating glaucoma with a monoadministration of the latter combination\(^2\) and versus the twice daily 0.50% timolol administration\(^6\).\(^7\).

The aim of our research was to assess the ocular hypotonizing effect and the tolerability both local and systemic of the fixed timolol 0.50% and latanoprost 0.005% combination administered once daily in a study with a follow-up of 24 months.

We compared the effects of such a combination with those of 0.50% timolol alone twice daily in a group of 24 patients suffering from prima-
ry open-angle glaucoma (POAG) and, moreover, with the effects of timolol 0.50% twice daily associated with once daily latanoprost in a second group of 20 patients.

Materials and Methods

The protocol was approved by the local Ethical Committee.

44 patients (20 males and 24 females) suffering from POAG after their informed consent, undergo the treatment. A total of 87 eyes (one patient was monocular) were observed with a follow-up of 24 months.

They were divided in two groups:

1st group: 24 patients in therapy with 0.50% timolol administered twice daily; (total 47 eyes) (one patient was monocular).

2nd group: 20 patients in therapy with 0.50% timolol twice daily + latanoprost once daily (total 40 eyes).

After a complete ophthalmic examination, including biomicroscopy of the anterior eye segment, tonometric curve, gonioscopy, computerized visual field (Humphrey Progr 30-2), provocative test with ibopamine and ophthalmoscopy (with cup/disc determination), the two groups of patients changed therapy and the fixed combination 0.50% timolol plus 0.005% latanoprost (Xalacom) was administered once daily.

The biomicroscopy and the intraocular pressure were determined, respectively, at the moment of therapy replacement and then after 1, 3, 6, 12 and 24 months, always at the same time in the morning (9 a.m.). Perimetry and ophthalmoscopy were perfomed every 12 months.

Moreover, local and systemic side-effects were noticed. The patients’ compliance and their tolerability as regards the two associated drugs and the fixed combination timolol-latanoprost were noted.

The statistical analysis was based on the Student’s “t” test for paired data; \( p=0.01 \) was considered significant. Data are means ± SD.

Results

The 87 eyes suffering from POAG examined in this study, showed the following mean parameters at the moment of therapy replacement:

The mean highest IOP recorded at the moment of the first examination: \( 24.8±4.43 \) mmHg

Computerized visual field (Humphrey, Progr. 30-2): mean MD = 5.72±2.90

Cup/disc: mean 0.38±0.10

Provocative test with ibopamine: positive in 94% of the eyes.

10 eyes had some side-effects as conjunctival hyperemia, burning (9.20%) and systemic side effects as bradycardia and asthmatic syndrome (2.27% of the patients) within 4-7 days and they were excluded from the statistical calculations of the two groups.

Figure 1 shows the average course of IOP (47 eyes) in the first group of patients that changed the twice daily 0.50% timolol therapy with the once daily fixed combination 0.50% timolol-latanoprost.

It may be observed that already after one month the IOP was reduced from a mean of \( 19.93 ± 2.11 \) to a \( 17.04±1.98 \) mmHg; the decrease was statistically significant (\( t=6.824; \ p=0.001 \)).

This reduction remained for the period of our observation (24 months) with a mean value of \( 17.00±2.26 \) mmHg (\( t=6.497; \ p=0.001 \)) at the third month, of \( 16.49±2.62 \) (\( t=7.011; \ p=0.001 \)) at the sixth month, of \( 17.04±2.02 \) (\( t=6.783; \ p=0.001 \)) at the twelfth month, of \( 16.00±1.98 \) at the eighteenth month (\( t=9.311; \ p=0.001 \)), and of \( 15.86±1.87 \) mmHg in the twenty-fourth month (\( t=9.897; \ p=0.001 \)).

In two eyes among 41 (4.87%) the fixed combination timolol-latanoprost was unable to keep IOP under control.

Therefore, it was necessary to add 0.50% timolol in the morning and satisfying tonometric results were obtained.

Figure 2 illustrates the IOP mean behavior in the second group of patients whose therapy (twice daily 0.50% timolol associated with once daily latanoprost) was replaced with the timolol-latanoprost fixed combination (Xalacom).

It may be observed that already after one month there was a statistically significant reduction (\( t=5.596; \ p=0.001 \)) from a mean of \( 17.04±2.11 \) to \( 16.84±1.98 \) mmHg in the 40 POAG eyes treated with twice daily 0.50% timolol associated with once daily latanoprost.

This reduction remained constant with mean values of \( 16.47±2.59 \) (\( t=5.547; \ p=0.001 \)) at the sixth month, of \( 16.20±2.12 \) (\( t=6.766; \ p=0.001 \)) at the twelfth month and of \( 16.00±2.26 \) mmHg (\( t=6.955; \ p=0.001 \)) at the twenty-fourth month of treatment.
Once daily Latanoprost-Timolol in POAG

**Discussion**

On the basis of the data obtained in the 24 months-study by comparing the ocular hypotensive effects and tolerability of a fixed combination 0.50% timolol + 0.005% latanoprost in a group of 44 patients suffering from POAG versus the twice daily administration of 0.50% timolol either associated or not with latanoprost we can make the following considerations:

![Figure 1](image1.png)

**Figure 1.** Mean tonometric values in a twice daily Timolol 50% therapy before and after replacement with the fixed combination Latanoprost-Timolol one daily. (Checkup at 1, 3, 6, 12 and 24 months from the beginning of the treatment). IOP: intraocular pressure.

![Figure 2](image2.png)

**Figure 2.** Average tonometric values in twice daily 0.50% Timolol therapy associated with once daily Latanoprost before and after replacement with the fixed once daily Latanoprost-Timolol combination. (Checkup at 1, 3, 6, 12 and 24 months). IOP: intraocular pressure.
Already after one month of treatment, the once daily fixed combination latanoprost-timolol proved to be more efficacious in reducing IOP (from a mean of 19.93±2.11 to 16.34±1.98 mmHg) versus twice daily 0.50% timolol (1st group). The IOP reduction was kept constant for the period of our observation (24 months).

The once daily fixed combination latanoprost-timolol allowed to furtherly reduce the IOP obtained after a twice daily 0.50% timolol administration associated with latanoprost. The mean reduction was of 2.56 mmHg (13.2%) after one month and of 3.4 mmHg (17.5%) after twenty-four months. In two eyes this combination was unable to control the IOP after three months; therefore it was necessary to add 0.50% timolol in the morning.

Both topical (9.25%) and systemic (2.27%) side effects were scarce.

In conclusion, the once daily fixed combination, in monoadministration, latanoprost-timolol (Xalacom®) can efficaciously replace the twice daily 0.50% timolol either associated or not with once daily latanoprost in most of the eyes.

It is therefore possible to improve the patient’s compliance and his quality of life.

References


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