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COMPARISON STUDY OF INTRAOCULAR PRESSURE REDUCTION EFFICACY AND SAFETY BETWEEN TIMOLOL AND BETAXOLOL IN IRAQI PEOPILS WITH NORMAL-TENSION GLAUCOMA

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ABSTRACT

Purpose: To evaluate and compare the intraocular pressure (IOP) reduction safety and efficacy between the ophthalmic solutions 0.5% timolol and 0.5% betaxolol in Iraqis patients with normal-tension glaucoma (NTG). **Methods:** In this non masked randomized study, we prospectively enrolled 40 Iraqis with NTG patients who had used timolol monotherapy for more than 4 weeks, and randomly divided them into the following two groups: 1) timolol-to-betoxolol group and 2) betoxolol-to-timolol group. At the beginning of the study, both groups were switched from initial timolol to timolol or betaxolol for 12 weeks, and then switched over to the other drug (crossover) for 12 additional weeks. At 0, 4, 12, 16, and 24 weeks, we evaluated each patient's IOP, conjunctival injection, and punctate keratitis at 0, 12, and 24 weeks. **Results:** The mean IOP of the timolol group (20 eyes) was 10.5, 10.6, and 11.1 mmHg, at 0, 12, and 24 weeks, respectively, whereas that of the betaxolol group (20 eyes) was 11.7, 11.1, and 10.5 mmHg at 0, 12, and 24 weeks, respectively. No significant differences were found between the two groups and in the intragroup comparisons. Moreover, no significant differences were found between timolol and betaxolol in regard to the conjunctival injection score. **Conclusion:** The findings of this study show that timolol and betaxolol have equivalent efficacy and safety in Iraqies patients with NTG.

KEYWORDS: timolol, betaxolol, normal-tension glaucoma, crossover.

INTRODUCTION

Glaucoma is one of the major leading causes of blindness worldwide.[1] glaucoma has become the third cause of blindness In Iraq since 2000.[2] Normal-tension glaucoma (NTG) is the second most common type of glaucoma in Iraq,[3] with a prevalence rate of 2.6% in people over 40 years of age. The ophthalmic solutions 0.5% timolol[4,5] and 0.5% betaxolol[6,7] are topical Betablokers. Both solutions reduce intraocular pressure (IOP) by decreasing the aqueous production, mediated by an effect on the ciliary epithelium.[8] Timolol was patented in 1968 and came into medical use in 1978. It is on the World Health organization"s List of Essential Medicine. betaxolol was approved by FDA as ocular solution in 1986. the most effective and safe medicines needed in a health system is reportedly equivalent to that of betaxolol[9] for patients with primary open-angle glaucoma or ocular hypertension.

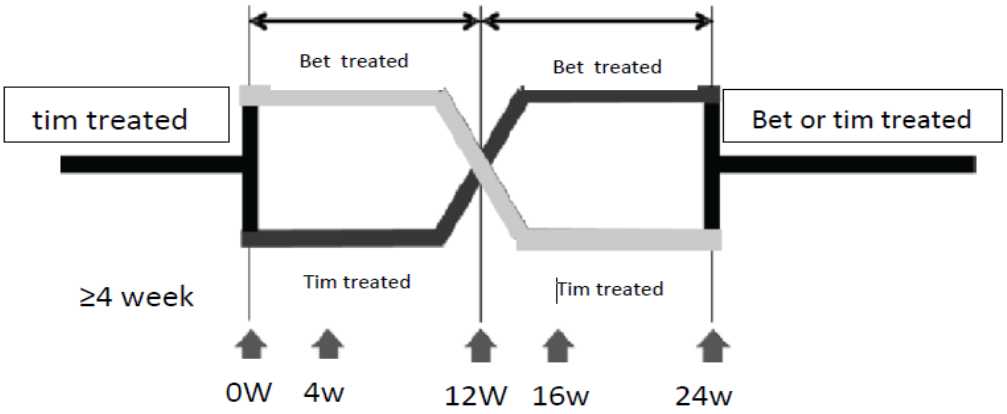
Although there have been report on the efficacy of timolol for NTG patients,[10,11] to the best of our knowledge, no comparison crossover studies have been conducted to investigate the efficacy and safety between timolol and betaxolol for NTG patients. In this prospective crossover study involving Iraqis NTG patients, the IOP reduction efficacy and safety of timolol were compared with those of betaxolol.

SUBJECTS AND METHODS

This study was a non-masked randomized study. All study participants were recruited between october 2021 and october 2023. We selected and enrolled 40 Iraqis NTG patients who had used timolol monotherapy at least 4 weeks at ophthalmological department in specialized center for ophthalmology. Written informed consent was obtained from all patients after receiving a detailed explanation of the nature and possible consequences of their participation in the study.

Each of the 40 enrolled patients were randomly divided into one of the following two groups: 1) timolol-to-betaxolol group (TB group: 20 patients, 9 male eyes and

11 female eyes; mean age: 63.5±11.5 years) and 2) betaxolol-timolol group (BT group: 20 patients, 11 male eyes and 9 female eyes; mean age: 69.1±8.8 years). At the beginning of the study, both groups were switched from initial timolol to timolol or betaxolol for 12 weeks, and then switched over to the other drug (crossover) to use for 12 additional weeks.



Measurement of IOP
Figure 1: study design.
Abbreviations: IOP, intraocular pressure; Bet, betaxolol; Tim, Timolol; W, week.

At 0, 4, 12, 16, and 24 weeks, we evaluated their IOP, conjunctival injection score (Grades 0–3),[12] and punctate keratitis score (area density [AD] score).[13] Then, at 0, 12, and 24 weeks.

In all patients, IOP was measured by using an applanation tonometer by the same glaucoma specialist throughout the protocol periods, and those IOP measurements were obtained at approximately the same time of day for each patient. If data were available from both eyes, then the right-eye data were used. We evaluated the mean deviation of the Humphrey 30-2 threshold of static visual field program at baseline or within 3 months. Statistical analysis was performed using the Student's *t*-test and Fisher's exact test.

For each patient, timolol and betaxolol eye drops were prescribed at the Glaucoma Special Clinic. As this was not a masked study, both the patient and the doctor knew which eye drop was being used. A calculated sample size of 20 enrolled subjects per arm providing the power of 80% was based on a non inferiority limit of 1.5 mmHg, a standard deviation of 1.5mmHg for change in IOP.

RESULTS

There were no dropout cases, and all patients completed the study. Of the total 40 subjects, 38 were newly prescribed timolol, yet 1 subject in both the TB and BT groups used timolol for more than 4 weeks. The backgrounds of the patients are detailed in Table 1.

Table 1: Background of the subjects.

	All subjects	timolol group	betaxolo l group
Number of subjects	40	20	20
Male/female	20/20	9/11	11/9
Mean age (years)	66.3±10.5	63.5±11.5	69.1±8.8
Baseline iOP at study starting (mmhg)	11.1±2.0	10.5±1.7	11.7±2.2
Nonmedication baseline IOP (mmhg)	13.8±2.2	13.9±2.3	13.6±2.0
Baseline MD (dB)	–4.2±42	–4.5±5.2	–3.9±3.3
Periods of Tim use before initiation of this study (weeks)	5.5±8.2	6.9±11.4	22.9±73.3

Note: Data presented as mean □ sD.
Abbreviations: TB, Timolol to Betaxolol; BT, Betaxolol to Timolol; IOP, intraocular pressure; MD, mean deviation Tim; Timolol.

There were no significant differences in age, sex ratio, or mean deviation obtained from Humphrey perimetry sita standard 40-2 between the TB and BT groups.

As for the IOP time course of all subjects, at 0, 12, and 24 weeks, respectively, the mean IOP of the TB group (20 eyes) was 10.5, 10.6, and 11.1 mmHg, whereas that of the BT group (20 eyes) was 11.7, 11.1, and 10.5 mmHg, and no significant differences were found between the two groups (Student's *t*-test) (Figure 2).

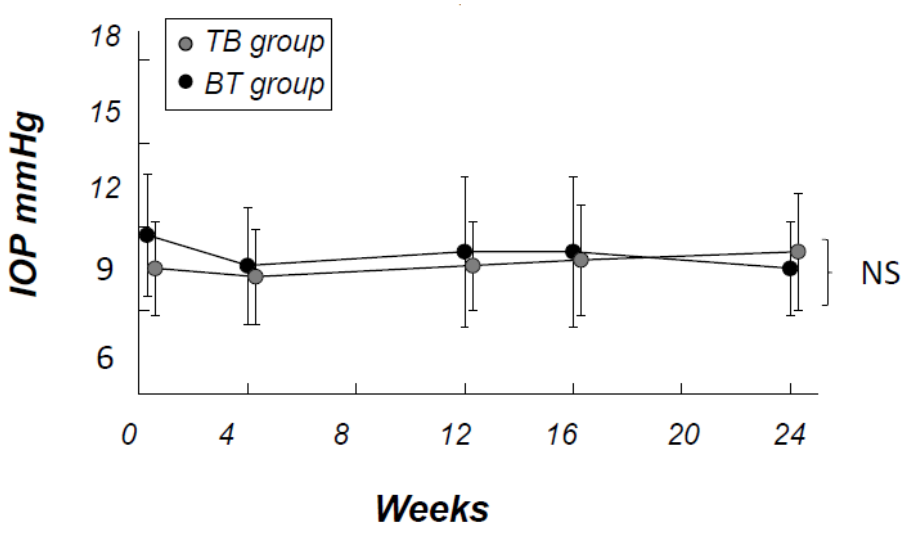


Figure 2: IOP time course of all subjects.

Note: No significant difference in IOP reduction was found between the timolol to betaxolo group and the TB toB T group throughout 24 months.

Abbreviations: IOP, intraocular pressure; TB, timolol to betaxolol; BT, betaxolol to timolol; NS, not significant.

At 0, 4, and 12 weeks, respectively, the mean IOP of the timolol intragroup (40 eyes) was 10.8, 10.6, and 10.5 mmHg, whereas that of Betaxolol intragroup (40 eyes) was 10.8, 10.7, and 11.1 mmHg, and no significant differences were found between the two intra- groups (Student's *t*-test) (Figure 3).

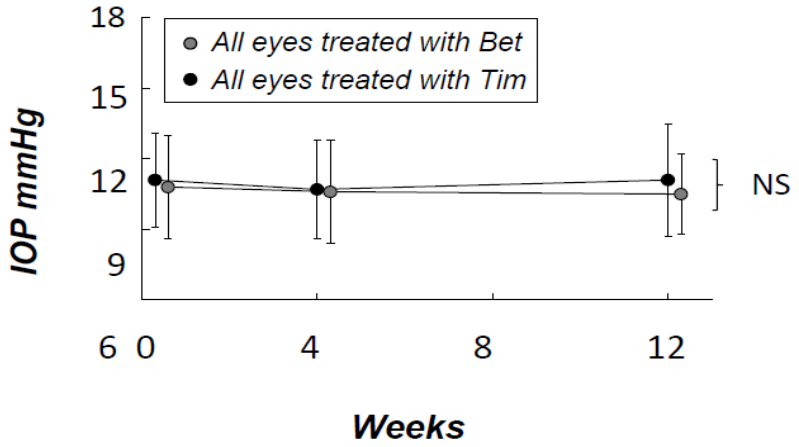


Figure 3: IOP reduction time-course between all subjects of Tim and Bet groups.

Note: No significant difference in IOPreduction was found between the two groups.

Abbreviations: IOP, intraocular pressure; Tim, timolol; Bet, betaxolol; NS, not significant.

The mean conjunctival congestion score at 0, 4, 12, 16, and 24 weeks, respectively, was 1.0±0.4, 1.0±0.5, 0.9±0.3, 0.9±0.4, and 0.9±0.4 in the TB group and 1.0±0.4, 1.1±0.5, 1.1±0.6, 1.0±0.5, and 1.1±0.5 in the BT group, and no significant differences were found between two groups (Student's *t*-test) (Figure 4).

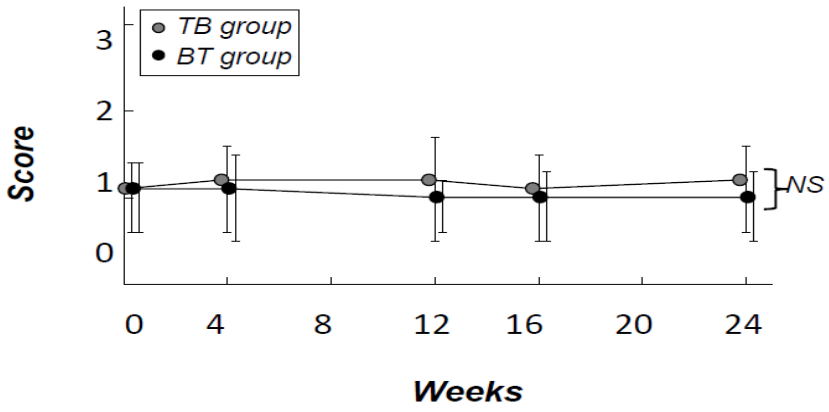


Figure 4: Conjunctival injection score.
Note: No significant difference in conjunctival injection score was found between the two groups.
Abbreviations: TB, timolol to betaxolol; BT, betaxolol to timolol; NS, not significant.

The respective mean AD score at 0, 4, 12, 16, and 24 weeks was 0.5±0.9, 1.0±1.4, 0.7±1.0, 0.9±1.4, and 0.7±1.0 in the TB group and 1.0±1.3, 0.7±1.0, 0.7±1.0, 0.5±1.0, and 0.8±1.3 in the BT group, and no significant differences were found between the two groups (Student's *t*-test).

DISCUSSION

Although there have been reports on the efficacy of betaxolol for NTG patients, to the best of our knowledge, this present study is the first crossover prospective report to investigate and compare IOP reduction efficacy and safety between timolol and betaxolol in NTG patients. In this study, no significant differences were found between timolol and betaxolol in regard to IOP reduction effects, conjunctival conjestion score, and punctat epithelial keratitis score, It has been reported that conjunctival conjestion becomes stronger when switching from timolol to betaxolol,[14,15] It should be noted that this study did include some limitations. The first limitation was that this was not a masked study, as both the subjects and the attending doctor knew which eye drop was being used.

The second limitation was that since the baseline IOP of all subjects using timolol was low, it was difficult to find the switching efficacy of the eye drop.

CONCLUSION

The findings of this study show that timolol and betaxolol have equivalent safety and efficacy in Iraqis NTG patients with low IOP.

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