COMPARISON OF LEVOBUNOLOL AND BRIMONIDINE IN PROPHYLAXIS OF INTRAOCULAR PRESSURE (IOP) RISE FOLLOWING ND:YAG LASER CAPSULOTOMY

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ABSTRACT

Objective: To compare the efficacy of topical 0.5% Levobunolol and 0.2% Brimonidine in preventing intraocular pressure rise after Nd: YAG laser posterior capsulotomy.

Study Design: Randomized controlled trial (RCT).

Setting and Duration of Study: Ophthalmology Department Combined Military Hospital Multan, from September 2010 to March 2011.

Patients and Methods: A total of 82 patients fulfilling the inclusion criteria were selected from out-patient department and randomly divided into two equal groups. Topical 0.5% levobunolol was instilled in group A while 0.2% brimonidine was instilled in group B one hour before and immediately after doing Nd:YAG laser capsulotomy. The intraocular pressure (IOP) was measured using Goldmann applanation tonometer 1, 3 and 24 hours later. Data was analyzed using SPSS version 15.0.

Results: There was no statistically significant difference in mean IOP between 0.5% Levobunolol group (Group A) and 0.2% Brimonidine group (Group B) at 1 hour, 3 hours and 24 hours after Nd:YAG laser capsulotomy. The mean intraocular pressure (IOP) one hour after Nd:YAG laser and topical treatment in group A was 16.10±1.60 mmHg while in group B was 15.65 ± 3.01 mmHg (P=0.401). Mean IOP after three hours in group A was 15.80 ± 1.35 mm Hg and in group B was 15.05 ± 2.15 mmHg (p=0.062). Mean IOP after 24 hours in group A was 15.13 ± 2.05 mmHg while in group B was 14.32 ± 1.62 mmHg (p=0.058).

Conclusion: Both 0.5% Levobunolol and 0.2% Brimonidine are equally effective in controlling the IOP spike after Nd: YAG laser capsulotomy. Either of these medicines can be used as a prophylaxis to prevent rise in IOP after Nd:YAG laser capsulotomy.

Keywords: Brimonidine, Levobunolol, Nd:YAG laser posterior capsulotomy, Posterior capsular opacification.

INTRODUCTION

Cataract is the leading cause of preventable blindness around the world and accounts for approx 48.0% of total blindness[1]. Posterior capsular opacification (PCO) is the most common late post-operative complication of uncomplicated cataract surgery, occurring in about one-third of patients despite the ongoing advances in surgical techniques[2]. PCO can drastically affect the vision over a period of time[3], forcing the patient to seek ophthalmic consultation[4]. The incidence of PCO in adults is 18-50% by two years post operatively[5]. The main reason for development of PCO is transformation of residual lens epithelial cells from the equatorial region of the capsular bag into Elschnig pearls and fibroblasts[6].

The current treatment of choice for PCO is Neodymium: Yttrium-Aluminum-Garnet (Nd: YAG) laser capsulotomy. Nd: YAG laser is a photo-disruptive laser which causes disruption of tissue by producing extreme heat of about 10,000°C along with an acoustic shockwave[7]. It is a simple and quick procedure, gives instantaneous results and can easily be done in an out-patient setting. It is, however, associated with several complications, the most common being an acute elevation in intraocular pressure (IOP)[8]. It is postulated that the release of lens epithelial cells and debris into anterior chamber causes the mechanical obstruction of the trabecular meshwork[9]. Rise in the IOP is also due to the breakdown of blood aqueous barrier[10]. Fortunately this rise in intraocular pressure is transient and can be easily managed. Other possible complications of laser capsulotomy include pitting of intraocular lens, vitreous floaters, cystoid macular oedema, iritis

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and endophthalmitis[11]. Retinal detachment and inadvertent damage to macula are also infrequent but vision-threatening complication[12-14].

Among these complications, the transient rise in IOP is the most important one. This rise in IOP usually occurs one to four hours after the laser treatment and can reach up to 30 to 40 mmHg which can lead to optic nerve damage and irreversible loss of visual field. The use of IOP lowering drugs in order to prevent these IOP spikes is mandatory[15,16] and prophylactic use of various drugs such as dorzolamide, apraclonidine, timolol, brimonidine and levobunolol has been documented to reduce the incidence of IOP spikes post Nd:YAG laser capsulotomy[8,9].

Levobunolol is a non selective beta blocker and blocks both beta-1 and beta-2 receptors. It is thought to reduce IOP by suppressing aqueous humor formation in the ciliary body. Topical levobunolol is available as 0.5% levobunolol hydrochloride ophthalmic solution and has been rapidly adopted as a standard treatment for open-angle glaucoma. Besides this, it is also useful in many cases of secondary glaucoma, aphakic glaucoma, and ocular hypertension. Brimonidine tartrate is a potent third generation alpha-2 adrenergic agonist and has more than 1000-fold selectivity for alpha-2 over alpha-1 receptors. It has IOP lowering characteristics similar to other alpha-2 agonists and acts by reducing aqueous humor production and increasing uveoscleral outflow.

PATIENTS AND METHOD

This randomized controlled trial (RCT) was carried out at the Department of Ophthalmology Combined Military Hospital Multan from 16th September 2010 to 15th March 2011. Approval from hospital ethical committee was obtained prior to the start of study. The patients having PCO who underwent uncomplicated cataract surgery at least six months ago were included. Any patient having IOP above 21 mmHg (with or without anti-glaucoma medication) or using any topical or systemic medication that could alter the IOP was excluded from the study. Patients having glaucoma, hypertension, diabetes mellitus, history of ocular trauma, uveitis, retinal detachment or angle anomalies were also excluded.

The sample size was calculated by using WHO sample size calculator and the study included 82 patients divided into two equal groups by simple randomization using lottery method.

- Group A (41 patients): 0.5% levobunolol eye drops.
- Group B (41 patients): 0.2% brimonidine eye drops.

Detailed history from each patient was taken and ocular examination with slit lamp biomicroscope and three mirror lens was carried out to ascertain the cause of reduced vision and to rule out optic disc cupping and predisposing factors of retinal detachment. Baseline IOP was measured using Goldmann applanation tonometer with fluorescein and all the data were collected using a proforma. Possible risks associated with the therapy were discussed in detail with every patient and informed written consent was obtained. One hour prior to Nd: YAG laser capsulotomy, a single drop of 0.5% levobunolol or 0.2% brimonidine was instilled into the eye under treatment depending upon the group of patient. Cornea was anaesthetized with one drop of topical 0.5% proparacaine hydrochloride a few minutes before laser application. Abraham YAG capsulotomy contact lens was applied and Nd: YAG capsulotomy was done with a Q-switched Zeiss VISULAS YAG III (Nd: YAG) laser system. An opening of 2-3 mm in the centre of the opacified capsule was made using minimum amount of total laser energy. One drop of the drug according to respective group was repeated just after capsulotomy. The IOP was measured at 1, 3 and 24 hours post-operatively using Goldmanns applanation tonometer by an ophthalmologist. All the capsulotomies were performed by same ophthalmologist in order to avoid operator bias. Patients from both groups were also given a combination of tobramycin and dexamethasone topical eye drops, one drop four times a day for next one week in order to prevent the intraocular inflammation and late post op

endophthalmitis.

DATA ANALYSIS

Data were analyzed using SPSS version 15.0. Mean and Standard Deviation were calculated for quantitative variables. Frequency and percentages were calculated for qualitative variables. Independent samples' t- test was used to compare the IOP recorded at various intervals between the two groups. Chi-square test was applied to compare IOP control between the two groups. A *p*- value of <0.05 was considered as significant.

RESULTS

A total of 82 patients were included in the study and randomly divided into two groups of 41 each. There were no drop outs as patients were selected after detailed history and examination and were briefed about the procedure and possible complications. Both the groups were comparable with respect to age (*p*=0.671) and gender (*p*=0.491) (Table-1).

In group A, the mean IOP pre Nd:YAG laser was 15.56 ± 2.72 mmHg while in group B, the mean IOP was 14.72 ± 2.92 mmHg (P= 0.181). The mean IOP after Nd: YAG laser and topical treatment in both the groups was similar at one hour (*p*=0.401), three hours (*p*=0.062) and 24 hours (*p*=0.058).

The comparison of change in IOP from baseline at different time intervals in both groups is also insignificant (Table-3).

DISCUSSION

The literature search on the subject revealed that although a lot of work has been done to evaluate and compare the efficacy of various pressure lowering drugs after Nd: YAG capsulotomy, specific literature on comparison of levobunolol and brimonidine is not available.

The hypothesis of the study was that topically administered 0.2% Brimonidine eye drops have better control over IOP rise after Nd: YAG laser capsulotomy than topically administered 0.5% Levobunolol eye drops. The results of the study have rejected the hypothesis of Brimonidine superiority over Levobunolol. IOP change at one hour, 3 hours and 24 hours showed that there was no statistically significant difference between these drugs in controlling the IOP after Nd: YAG capsulotomy.

In our study both the groups were comparable statistically in terms of age and

Table-1: Demographic distribution of patients.

		Group A (n=41)	Group B (n=41)	*P* Value
Age (Years)		59.24 ± 6.35	59.85 ± 6.61	0.671
Gender	Male	27(65.9%)	24 (58.5%)	0.491
	Female	14 (34.1%)	17 (41.5%)	

Table-2: Comparison of mean intraocular pressures at different time intervals in the two groups.

Group	Pre Nd:YAG laser IOP	IOP Post Nd:YAG laser and topical treatment		
		After 1 hour	After 3 hours	After 24 hours
A	15.5 6 ± 2.72	16.10±1.60	15.80 ± 1.35	15.13 ± 2.05
B	14.72 ± 2.92	15.65 ± 3.01	15.05 ± 2.15	14.32 ± 1.62
p-value	0.181	0.401	0.062	0.058

Table-3: Comparison of mean change in IOP from baseline at different time intervals in the two groups.

Group	IOP change after 1 hour	IOP change after 3 hours	IOP change after 24 hours
A (n=41)	0.54 ± 3.16	0.24 ± 3.03	- 0.46 ± 3.40
B (n=41)	0.93 ± 4.19	0.33 ± 3.62	- 0.40 ± 3.33
p-value	0.635	0.903	0.935

gender distribution. This study is also comparable to other studies in terms of demographic distribution of patients. In a study conducted by Minello et al[17] the mean age of the patients was 63.67 years. Similarly Awan et al[15] conducted similar study where mean age was 63-60 years.

In our study the mean baseline IOP in group A was 15.56 mmHg and in group B was 14.72 mmHg. According to Latif et al[9] the mean baseline IOP in all groups was 12 mmHg. Chen TC[18] reported the mean baseline IOP of 14.1 mmHg in the brimonidine group and 16.2 mmHg in the apraclonidine group. Study conducted by Minello et al[17] showed baseline IOP in Brimonidine group as 11.2 mmHg. In the study conducted by Cai PJ et al[19] the mean baseline IOP in Timolol group was 14.8 mmHg while in placebo group the mean baseline IOP was 15.1 mmHg.

In our study the mean IOP 1 hour after laser application and topical treatment in Group A was 16.10 mm Hg and in Group B it was 15.65 mm Hg. Although rise in IOP was noted in both groups at 1 hour, the change in IOP in the two groups was not statistically significant. Minello et al[17] conducted a study which revealed IOP after one hour in Timolol group as 10.8 mmHg while in Brimonidine group it was 11.3 mm Hg, showing a slight increase in the Brimonidine group. Nisar et al[20] noted 2 hour Post YAG mean IOP of 13.02 mmHg in levobunolol group.

In our study the mean IOP after three hours in group A was 15.80 mmHg and in group B was 15.05 mmHg. Minello et al[17] reported IOP at 2 hours in Timolol group as 10.3 mm Hg while that of Brimonidine was 10.1 mm Hg. There was no statistically significant difference between two groups in his study too and both drugs were equal in potency at 2 hours. Minello et al[17] also observed that no spike was noted after 2 hours of Nd: YAG capsulotomy.

In our study the mean IOP after twenty four hours of laser treatment and drug instillation in group A was 15.13 mmHg and in group B was 14.32 mmHg with insignificant difference. Nisar et al[20] observed that the mean IOP of 13.12 mmHg in levobunolol group after twenty four hours. We also noticed that the change in mean IOP in both the groups after one hour, three hours and twenty four hours post laser / drug treatment, as shown in Table-3, was consistent with various other studies. Both of the groups were comparable to each other as evident by insignificant P-values. Nisar et al[20] observed the change of 0.85 mmHg at two hours and -0.38 mmHg at twenty four hours post laser in levobunolol group.

It is thus proved by our study that both 0.5% levobunolol and 0.2% brimonidine are equal in efficacy in lowering the IOP after Nd: YAG laser capsulotomy and thus either can be used for prophylaxis of IOP rise after this procedure. In patients having contra-indication to levobunolol, brimonidine can be considered as an alternative for prophylaxis of IOP elevation after Nd:YAG capsulotomy. However keeping in view the scarcity of literature on specific comparison of these two drugs, more research with longer follow ups is required in order to completely ascertain their effects.

CONCLUSION

The acute rise in intraocular pressure which occurs after Nd: YAG laser posterior capsulotomy can effectively be prevented by prophylactic instillation of either 0.5% Levobunolol or 0.2% Brimonidine, administered before and after the procedure..

CONFLICT OF INTEREST

The authors of this study reported no conflict of interest.

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