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A COMPARATIVE STUDY OF EFFICACY AND TOLERABILITY OF DORZOLAMIDE AND TIMOLOL MALEATE IN PRE-OPERATIVE CATARACT PATIENTS

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ABSTRACT

The drugs currently available for treatment of glaucoma are â-blockers, sympathomimetics, carbonic anhydrase inhibitors (CAIs) and prostaglandin analogues[1]. Apart from their use in glaucoma to reduce IOP, the antiglaucoma drugs are also used routinely for pre-operative reduction of IOP even in non-glaucomatous patients subjected for intraocular surgery to prevent expulsive haemorrhage and bulging of anterior segment.

Objectives: To assess the safety and tolerability of 2% dorzolamide and 0.5% timolol maleate in Pre-operative Cataract patients.

Materials and Methods: A prospective, comparative study enrolling 60 Pre-operative Cataract patients (30 in each group) attending Ophthalmology inpatient department in Kempe Gowda Institute of Medical Science Hospital and Research Centre. Dorzolamide was instilled thrice daily and timolol maleate twice daily for 2 days. IOP was measured on zero, 2nd, 24th and 48th hours and also looked for side effects.

Results: The mean reduction of IOP was 17.1% with dorzolamide and 18.9% with timolol maleate. Both the drugs were tolerated very well without any systemic adverse effect and the local side effects were comparatively less with dorzolamide.

Conclusion: Efficacy of dorzolamide in decreasing IOP in Pre-operative Cataract patients was almost comparable to timolol, and dorzolamide appeared to be relatively better tolerated.

Keywords: *Pre-operative, cataract; IOP; dorzolamide; timolol maleate.*

INTRODUCTION

The drugs currently available for treatment of glaucoma are â-blockers, sympathomimetics, carbonic anhydrase inhibitors (CAIs) and prostaglandin analogues[1]. Apart from their use in glaucoma to reduce IOP, the antiglaucoma drugs are also used routinely for pre-operative reduction of IOP even in non-glaucomatous patients subjected for intraocular surgery to prevent expulsive haemorrhage and bulging of anterior segment.

Timolol, a non-selective □-blocker, is one of the widely used topical agents, which reduces the IOP by decreasing the aqueous humor secretion. However it carries the risk of worsening bronchospasm in asthmatics, worsening A-V block and masking hypoglycemia in IDDM. Dorzolamide is a topical CA inhibitor, which reduces IOP by decreasing aqueous humor production and secretion, and is used as an effective adjuvant or alternative when □-blockers are contraindicated or ineffective to control IOP.

As there are few studies done to compare its relative efficacy and tolerability with timolol in Indian population, this study was taken up. In this study, the clinical efficacy and tolerability of topical dorzolamide was assessed in comparison with topical timolol maleate for pre-operative reduction of IOP in patients subjected to cataract surgery.

OBJECTIVES

To assess the clinical efficacy & tolerability of 2% dorzolamide eye drops instilled thrice daily in comparison with 0.5% timolol maleate eye drops instilled twice daily in producing clinically relevant reduction of IOP in pre-operative cataract patients.

METHODOLOGY

This prospective study was done to assess the efficacy and tolerability of topical dorzolamide in comparison with topical timolol maleate to reduce IOP in pre-operative cataract patients who have admitted for inpatients Ophthalmology department of KIMS Hospital and Research Centre, Bangalore for a period of one year. After obtaining approval and clearance from the Institutional Ethical Committee, 60 subjects were recruited for the study. Patients were randomly selected into 2 groups (30 each)

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Inclusion criteria include pre-operative cataract patients between 40-60 years of age & who were willing to give written informed consent. Exclusion criteria include pregnant and lactating woman, patient with history of allergy or tolerance to CAIs, angle closure glaucoma, intra ocular surgery within previous six months, argon laser trabeculoplasty within three months, any ocular inflammation or infection within past three months, bronchial asthma / chronic obstructive pulmonary disease, Sinus bradycardia/second or third degree heart block, overt cardiac failure & cardiogenic shock.

Informed consent was obtained after fully explaining the procedure and the consequences, in patients' own language. A thorough evaluation of all the patients was done by detailed history taking followed by general, systemic and ocular examination.

To one group, dorzolamide 2% ophthalmic solution instilled in the affected eye, one drop three times a day and for the second group timolol maleate 0.5% ophthalmic solution instilled in the affected eye, one drop two times a day. Study drugs were started 48 hrs before surgery and duration of therapy was for 2days. The follow up was done after 24 and 48 hours to assess IOP & any side effect of the drug.

In this study, the clinical efficacy and tolerability of topical dorzolamide was assessed in comparison with topical timolol maleate in patients subjected to cataract surgery. The age of the patient included in the study ranges between 41 and 60 years. 26 patients in DRZ group and 28 patients in TML group were in the age group 51 to 60 years (Fig 1). The mean age of the patients was 55.86yrs in DRZ group and 57.26yrs in TML group. 18 patients were male and 12 female in each group (Fig 2). The demographic features (age & sex) of the patients chosen for pre-operative reduction of IOP before cataract surgery were not significant between groups. All the patients from both the groups had normal IOP, the pre-operative reduction of normal IOP deemed necessary to prevent perioperative complications like expulsive haemorrhage and bulging of anterior segment[2].

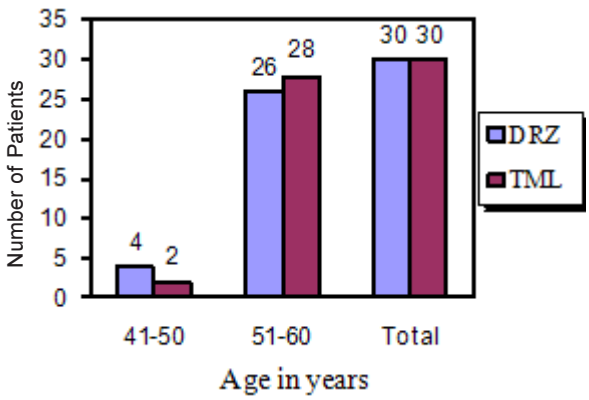


Fig. 1 : *Age Distribution*

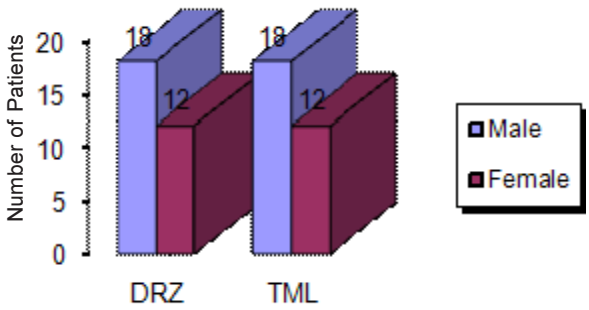


Fig. 2 : *Sex Distribution*

All the patients complained of diminution of vision and some also had headache (13.33%) and watering (10%) (Table 1). Among the patients selected from both the groups, 43(71.67%) were having senile immature cataract and 17(28.33%) having senile mature cataract (Table 2).

Table 1: *Chief complaints*

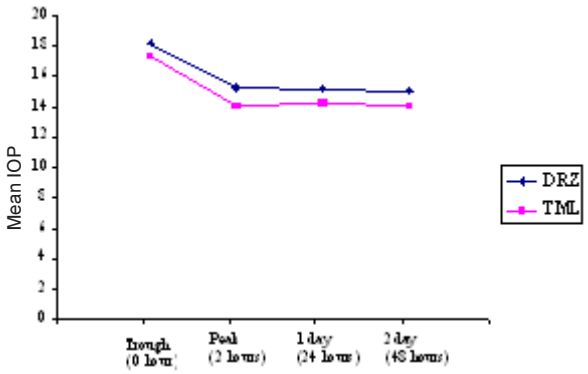
Chief complaints	DRZ (30)	TML (30)	Total (60)
	n (%)	n (%)	n (%)
Diminution of vision	22(73.33)	24(80.00)	46(76.67)
Diminution of vision with headache	06(20.00)	02(06.67)	08(13.33)
Diminution of vision with watering	02(06.67)	04(13.33)	06(10.00)

Table 2: *Distribution of type of cataract*

	DRZ	TML	Total
	n (%)	n (%)	n (%)
SIMC	19(63.33)	24(80)	43(71.67)
SMC	11(36.67)	06(20)	17(28.33)

The effect of drugs on IOP in pre-operative cataract patients is depicted in Figure 3. The drugs were started 48 hours before surgery and the IOP were recorded at trough, peak, at the end of 24 and 48 hours and the % reduction was calculated after 48hrs. In both the groups the maximum decrease in IOP occurred within 2 hours, with little further decrease after 24 hours and 48 hours. The fall in IOP in the two groups was almost comparable, DRZ achieving a mean fall of 3.1mm Hg(17.1%) and TML 3.27 mm Hg (18.9%) from the trough, at the end of the study period and the difference was not statistically significant (p-value >0.05).
Both the drugs were well-tolerated and only 6 patients (10%) in DRZ group and 11 patients (18.33%) in TML group experienced side effects like headache, burning

sensation and bitter taste (Fig 4). The main complaint in the DRZ group (3 patients) was bitter taste, whereas in TML group 6 patients complained of burning sensation. Side effects occurred after 24 hours and among the two drugs dorzolamide was relatively better tolerated.



p > 0.05 (between groups)

Fig. 3 : *Effect of Drugs on IOP*

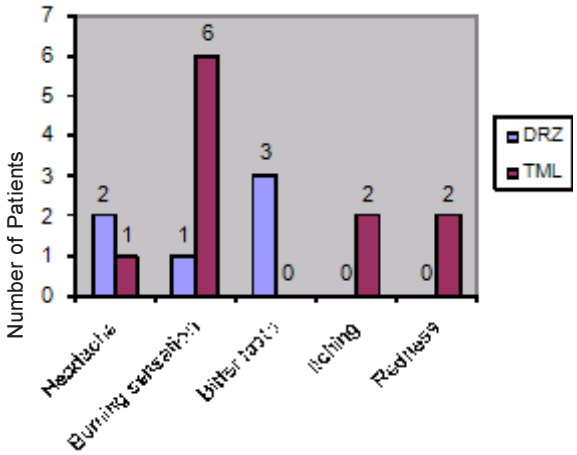


Fig. 4 : *Side effects*

Dorzolamide being a topical CA inhibitor is free from systemic adverse effects metabolic acidosis, crystalluria, and hyperkalemia unlike oral acetazolamide. Studies have shown that the efficacy in lowering IOP was comparable to oral acetazolamide and topical timolol[3], betaxolol[3] and brimonidine[4] though some studies have shown timolol to be marginally better[3].

For pre-operative reduction of IOP, both the drugs were almost equally effective achieving nearly maximal effect after two hours. Though there is no clearly defined target level of IOP to be reached; it is generally advisable to maintain hypotonic IOP around 14 mm of Hg in view of preventing perioperative and postoperative complications[5]. The IOP lowering drugs may be continued for 2-3 days in the postoperative period. However in the present study the follow up measurement of IOP was not done, as it was not feasible in the postoperative period. Other measures used for pre-operative decrease in IOP include acetazolamide [250mg-oral, 2 hours before or i.v. 15 min before surgery [2], mannitol [i.v.infusion] and glycerol [oral]. In one study, topical dorzolamide compared very well with oral acetazolamide [6]. There are no extensive and systematic studies to show the efficacy of topical timolol maleate for pre-operative decrease in IOP. In the present study both the drugs achieved desirable and acceptable level of IOP reduction. Since the maximum effect is achieved within two hours, it may be advisable to start the IOP lowering drugs just 2 hours prior to surgery instead of 48 hours before, as there seems to be little advantage if started earlier and also because side effects seem to be less likely within 2 hours.

In the present study both the drugs were tolerated very well, pre-operative reduction of IOP and the adverse effects were mild and infrequent. Only 10% of patients receiving dorzolamide experienced mild side effects like bitter taste, headache and burning sensation in the eye. In timolol group 18.33% of preoperative cataract patients experienced side effects, which mainly included burning sensation. With both the drugs, the side effects were not evident at peak but developed with repeated administration and therefore seem to be related to the duration of administration and hence the occurrence of side effects being of much concern with long-term administration.

Thus, the present study suggests that the efficacy of topical dorzolamide in reducing IOP in pre-operative cataract patients is almost comparable to topical timolol maleate, and dorzolamide was relatively better tolerated than timolol maleate and also totally free from systemic and biochemical adverse effects characteristic of oral CAIs. Thus, dorzolamide can be better option or preferable drug in the naturalistic setting of the general population. Though dorzolamide can be effective as monotherapy, in patients with inadequate response it can be combined with timolol and this combination appears to be synergistic for achieving maximal reduction in IOP [7]. Since there is no additional advantage by using dorzolamide in concentration more than 2% [8], such a combination would be of considerable clinical advantage for achieving maximum IOP reduction. Further, detailed and extensive studies in Indian population with dorzolamide alone or other topical CAIs, and also fixed dose combination of dorzolamide (or other topical CAIs) and timolol seems to be worth undertaking.

CONCLUSION

The present study suggests that efficacy of topical dorzolamide in decreasing IOP in preoperative cataract patients, was almost comparable to topical timolol maleate. Both the drugs were very well tolerated throughout the study period and the side effects were mild and local in nature and dorzolamide appeared to be relatively better tolerated.

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