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A COMPARATIVE STUDY ON EFFICACY OF FIXED COMBINATION TIMOLOL/BRINZOLAMIDE VERSUS TRAVOPROST MONO-THERAPY IN DRUG-NAÏVE OPEN-ANGLE GLAUCOMA PATIENTS.

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Abstract:

Background: Glaucoma is the cause of blindness. Beta blocker and prostaglandins are used as a first line treatment of open angle glaucoma. The exact target with mono therapy for reducing intraocular pressure is achieved within 2 years, so patient prefers fixed dose combination therapy.

Objective: For reducing intraocular pressure efficacy, travoprost mono therapy and timolol/brinzolamide fixed dose combination therapy is compared.

Material and methods: For 3 months, patients are randomly received 0.5% timolol and 0.2% brinzolamide twice daily and travporost once daily 0.004%.Then compared intraocular pressure, pulse rate, blood pressure, and cup disc ratio over 12 weeks of treatment.

Results: 27.99% and 30.49% reduction in intraocular pressure is observed with mono therapy and fixed dose combination respectively. Pulse rate (9beats/min) and systolic pressure reduction by (2.35mmHg) were seen with fixed dose combination but no cup disc ratio observed.

Conclusion: It is proved that 0.5% timolol and 0.2% brinzolamide causes more reduction in intraocular pressure than the 0.004% travporost mono therapy.

Keywords: Glaucoma, travporost and lantoprost

Introduction

Most common disease of blindness is caused by degeneration of retinal ganglion or retinal nerve fiber. Beta blockers and carbonic anhydrase inhibitor and prostaglandin analogues are used to treat open angle glaucoma, but most commonly we used beta blockers and prostaglandin analogues. [1] Seven years of study show that timolol causes 27.8 ± 0.3 mmHg reductions in Intra ocular pressure, which is better than other beta blockers. [2] PGA analogues cause a 30 % reduction and a 26.5 % reduction is seen with travporost and lantoprost. Medical guideline suggests that 20% reduction is caused by BB and 30% with the PGA. And this is costly, so combination therapy is used by BB, AA, and PGA. [3]

Results with mono therapy are obtained after 2 years and it is seen only in 50% people. [4] So, Multiple studies, like Normal Tension Glaucoma Treatment Study, the Collaborative Initial Glaucoma Treatment Study and the Ocular Hypertension Treatment Study (OHTS) proved that to achieve the target multiple drug therapy must be used. [5]

Topical medication absorbed into systemic circulation through nasal, orapharyngeal and the gastrointestinal mucosa. But the results with topical administration are not as strong as achieved through oral administration. Topical beta blockers produces bradycardia and heart blockade in patients with conduction system diseases. [6]

Timolol ocular instillation causes exacerbation of cardiopulmonary disease so its use is restricted in patients with pulmonary diseases. [7] FP receptors are most commonly present in the kidney and their role is to maintain water and electrolyte homeostasis. PGF2a causes the release of rennin, which increases BP by increasing rennin- angiotensin- aldosterone system. As age increases, risk of cardiopulmonary diseases increased. [8]

It is proved that clinical performances are altered by neurobiological changes. Various psychological mechanisms can explain these behavioral changes by conditioning, reward, expectations, and anxiety. And we can transform it by desire, motivation, and memory of a person. [9] These factors fall into the category of conscious, associative and social learning. For 12 weeks case report, a single blinded, parallel study was performed to compare

travporost mono therapy and timolol/ brinzolamide fixed dose combination therapy. [10]

Material and Methods

We selected 109 patients, among them only 104 patients completed the study. A written informed consent was signed by all of them to aware the effects of their contribution in the study by explaining all these factors. Patients were given 0.004% travporost randomly only one drop per day and were given 0.5% timolol and 0.2% brinzolamide twice drops per day. These drugs are chosen because they have the same dimensions, availability. And these are mostly commonly chosen drugs by all ophthalmologists.

Then we measured mean arterial blood pressure, systolic blood pressure, diastolic blood pressure after 2nd, and 4th, 8th, 12th week of case study. Goldmann applanation tonometer was used to measure intraocular study. The things remain constant during the whole study were Fluorescein dye and anesthetic agents. And between 10:00 a.m. – 12:00 p.m., All IOP measurements are performed by the same operator to mitigate circadian variation.

In a separate room, by using same equipments, hydrodynamic parameters were assessed. After taking the rest of 5 min, readings were taken. Readings taken are consecutive three but less value didn't take.

The persons who participated in the case study are directed to take pictures, and showed in the next follow up visit, if in case any adverse effects are noticed. Adverse drug reactions if reported are submitted to ADR monitoring center.

Statistical Analysis

Shapiro Wilk test was used to assess the possible results obtained from the case study. Since IOP data are normally spread, w= 0.97, p=0.24 and normal values for pulse rate, systolic blood pressure and diastolic blood pressure. The mean value will always be normal, unless in the population how the values are distributed, the mean value will always be normal for a larger size sample population. By repeated measure analysis of variance and unpaired student's t test for intra group and inter group comparison, data analysis for IOP, pulse rate, systolic blood pressure and diastolic blood pressure and CDR measurements were performed. Dunnett's test was performed for post hoc analysis. Analysis was performed by SPSS 17.0 statistical software. The statistically significant figure for p was <0.05.

Results

The study population mean age was 51.49 ± 7.00 years (range: 40–67 years), mean age of patients was 51.13 ± 7.32 and 51.83 ± 6.75 years in groups 1 and 2, respectively. Sixty-six patients (63.5%) were male. The baseline demographic characteristics, CCT, average RNFL, VF-MD and VF-PSD were comparable among both groups.

Table: Baseline characteristics of patients in two treatment groups of newly diagnostic drug naïve open angle glaucoma patients.

	Travoprost (*n* = 52)	Timolol/brinzolamide (*n* = 52)	*p* value
Mean age ± SD (range)	51.13 ± 7.32 (40–65)	51.83 ± 6.75 (41–67)	0.198
Female (%)	21 (40.4%)	17 (32.7%)	0.415
Male (%)	31 (59.6%)	35 (67.3%)	
IOP (mean ± SD)	23.40 ± 1.83	23.35 ± 1.55	0.862
Pulse rate (mean ± SD)	81.23 ± 9.66	80.50 ± 10.29	0.710
Systolic BP (mean ± SD)	129.69 ± 13.57	128.96 ± 14.67	0.793
Diastolic BP (mean ± SD)	82.92 ± 6.43	82.08 ± 6.50	0.506
Mean arterial pressure (mean ± SD)	98.51 ± 8.33	97.71 ± 8.92	0.634
CDR (mean ± SD)	0.65 ± 0.13	0.62 ± 0.14	0.606
Average RNFL (mean ± SD)	81.27 ± 7.28	83.17 ± 6.16	0.418
CCT (mean ± SD)	524 ± 36.11	512.8 ± 39.23	0.059
VF-MD (Mean ± SD)	–10 ± 7.5	–9.8 ± 8.7	0.127
VF-PSD (mean ± SD)	8.1 ± 3.9	7.9 ± 3.4	0.213

Primary Output

At 12th week, by comparison with baseline, a significant reduction in Intra ocular pressure by 6.56 mm Hg is observed by travporost. And 7.12 mmHg reductions in intraocular pressure are seen with the fixed dose combination by comparing with the baseline. When compared with travoprost patients, the reduction in Intra ocular pressure of FDC was significantly more by the end of case study.

Secondary Output

Mean pulse rate per minute (mean SD) 81.23 ± 9.66 and 80.50 ± 10.29 are comparable at baseline in group 1,2 and a significant reduction in pulse rate was observed at all follow -up visits as compared with baseline. But pulse rate reduction in group 2 is comparatively higher as compared to group 1 at all next follow –up visits.

But in the next follow- ups, between group 1, 2, no significant changes in mean arterial blood pressure and diastolic blood pressure and systolic blood pressure.

The values of CDR (mean ± SD) at the time of recruitment in group 1 and 2 are 0.66 ± 0.13 and 0.62 ± 0.14 respectively. When compared with the baseline, insignificantly reduction in intraocular pressure is seen at the end of the study.

Adverse Drug Effects

In group 1, at the next follow up visits between 4^{th} and 8^{th} week, 14 people developed conjunctival hyperemia. At 2^{nd} week, 4 people suffered from ocular discomfort. Foreign body sensation is seen in 4 different people and 2^{nd} follow up visit. Because of apparent changes in eyelashes at 12^{th} week follow up, two people complained of difficulty wearing spectacles. Transient blurred vision is seen in 16 patients of group 2. Total 18 (35%) and 20 (38.5%) patients developed different ADR's till 12 week treatment plan.

Discussion

Both of medicines showed significant reduction in intraocular pressure was 6.56 mmHg and 7.12 mmHg with the mono therapy travporost and fixed dose combination medication timolol and brinzolamide respectively at the end of case study. [20] Different percentages of reduction in IOP were seen at 2^{nd}, 4^{th}, 8^{th}, 12^{th} week, which were 20%, 22.64, 24.5, 28%, 20.34%, 24.36%, 26.46% and 30.5% [11] in brinzolamide and timolol respectively. In the efficacy of Latanoprost, the genetic polymorphism in prostanoid receptors correlates to the difference. [12]

The IOP reduction in each follow up was more than in fixed dose combination brinzolamide and timolol FDC than mono therapy travporost. [19] And this is just possible due to the combined effect of both fixed dose drugs brinzolamide and timolol. [13]

Most commonly observed adverse effects were conjuctival hyperemia and blurred vision in both drug combinations of group 1 and 2. [15] And these adverse effects were not as much as troublesome and mild to cause any serious harm to patients and these adverse effects are bearable. [14]

Most important diagnostic parameter for glaucoma and evaluating efficacy of treatment was CDR values. [15] And CDR reduction was seen was both treatments at the end of the 12th week. But we considered this reduction was not useful, but the CDR reversal potential was observed. [16]

The consequences of brinzolamide and timolol versus travporost were the main purpose of the study on hemodynamic parameters and CDR values when the drug was instilled topically. [17] The study not only concerned with the lowering of IOP but also discussed CDR reversibility. And ADR's associated with them were not passive and need to learn to reduce them. [18]

Conclusion

It is proved in our study that 0.5% timolol and 0.2% brinzolamide fixed dose combination FDC was better than the 0.004% travporost mono therapy. And no significant changes were seen with the mean arterial blood pressure, systolic blood pressure and diastolic blood pressure and CDR measurements by both pharmaceutical groups. Everything is tolerable with these medications; no new safety findings were established.

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