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Research Article

Pharmacoeconomic analysis of brimonidine/timolol and travoprost 0.004% in the treatment of primary open angle glaucoma in Indian settings

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ABSTRACT

Background: As we know primary open angle glaucoma need lifelong treatment. It possess financial burden to patient. We have done this study to compare the monthly cost and cost effectiveness of brimonidine /timolol fixed combi-nation and Travoprost 0.004% eye drops in patients of primary open angle glaucoma.
Methods: Drops were dispensed at room temperature from 2.5-mL bottles of Travoprost, and 5ml of Brimonidine/Timolol. Two determinations of drop count were taken, each made from bottles held vertically and at a 45-degree angle. The total volumes of medication dispensed from each bottle were measured. Drops in five new bottles were counted and averaged for each drug. Drugs given to patients and asked them to come back with empty bottles for follow up after 2, 4, 8, 12 wks. IOP was measured and another bottle of drug is given. Average retail price was determined by survey of different brands available in market. Drop count, average retail price, and IOP reduction data were used to compute annual cost and cost effectiveness (annual cost per mmHg of IOP reduction) of both of the drugs.
Results: Drops per 2.5ml bottle averaged 83 for Travoprost 0.004% and 100 drops per 5ml bottle for Brimonidine/Timolol. Average retail cost per bottle was 498 for Travoprost 0.004% and 204 for Brimonidine/Timolol. Annual re-tail cost was 3545 for Brimonidine/Timolol and 4910 for Travoprost 0.004%. Cost effectiveness ranges were 328 to 361 for Brimoni-dine/Timolol and 629 to 637 for Travoprost 0.004%.
Conclusions: Brimonidine/Timolol had the lower monthly cost and annual cost and it is more cost effective than Travoprost 0.004%.

Keywords: Pharmacoeconomic analysis, Travoprost, Brimonidine/Timolol, cost effec-tiveness, IOP

INTRODUCTION

Glaucoma is a major public health problem, being the largest cause of bilateral blindness, second only to the cataract.[1-3] accounting for 12.3 % of the 37 million people with bilateral visual loss around the world in 2002. The World Health Organization (WHO) projected that the number of affected individuals would escalate to 80 million by 2020, 11.2 million of whom would suffer bilateral blindness attributable to the disease.

Lowering intraocular pressure (IOP) is the standard treatment of glaucoma. Its effectiveness in halting glaucomatous progression in primary open angle glaucoma (POAG) was confirmed by various randomized control trials (RTCs).[4-6]

Management of primary angle closure glaucoma (PACG) is similar once the anterior chamber predisposition is reverted.[7] Glaucoma needs long term treatment. This life time treatment poses a financial challenge to the patient and adversely affects the drug compliance, which is, as in any chronic diseases, plays a major role in treatment outcome. Since glaucoma is a disease of elderly, the impact on productivity loss is relatively lower but financial burden is immense. The financial burden of

glaucoma increases as disease severity increases.[8] Efforts have been made to estimate the cost effectiveness to identify and to treat glaucoma and ocular hypertension.[9-12]

The analytical tools of economic evaluation like cost-effectiveness are most valuable with respect to chronic diseases like glaucoma with many alternative treatments.[13] Treatment strategies of glaucoma aim at lowering IOP which helps to prevent optic nerve damage and glaucoma related blindness. Even a single unit lowering of IOP has been associated with significant clinical improvements.[14]

METHODS

All the cases studied were attending the outpatient Department of Ophthalmology at Peoples College of Medical Science and Research Centre Bhanpur Bhopal. Study duration was 18 months. While selecting the cases for the study special care was taken to include only newly diagnosed cases of primary open-angle glaucoma (POAG).Necessary approval were taken (CTRI/2011/11/002105). Informed consent from the patient was obtained after explaining to them the details of the study. Patients were divided into two groups a and b based on simple random sampling. One group was treated with 0.004% of Travoprost eye drops once a day in both eyes in the morning and the other with fixed combination of Brimonidine/Timolol eye drops twice a day. Ocular improvement and efficacy of the drug were assessed by a follow-up study done 2, 4, 8, and 12 weeks.

Retail prices of both the drugs were obtained from 4 pharmacies.The contents of 5 new bottles of each drug (brimonidine /timolol and Travoprost 0.004%) were measured in terms of drops per bottle by a procedure designed to mimic actual medication use by patients. Drops were counted while the contents were at room temperature. Each bottle was inverted to a vertical position and squeezed until 1 drop came out. The bottle was then placed upright. This procedure was repeated until the bottle was emptied. The same person dispensed all drops for 2 drugs and was masked to the purpose of the study and the identity of the drugs. Because a secondary observer might be more likely to miss seeing a drop, the same person that squeezed the bottles also counted the drops. The average of the values for the 5 bottles was used in further analyses. Daily Cost of a particular anti-glaucoma medication was calculated by dividing the cost of one bottle by total number of drops in a bottle and multiplying by number of drops required daily. It was assumed that all the patients were treated for both eyes.

Cost-minimization analysis was conducted using the average retail price, determined from the pharmacy survey, for 1 bottle of drug. The number of days per bottle was calculated by dividing the number of drops per bottle by 2 (drops per day), based on treatment of both eyes once per day for Travoprost and dividing the number of drops per bottle by 4 for Brimonidine/timolol as it was given twice per day. Annual usage (bottles per year) was calculated by dividing 365 (days per year) by the number of days per bottle. Annual cost is the bottle cost times the annual usage, and the monthly cost is the annual cost divided by 12 (months per year).

Cost effectiveness was determined by dividing the drug cost by the drug's efficacy. In this study, efficacy is defined as the degree of IOP reduction (mm Hg). Cost effectiveness data for the two drugs in this study are expressed as ranges calculated from the ranges of IOP lowering capacity.

Statistical analysis

The data collected were tabulated and analyzed using descriptive statistical tools mean, standard deviation, and comparison between the groups by using Student's t-test.

RESULTS

Table 1: List of different pharmacies (brimonidine /timolol).

Name of drug (brimonidine/ timolol)	Qty.	Pharma-ceutical company	Cost per bottle	
Combigan	5 ml	Allergan	265	Average
Brimonist	5 ml	Neiss	165	819/4=204
Brimolol	5 ml	Sun	208	
Brimocom	5 ml	Cipla	181.5	

Table 2: List of different pharmacies (travoprost).

Name of drug (Travoprost)	Qty.	Pharma-ceutical company	Cost per bottle	
Optrvo	2.5 ml	Eye care	447	Average
Travatan	2.5 ml	Alcon	652	1994/4= 498.7
Xovotra	2.5 ml	Cipla	450	
Travo z	3 ml	Microlabs	535	

Based on average retail prices, calculations for the number of days per bottle, annual usage, annual cost, monthly cost, bilateral daily cost and cost per drop appear in Table 2. On the pharmacoeconomics parameter too Brimonidine/ timolol fixed combination proved better than the costly Travoprost which might affect the patient compliance in terms of the cost effectiveness of treatment. Travoprost is a longer acting drug hence require once daily administration in comparision to Brimonidine/ timolol fixed combination which requires twice daily administration. But this disadvantage with Brimonidine/timolol fixed combination did not

significantly affect the compliance of the patient in the study group.

We observed in our study that the treatment with Travoprost is less cost effective than with Brimonidine /timolol. The efficacy of Travoprost, in reducing mean IOP at the end of 6 months (7.7 mm Hg) was less than that of (10.8 mm Hg). Therefore, Brimonidine /timolol are clearly a better combination in our study in terms of being less costly and more efficacious than Travoprost.

Table 3: Comparison of cost.

	Drops per Bottle	Days per Bottle	Annual usage (bottles per year)	bottle cost	monthly cost	annual cost	Cost per drop
Travoprost 0.004%	83	37	9.86	498	409	4910	6
Brimonidine /timolol	100	21	17.3	204	295	3545	2.04

Table 4: Mean change in IOP after 3 months of treatment.

Group	Baseline IOP (mmhg)	IOP after 3 mnths	Mean change in IOP
Travoprost	27	19.2	7.8
Brimonidine/ timolol	28	19.0	11.0

Table 5: Cost-minimization analysis of brimonidine/timolol and travoprost 0.004%.

	Travoprost 0.004%	Brimonidine /timolol
Annual Cost*	4910	3545
IOP Reduction, † Lower Value (mm Hg)	7.6	9.9
IOP Reduction, Upper † Value (mm Hg)	7.8	10.9
Cost Effectiveness Range ($/mm Hg decrease in IOP)	629 to 646	325 to 358

Table 6: Cost effectiveness (CE) analysis of brimonidine/timolol and travoprost 0.004% at 3 months.

Group	Average IOP reduction for 3 months (mm hg)	CE for 3 months (rs/mm fall)	Calculated yearly CE (rs/mm fall)
Travoprost	7.7	159	637
Brimonidine /timolol	9.8	90	361

DISCUSSION

Pharmacoeconomics is the branch of economics that uses cost-benefit, cost-effectiveness, cost-minimization, cost-of-illness and cost-utility analyses to compare pharmaceutical products and treatment strategies.[15]

Here we have done cost-minimization analysis and cost-effectiveness analysis.

Cost incurred by the patient per mm Hg of IOP reduction was calculated for a period of three months of study period. Cost per mm of Hg reduction is calculated as, Cost per mm of Hg reduction = Mean total cost of treatment per year ÷ Mean change from baseline IOP (mm Hg).

Brimonidine/timolol was the most economical of the 2 IOP-lowering drugs evaluated in this study in terms of both cost minimization and cost effectiveness.

The monthly and annual costs of Brimonidine /timolol were lower of than Travoprost in the cost minimization analyses because of the greater number of drops dispensed per bottle, a measurement that mimics actual use of medication by patients. In this study, 83 drops per 2.5 mL bottle of Travoprost and 100 drops per 5ml bottle of brimonidine /timolol, were measured.

A literature review conducted by Hommer A, et al, found out that fixed drug combination of brimonidine and timolol or brimonidine adjuvant to timolol was cost-effective than fixed drug combination dorzolamide and timolol or dorzolamide adjuvant to timolol in European countries over a period of three and twelve months of follow-up.[16] Further studies are needed to focus on cost-effectiveness by taking more objective parameters using perimeter, monitoring of POAG progression using fundus camera, which can provide observable changes in POAG, over long period.

Because of lack of data on drug loss during drug administration we assumed it to be as 2 drops/wk for Travoprost and 4 drops/wk for Brimonidine /timolol. But with the improvements in dropper tips in recent years, the drug loss during administration may be minimal in future studies. With drugs cost is expected to come down in coming years in addition to improvements in drug delivery methods, the glaucoma pharmacotherapy is expected to be more cost effective in future.[17] The cost of drug treatment in India is cheaper unlike in developed countries like UK, Australia & USA.[18-20]

This study was limited by the number of bottles of each drug that were counted. The volume of ophthalmic solution (drops per bottle) could vary considerably with each medication and across medications. Each medication in this study was dispensed from a vertically-positioned bottle, but the angle of instillation has been found to differentially affect drop size and thus the number of days of therapy achieved.[17] Additionally, a small number of pharmacies were surveyed, although most were members of large chains that were felt to be representative retailers to consumers. We tried to be unbiased in our pharmacy selection; however, it is clear that retail costs to patients with no drug coverage may vary among these and other pharmacies. Furthermore, although patients with drug coverage may be less affected depending on their deductible level, these cost variances may still be consequential.

CONCLUSION

Brimonidine/Timolol had the lower monthly cost and annual cost and it is more cost effective than Travoprost 0.004%.

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