

Volumetric and cost evaluation study of glaucoma medical therapy

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ABSTRACT

Aim: The aim of the study was to evaluate the difference in mentioned volume and measured volume of the eye drops and to find out the yearly cost of various antiglaucoma drugs. **Methods:** It was an experimental and purely laboratory study. Total of 245 bottles of 49 different brands, five of each brand of antiglaucoma drug were analyzed. Number of drops were counted, and volume was measured from each bottle. On the basis of data collected yearly cost of each brand was calculated. **Results:** Of the 245 bottles, 152 bottles (62.04%) had underfilling. Yearly cost of most of the antiglaucoma drugs lies between Rs. 423.40 and Rs. 6263.40. **Conclusion:** Measured volume and drops are the major determinants of the cost of medical therapy of glaucoma. Most of the bottles showed underfilling and it was the significant finding. Less number of drops and lesser volume increases the cost of treatment indirectly.

Key words: Cost, drops, glaucoma, medical therapy, volume

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INTRODUCTION

The rising cost of healthcare is a major concern for health Authorities as well as for public. The same is applicable for the treatment of glaucoma. Glaucoma is the second leading cause of blindness worldwide, disproportionately affecting women and Asians. The prevalence of glaucoma in Asia is high. The total cases of glaucoma in 2020 in India will be 16.1 million.^[1] In country like India where financial sources are limited, it becomes necessary to provide treatment of glaucoma in cost effective manner.

Glaucoma requires long-term medical therapy. Up to 80% of patients may not take their medication as prescribed.^[2] Cost may be the deciding factor for adherence to medical therapy

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of glaucoma. There are not many studies in India on the cost of glaucoma therapy. Thus, there is an urgent need to assess the cost of glaucoma therapy. This study aimed to calculate the cost of various brands of different topically instilled antiglaucoma drugs. This study is intended to help ophthalmologists to choose the appropriate medication of a specific class according to the need of patients.

METHODS

It was a prospective, experimental and purely laboratory study. This study was conducted from December 1, 2012 to January 17, 2013. Five bottles of each 49 brands of various antiglaucoma drugs were analyzed by calculating the yearly cost of medication.

The volume and maximum retail price (MRP) of each drug were recorded. Graduated glass cylinder having total capacity of 10 ml, marked with 0.2 ml gradation was used for measuring the volume and number of drops in one vial. Before the measurement of eye drops, it was ensured that measuring cylinder was dry.

Each bottle was opened by breaking the seal and tightly screwing cap of the bottle to create an opening at the tip of the bottle. The bottles were held at approximately 135 angle and drops were collected in glass cylinder. After drops had

ceased to flow, bottles were inverted to 180° to try to obtain last drops in the bottle. Products that contain gel forming solutions were placed upside down for an additional 15-30 sec. To determine if any additional drop could be obtained. The total number of drops and total volume in the bottle were recorded. After each measurement, the cylinder was dried thoroughly after washing it using a scrub brush and rinsing with isopropyl alcohol.

The number of drops per ml was calculated by dividing number of drops with the actual volume that is, number of drops per ml = number of drops ÷ actual volume. Cost per drop was calculated by dividing MRP by total number of drops in each vial. For each drug cost/day was calculated by -cost/day = total number of drops instilled in both eye/day × cost per drop. After calculating cost/day, cost for 3 months, 6 months and 12 months were calculated. Overfilling and underfilling percentage was calculated for all the eye drops by - ([actual volume - labeled volume] ÷ actual volume) × 100. All measurements and calculations were presented in a tabulated form.

RESULTS

Of the 245 bottles, 86 bottles (35.1%) had correct volume of drug as mentioned on the bottle, 7 bottles (2.86%) had overfilling with volume and rest 152 bottles (62.04%) had underfilling of volume [Tables 1-4].

In Tables 1-4, the difference in volume is appreciable. This difference was calculated by taking average of measured volume of 5 bottles. From the tables, it can be seen that the percentage of volume difference is mostly in negative (-ve), which indicates the underfilling of bottles. Some brands

showed even higher level of difference in volume like in case of bimatoprost Brand D, latanoprost Brand B, timolol Brand B, brimonidine tartrate brand D.

Drop size varies from 29.4 µl to 67.47 µl. The number of drops per ml were highest for travoprost Brand A and latanoprost Brand B. Bottles of latanoprost + timolol Brand A, bimatoprost Brand B and C, travoprost Brand D, bimatoprost + timolol Brand A shows ≥30 average drops per ml. Number of drops varies from 14.85 ± 1.53 to 34.03 ± 0.69 drops per ml. The bottles of dorzolamide Brand A, brimonidine tartrate brand A and C, lies on the lower side that is, they contained <20 average number of drops per ml.

Dorzolamide Brand A was the most expensive antiglaucoma drug with an annual cost of treatment being Rs. 6263.4. The other expensive drug that cost >Rs. 5000/year is dorzolamide Brand B. Most of the other drugs lie in between Rs. 1000 and Rs. 5000/year. On the cheaper side that is, the drugs that cost ≤Rs. 1000/year are all brands of timolol maleate (i.e. Brand A, B, C, D, E, F), Travoprost brand A and betaxolol Brand A. Of various combinations, travoprost + timolol maleate Brand A was the most expensive one (Rs. 6098.4/year). On the other hand, Brand B and C of travoprost + timolol maleate were far cheaper than Brand A. Bimatoprost + timolol Brand B was the cheapest combination available in the market.

As a group, β-blockers were found to be the most economical, their cost ranged from Rs. 0.32 to 2.80/day, while carbonic anhydrase inhibitors were the most expensive, where the cost of TDS dorzolamide Brand A was Rs 17.16/day. There is a large variation in the range of cost per day in case of prostaglandin (PG) analogue and price varies from Rs. 2.22 to Rs. 15.34/day.

Table 1: Analysis of prostaglandin ophthalmic solutions

Coding of drugs	Mentioned volume in ml*	Measured mean volume in ml*	Percentage overfill (+) or underfill (-)	Mean drop/ml**	Cost per year in Rs.
Bimatoprost Brand-A	3	2.28±0.08	-5.33±2.61	24.28±0.39	3000.3
Bimatoprost Brand-B	3	2.36±0.10	-21.33±3.3	30.79±0.06	2744.5
Bimatoprost Brand-C	3	2.9±0.09	-3.33±2.92	32.98±0.55	2708.3
Bimatoprost Brand-D	3	3.02±0.10	+0.66±3.2	27.76±0.80	2577.6
Bimatoprost Brand-E	3	2.88±0.11	-4±3.81	30.28±0.87	799.2
Travoprost Brand-A	2.5	2.4±0.06	-4±2.48	34.03±0.69	5599.1
Travoprost Brand-B	3	2.94±0.08	-2±2.61	21.74±1.61	4730.4
Travoprost Brand-C	3	2.82±0.16	-6±5.22	27.81±1.34	4102.6
Travoprost brand-D	2.5	2.48±0.07	-0.80±2.93	32.01±1.22	4051.5
Travoprost Brand-E	3	2.7±0.17	-10±5.84	24.20±1.54	3723
Travoprost Brand-F	2.5	2.36±0.05	-5.6±1.92	26.17±1.73	1843.2
Travoprost Brand-G	3	2.88±0.10	-4±3.2	23.14±2.17	1606
Latanoprost Brand-A	2.5	2.16±0.15	-13.6±5.87	28.31±2.10	4694.4
Latanoprost Brand-B	2.5	2.5±0.06	+0±2.48	33.97±0.72	3808.8
Latanoprost Brand-C	3	2.8±0.11	-6.66±3.58	27.74±0.78	2350.6
Latanoprost Brand-D	2.5	2.48±0.07	-0.80±2.93	26.70±1.93	2270.3

*ml: Milliliter, **drops/ml: Drops per milliliter

Table 2: Analysis of beta blocker and alpha adrenergic agonist ophthalmic preparations

Coding of drugs	Mentioned volume in ml*	Measured mean volume in ml*	Percentage overfill (+) or underfill (-)	Mean drop/ml**	Cost per year in Rs.
Timolol Brand-A	5	4.88±0.10	-2.4±1.92	23.37±1.87	1022
Timolol Brand-B	5	3.84±0.45	-23.2±9.08	22.784±3.40	751.9
Timolol Brand-C	5	4.9±0.09	-2±1.75	21.46±2.00	720
Timolol Brand-D	5	4.72±0.20	-5.6±4.00	24.30±2.19	686.2
Timolol Brand-E	5	4.92±0.10	-1.6±1.92	28.23±1.41	467.2
Timolol Brand-F	5	4.76±0.23	-4.8±4.57	26.51±3.52	423.4
Betaxolol Brand-A	5	4.9±0.09	-2±1.75	23.79±3.10	569.4
Brimonidine Brand-A	5	4.86±0.12	-2.8±2.35	17.79±1.77	3431
Brimonidine Brand-B	5	4.52±0.20	-9.6±4.00	18.87±2.20	3124
Brimonidine Brand-C	5	4.16±0.34	-16.8±6.74	23.83±1.32	2146.2
Brimonidine Brand-D	5	5.02±0.10	+0.40±1.92	23.21±0.99	1562.2
Brimonidine Brand-E	5	4.86±0.15	-2.8±2.93	29.79±1.44	1416.2
Brimonidine Brand-F	5	4.68±0.20	-6.4±4.00	24.67±1.74	1328.6

*ml: Milliliter, **drops/ml: Drops per milliliter

Table 3: Analysis of carbonic anhydrase inhibitor and cholinergic agonist ophthalmic preparations

Coding of drugs	Mentioned volume in ml*	Measured mean volume in ml*	Percentage overfill (+) or underfill (-)	Mean drop/ml**	Cost per year in Rs.
Dorzolamide Brand-A	5	4.2±0.28	-16±5.54	14.85±1.53	6263.4
Dorzolamide Brand-B	5	4.74±0.21	-5.2±4.22	21.52±1.80	5321.7
Dorzolamide Brand-C	5	4.54±0.23	-9.2±4.57	22.59±1.33	4226.7
Dorzolamide Brand-D	5	4.84±0.14	-3.2±2.93	28.25±1.64	3723
Brinzolamide Brand-A	5	4.64±0.23	-7.2±4.57	23.77±1.41	4599
Pilocarpine Brand-A	5	4.9±0.09	-2±1.75	27.66±0.76	1123.2

*ml: Milliliter, **drops/ml: Drops per milliliter

Table 4: Analysis of combinations ophthalmic preparations

Coding of drugs	Mentioned volume in ml*	Measured mean volume in ml*	Percentage overfill (+) or underfill (-)	Mean drop/ml**	Cost per year in Rs.
Brimonidine+timolol Brand-A	5	4.94±0.08	-1.2±1.57	23.64±1.06	2759.4
Brimonidine+timolol Brand-B	5	4.7±0.09	-6±1.75	24.09±0.95	2511.2
Brimonidine+timolol Brand-C	5	4.96±0.07	-0.80±1.57	28.60±1.75	2482
Brimonidine+timolol Brand-D	5	4.76±0.18	-4.8±2.93	25.49±1.19	2131.6
Brimonidine+timolol Brand-E	5	4.92±0.12	-1.6±1.92	27.79±1.39	1454.4
Brimonidine+timolol Brand-F	5	4.84±0.14	-3.2±2.93	26.65±1.18	1211.8
Bimatoprost+timolol Brand-A	3	3±0.12	+0±4.13	31.35±0.96	4348.8
Bimatoprost+timolol Brand-B	3	2.74±0.07	-8.66±2.61	22.23±1.00	921.6
Travoprost+timolol Brand-A	2.5	2.42±0.09	-3.2±3.84	34.03±0.69	6098.4
Travoprost+timolol Brand-B	3	2.9±0.12	-3.33±4.13	25.20±0.22	3650
Travoprost+timolol Brand-C	2.5	2.8±0.13	+12±4.96	22.04±1.13	1934.5
Dorzolamide+timolol Brand-A	5	4.64±0.14	-7.2±2.93	23.19±1.18	4406.4
Dorzolamide+timolol Brand-B	5	4.78±0.09	-4.4±1.92	27.49±0.71	2707.2
Latanoprost+timolol Brand-A	2.5	2.46±0.07	-1.6±3.14	33.15±0.76	4464

*ml: Milliliter, **drops/ml: Drops per milliliter

This large variation is also seen for the various combinations available in the market. The cost per day for various combinations varies from Rs. 2.56 to Rs. 23.22/day [Figure 1].

DISCUSSION

Glaucoma is a chronic debilitating ophthalmic disease and is the leading cause of irreversible blindness throughout the world. Although β -blockers enjoyed great success as the first line anti-glaucoma therapy for many years, recently PG

analogues have gained favor as the initial treatment of choice for most patients.^[3] The prescription rates of pilocarpine and β -blockers have shown constant decline while latanoprost and brimonidine increased steadily.^[4]

In a study, Fiscella *et al.* observed that the cost of combination agents was less than the separate bottles of individual constituents, as observed by the present study as well. In all these studies, β -blockers were found to be the most economical group of topical anti-glaucoma medications.^[5]

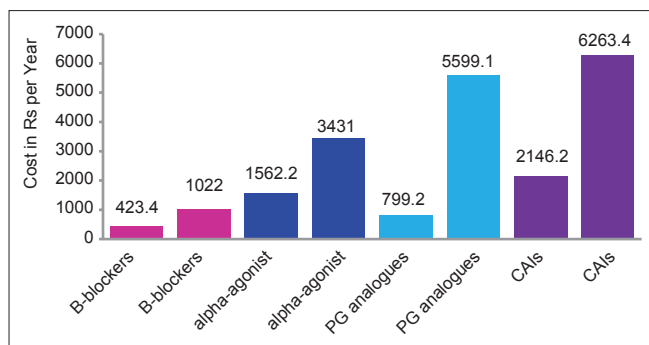


Figure 1: The price range of various drugs

Like present study, in another study,^[6] travoprost was found to have the maximum number of drops per ml at 34 and 40.86 drops/ml respectively. In our study, dorzolamide Brand A was found to have the least number of drops per ml (14.85 ± 1.53), while they found that timolol maleate had the least number of drops per ml (21.62 drops/ml).^[6]

Overfilling or underfilling needs to be considered while determining the baseline per day and per year costs. The higher the volume, the lower would be the cost incurred per day and per year. Overfill in the bottle helps to offset the high cost and in one way helps to counter the effects of inefficiencies resulting from the application error and provide a beneficial economic factor to the patient. As the number of drops per ml increased, the cost per day decreased and vice versa. In the present study, the average number of drops per ml varied widely from 14.85 ± 1.53 for dorzolamide Brand A to 34.03 ± 0.69 for travoprost Brand A. Cost per day and cost per year ranged widely depending on the class of medication and recommended daily dosing. Improved patient compliance with fewer daily drops is an important benefit of the newer anti-glaucoma medication.^[5] The convenient regimen and longer duration of action also improve compliance.

A single bottle of combination eye drops simplifies the therapy for patients by eliminating two separate bottles of

each constituent and reducing the number of drops that must be placed in the eye daily. This may also help to reduce the potential for loss of another drug's pharmacological effect which is believed to be related to a dilutional pharmacological effect that occurs when second medication is administered before complete absorption of the first medication. The combinations also decrease the side effects caused by preservatives in the medication and improve compliance.^[7] In the present study, the costs of combination agents were less than the combined costs of separate bottles of individual constituents. This study raises the serious issue of underfilling of ophthalmic solutions. Pharmacologists have an important role to play in giving appropriate drug in right dosage form to the patients. Nor the ophthalmologist neither the patient can check these issues. Health policies should be made stronger for giving right volume of drug with right cost to the patients.

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