ORIGINAL ARTICLE

Cost-effectiveness of glaucoma management with monotherapy medications in Egypt

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J. Adv. Pharm. Technol. Res.

ABSTRACT

Glaucoma is a serious chronic ophthalmic disease since it causes irreversible visual disability if untreated can lead to blindness. Treatment options include medications (classified into five major classes of drugs which are muscarinic cholinergic agonists, alpha-2 adrenergic agonists, beta-1 adrenergic antagonists, prostaglandins [PGs], and carbonic anhydrase inhibitors); use of laser therapy or conventional surgery. Pharmacoeconomic analysis helps in choosing among this variety of treatments. There is a great need for such analysis in Egypt since undergoing of it in different countries or societies may produce different results. This work aimed to compare cost-effectiveness of bimatoprost 0.03% once daily versus brimonidine 0.2% twice daily and timolol 0.5% twice daily as monotherapy treatment in Egyptian patients with open-angle glaucoma or ocular hypertension. Clinical data revealed that all treatments decreased intraocular pressure (IOP) significantly but bimatoprost 0.03% showed the highest efficacy (27.7% decrease in IOP from baseline), while timolol 0.5% reduced IOP by 22.5% then brimonidine 0.2% which decreased IOP by 20.8%. From the cost-effectiveness view, it would be preferable to initiate treatment with timolol in case of absence of any contraindications. PG analog can be used as add-on therapy in low responder patients or as alternative treatment in case of presence of contraindication to use of beta blockers.

Key words: Cost-effectiveness, glaucoma, pharmacoeconomic analysis

INTRODUCTION

Glaucoma is a condition of the eye in which there an increase in the intraocular pressure (IOP), causing progressive atrophy of the optic nerve with deterioration of vision and if untreated, blindness. The higher the IOP, the greater the risk of optic nerve damage, visual loss, and blindness.[1-3] Early, pressure-lowering treatment is a dominant cost-effective treatment strategy over a strategy to start the same treatment approach later, after glaucoma has occurred for patients with ocular hypertension.[4]

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Access this article online

Quick Response Code:

Website: www.japtr.org

DOI: 10.4103/2231-4040.197384

Treatment options of glaucoma include medical treatment, laser therapy, and incisional surgery. The major classes of drugs for glaucoma treatment are muscarinic cholinergic agonists, alpha-2 adrenergic agonists which acts to reduce aqueous humor production and increase the outflow of aqueous humor, carbonic anhydrase inhibitors that acts by inhibition of carbonic anhydrase in the eye so decreases aqueous humor secretion, resulting in a decrease of IOP, beta-1 adrenergic antagonists. The advantages of beta-blockers are good efficacy in primary and secondary types of glaucoma, easy use in combination with all other glaucoma drugs, and low costs. Timolol is the most frequently used drug in fixed glaucoma medications. In comparison with other glaucoma

How to cite this article: El-Khamery AA, Mohamed AI, Swify HE, Mohamed AI. Cost-effectiveness of glaucoma management with monotherapy medications in Egypt. J Adv Pharm Technol Res 2017;8:25-8.

drugs, beta-blockers have the most severe systemic side effects and may interact with other systemic medication,[5,6] and prostaglandin (PG) analogs that are highly efficient in lowering the IOP. In particular, they appear to have a good control of 24 h IOP fluctuations by primarily improving the outflow pathways. Furthermore, they have less systemic side effects than beta-blockers. However, their use is often associated with higher costs.[7]

Cost-effectiveness analysis (CEA) is used to compare medications that have different costs and quantitatively different outcomes with the latter expressed in the same natural units.[8]

Scope of work

The objective of this study was to perform a CEA between different drugs used as a single first-line treatment of glaucoma.

PATIENTS AND METHODS

Patients

Inclusion criteria were adult patients (>18 years), diagnosis of ocular hypertension or glaucoma (i.e., IOP ≥22 and ≤34). Exclusion criteria were pregnant or nursing females, any conditions or medication that would put the patient at risk or interfere with study results, any sensitivity or contraindication to medication used.

Drug products

- Lumigan™ (bimatoprost 0.03%): Manufactured by Allergan, USA. Marketed in Egypt by Sofico Company, Batch No. 1399
- Timolol (timolol maleat 0.5%): Manufactured by Nile Co., for Pharmaceuticals and Chemical Industries, Egypt. Batch No. 912418
- Brimonidine (brimonidine tartrate 0.2%): Manufactured by Jamjoom Pharmaceuticals, Saudi Arabia. Marketed in Egypt by Malty Pharma Company Batch No. PL 0118.

Equipment

- Haag-Streit 900 series slit lamp +78D lens (Japan)
- Applanation Tonometer 900AT® which is a powerful accessory to the Haag-Streit 900 series slit lamps for measurement of IOP (Japan)
- Humphrey visual field (VF) 740i analyzer (USA).

Methodology

Clinical examination of study patients

Physician saw the patient (long visit) at baseline and patient assigned to monotherapy treatment. All patients undergo an established follow-up visit (short visit) 1 month after baseline. The second short visit was 3 months after initiation of monotherapy treatment to determine tolerability and initial response. If patient achieved lower IOP, he/she would remain on the assigned monotherapy treatment, and the next visit would be at month 9. Patients showed intolerability or lack of response at month 3 excluded from the study and shifted to another treatment or adjunctive treatment was prescribed. Treatment algorithm was shown in Figure 1.

Treatment protocol

- Lumigan™ (bimatoprost 0.03%) one drop was administered once daily in the evening in the first group
- Timolol (timolol maleat 0.5%): One drop was administered twice daily in the second group
- Brimonidine (brimonidine tartrate 0.2%): One drop was administered twice daily in the third group.[8]

Statistical analysis of data

Statistical analysis was carried out using SPSS program software version 11 (Echo Soft Corp., USA).

Paired *t*-test for comparison between each two dependent groups (before and after administration of treatment) was conducted to test the significance for each measured parameter.

One-way ANOVA test was conducted to test the significance between parallel groups for measured parameter before administration data. The same was done for parallel group after administration data.

$P \leq 0.05$ was considered as a criterion of significance.

Table 1: Clinical effect of treatment administration

Item	Before	After	Significance
Bimatoprost (Lumigan)	25.20±0.39	18.22±0.28	Sig
Timolol (Timolol)	25.03±0.57	19.40±0.48	Sig
Brimondin (Brimondin)	25.09±0.58	19.87±1.02	Sig

This table shows that IOP level significantly decreased in all groups after administration of glaucoma medication

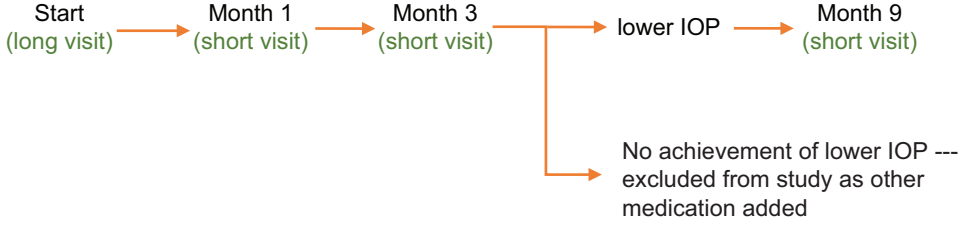

Figure 1: Treatment algorithm of patients undergoing the clinical study. IOP: Intraocular pressure

Table 2: One-way ANOVA before treatment

Source of variation	SS	df	MS	*F*	*P*	F crit	Significance
Between Groups	0.294333	2	0.147167	0.285663	0.752585	3.158843	Non-sig
Within Groups	29.365	57	0.515175				
Total	29.65933	59					

This table shows No significant difference could be determined when comparing parallel groups data before administration of treatment

Table 3: One-way ANOVA after treatment

Source of variation	SS	df	MS	*F*	*P*	F crit	Significance
Between Groups	29.09433	2	14.54717	24.59953	1.99E-08	3.158843	Sig
Within Groups	33.7075	57	0.59136				
Total	62.80183	59					

This table reveals significant difference could be determined upon comparing parallel group data after administration of treatment

Table 4: Significance of clinical effect difference between groups after treatment administration

Item	Variable I	Variable 2	Significance
Bimatoprost vs. Timolol	18.22±0.28	19.40±0.48	Sig
Bimatoprost vs. Brimondin	18.22±0.28	19.87±1.02	Sig
Timolol vs. Brimondin	19.40±0.48	19.87±1.02	Non-Sig

This table reveals that Bimatoprost significantly decrease IOP when compared with Timolol or Brimondin while no significant difference could be determined upon comparing Timolol and Brimondin

Table 5: Cost-effectiveness ratio of the interventions

Groups	Cost/ patient (L.E)	Total cost (cost of all patients) (L.E)	Effectiveness (% reduction in IOP)	ACER*
Bimatoprost	3480	69600	27.7	2512.64
Timolol	1716	34320	22.5	1525.33
Brimondin	4470	89400	20.8	4298.08

*ACER: Average cost effectiveness ratio. This table revealed that Timolol was the dominant treatment intervention

RESULTS

Clinical results are summarized in Tables 1-4. Clinical effect of treatment administration on mean IOP is shown in Table 1. For testing presence of a significant difference between parallel groups, one-way ANOVA is used; data of before administration of treatment is represented in Table 2 while data of after administration of treatment is represented in Tables 3 and 4.

PHARMACOECONOMIC COMPARISON BETWEEN TREATMENTS

A CEA was performed. Only direct medical costs were considered in the present pharmacoeconomic analysis between bimatoprost and timolol and brimondin.

Costs

The costs of medical resources were assigned in Egyptian pounds (year 2013–2014 values). Costs for patient care and physician services were based on Egyptian Medicare reimbursement rates. In this study, the cost assessment was done for each patient by calculating the total costs paid per patient.

Effectiveness

Efficacy of treatment was defined as "percentage reduction in IOP compared with baseline." Direct costs only were considered in the study (medical costs assuming that all patients received treatment for both eyes, physician services, VF testing, and IOP measure cost). Cost-effectiveness ratio of all interventions is declared in Table 5.

DISCUSSION

Results of this study demonstrate that bimatoprost significantly decrease IOP when compared with timolol or brimonidine while no clinically meaningful difference could be determined on comparing timolol and brimonidine.

This was in consistence with results of some other studies which stated that bimatoprost significantly decrease IOP[9-11] and those which stated that topically applied twice daily for 1 month, brimonidine tartrate 0.2% has clinical effectiveness equivalent to timolol 0.5% in Taiwanese patients with glaucoma.[12]

In contrast to results of this study was that done by Araie *et al*. which stated that topical brimonidine showed a significant IOP-lowering effect, although its IOP-lowering effect was inferior to topical timolol as monotherapy.[13]

Concerning cost-effectiveness this study revealed that timolol is more dominant than bimatoprost and brimonidine. This was in consistence with results of the study by Rylander and Vold.[14]

In contrast to that was results obtained by van Gestel *et al*. which stated that initiation of monotherapy with a PG analog may be acceptable depending on the cost-effectiveness outcomes and reduction in the frequency of VF testing.[15]

CONCLUSION

Treatment of open-angle glaucoma with any of used monotherapy is clinically effective. Although bimatoprost is most clinically effective treatment from the cost-effectiveness view, it would be preferable to initiate treatment with timolol in case of absence of any contraindications. PG analog can be used as add-on therapy in low responder patients or as alternative treatment in case of presence of contraindication to use of beta blockers.

Financial support and sponsorship
Nil.

Conflict of interest
There are no conflicts of interest.

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