

IMPACT OF ADVERSE DRUG REACTIONS OF TOPICAL ANTI-GLAUCOMA MEDICATIONS ON THE VISION-RELATED QUALITY OF LIFE IN PRIMARY OPEN ANGLE GLAUCOMA

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ABSTRACT

BACKGROUND

Adverse drug reactions (ADR) to topical medications form an important cause for noncompliance in the long term management of glaucoma. This study was aimed to determine the different types of adverse drug reactions associated with glaucoma medications and their impact on the vision-related Quality of Life (vQOL) in patients with Primary Open Angle Glaucoma.

MATERIALS AND METHODS

Patients with Primary Open Angle Glaucoma, fulfilling the inclusion criteria were interviewed and data collected. Adverse drug reactions to topical anti-glaucoma medications were evaluated using the 'Comparison of Ophthalmic Medications for Tolerability Questionnaire' and quality of life related to vision was evaluated using the 'National Eye Institute Visual Function-25 Questionnaire'. Statistical analysis was performed using the SPSS version 22. The effect of ADR on the vQOL was analysed both by a univariate and multivariate analysis using a linear regression model.

RESULTS

The study population included 115 patients (28% females) with mean age of 53.22 ± 11.46 years. At least one adverse drug reaction was reported in 71.2% of cases. Adverse drug reaction (ADR) was reported in nearly all patients on dorzolamide eye drops followed by timolol (74.1%), brimonidine (50%), bimatoprost (31.8%), latanoprost (39.3%) and travoprost (15%). The three most common adverse drug reactions reported were burning (60.75%), blurred vision (45.56%) and bitter taste (44.3%). The vision-related Quality scores in all subset domains were well above 50, the lowest being the general health and near activities domain. Significant association was noted between patients with ADR and low vQOL scores ($P = 0.03$) on multivariate analysis.

CONCLUSION

Adverse drug reactions to topical anti-glaucoma medications were found to have a negative impact on the vision-related quality of life in glaucoma patients, emphasising the integration of proper patient education and counselling in the long-term management.

KEYWORDS

Adverse Drug Reactions, Anti-glaucoma Medications, Quality of Life.

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BACKGROUND

The term 'Glaucoma' relates to a group of conditions characterised by distinctive optic neuropathy and visual field loss, raised intraocular pressure being the major risk factor. It is one of the leading causes of irreversible blindness worldwide.^{1,2} The estimated prevalence of glaucoma in India is about 11.9 million² and the country is expected to be the second largest home to glaucoma by 2020.^{1,3}

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Primary Open Angle Glaucoma (POAG) has been referred to as "the silent thief of sight," as most patients are unaware of the disease until permanent visual damage ensues. The cornerstone of treatment for POAG involves reduction of intraocular pressure by medical, laser or surgical means. In majority of patients, medical treatment with topical medications alone is said to achieve the target pressure that prevents further progression of the disease. However, ensuring lifelong adherence, tolerance and compliance to topical medications form a critical issue in the long-term management of the disease.

A subjective assessment of Adverse drug reactions (ADR) associated with topical glaucoma medications and vision-related quality of life (vQOL), using validated patient-reported outcome (PRO) questionnaires form an important tool in understanding the impact of glaucoma and its treatment on the daily life activities of an individual. However, vQOL has been perceived to differ between individuals, with variability based on cultural beliefs, social circumstances and personal expectations.⁴

This study was hence designed to determine the different types of ADR associated with topical glaucoma medications and its effect on the vision-related quality of life in patients with POAG attending the Glaucoma Clinic in a tertiary teaching eye hospital in Kerala, India.

MATERIALS & METHODS

This cross-sectional observational study was conducted at a tertiary eye hospital in Kerala, South India during July-December, 2016. The participants included POAG cases above 40 years of age who were on treatment with topical glaucoma medications. The diagnostic criteria included baseline intraocular pressure above 22 mmHg, open angles on gonioscopy, characteristic glaucomatous optic nerve disc changes and corresponding visual field defects. The exclusion criteria included patients on chronic ocular medication other than anti-glaucoma drugs, patients with prior ocular surface disorders, corneal disorders, ocular inflammations and patients with chronic systemic diseases that would affect the QOL such as diabetes, arthritis, neurological disorders, cardiac diseases and malignancies. The study was approved by the institutional ethics committee and was conducted in adherence to the tenets of the Declaration of Helsinki.

Information relevant to the study was collected by direct interview of the patients. The sociodemographic data and history related to glaucoma of each patient was recorded. The ADR of topical anti-glaucoma drugs was assessed using the 'Comparison of Ophthalmic Medications for Tolerability (COMTOL) questionnaire'.^{5, 6, 7} The COMTOL questionnaire is designed and validated for comparing the tolerability of topical glaucoma medications.⁸ The ocular symptoms listed are burning, stinging, conjunctival hyperaemia, itching, ocular secretion, ocular pain, tearing, brow ache, dryness, foreign body sensation, eyelid redness and eyelid oedema. The other domains included frequency and bothersomeness of blurred vision, accommodation difficulties and taste side effects as well as limitations on driving, reading and moderate activities.

The vision-related quality was assessed using the 'National Eye Institute- Visual function questionnaire 25' (NEI VFQ-25).⁹ A local language (Malayalam) validated questionnaire was used to record the data. The VFQ-25 consists of a base set of 25 vision targeted questions representing 11 vision-related domains, plus an additional single-item general health rating question. The vision-targeted domains are related to a specific functional ability, for which the patient grades a response reflecting the severity of the problem. Subset scores reflect the impairment related to each domain and the total score reflects the composite QOL. The different subsets and the number of inclusive questions (in brackets) include: global vision rating (1), difficulty with near vision activities (3), difficulty with distance vision activities (3), limitations in social functioning due to vision (2), role limitations due to vision (2), dependency on others due to vision (3), mental health symptoms due to vision (4), driving difficulties (3), limitations with peripheral (1) and colour vision (1), and ocular pain (2). Additionally, it also contains a single general health rating question which has been shown to be a robust predictor of future health and mortality in several population-based studies.⁹

Statistical analysis was performed using the SPSS version 22. Descriptive statistics of the sociodemographic data, data relating to glaucoma treatment and ADR of glaucoma medications were analysed. NEI-VFQ-25 QOL scores were calculated according to the instrument author's algorithm. The effect of ADR on the vQOL were analysed both by a univariate and multivariate analysis using a linear regression model. Comparison of variables in patients with and without ADR were done using Chi square and t test.

RESULTS

One hundred and fifteen (115) cases of POAG were enrolled for the study, out of which 4 were excluded later due to incomplete data. The mean age was found to be 53.22 ± 11.46 years. Males constituted 72.1% while females formed 27.9% of the study group. Nearly half the total number of patients resided in rural areas and 38.7% belonged to the low socioeconomic group. The duration of medical treatment for glaucoma was found to be more than 5 years in 4.5% of patients; 1-5 years in 65.8% of patients and less than 1 year in 29.7% of patients.

Timolol was the most prescribed drug in nearly 52.3% patients followed by latanoprost (25.2%), Travoprost (18%), Bimatoprost (19.8%), Brimonidine (19.8%) and Dorzolamide (4%). Fixed combination drug (Dorzolamide with timolol) was used only in 9% of patients. At least one ADR was reported in about 71.2%. ADR was reported in nearly all patients on dorzolamide and (dorzolamide + timolol) combination. This was followed by timolol (74.1%), brimonidine (50%), bimatoprost (31.8%), latanoprost (39.3%) and travoprost (15%). The most common ADR reported was burning (60.75%) followed by blurred vision (45.56%), bitter taste (44.3%), dry eye (34.17%), redness (26.58%), tearing (20.25%), itching (18.98%) and stinging (13.92%).

The vQOL scores in different domains among POAG patients are shown in Table 1. All subset domain scores were above 50. The lower scores were found within the general health and near activities domain. The scores related to domains of social functioning, mental health and dependency showed high scores above 70. A univariate analysis of ADR and vQOL scores in different domains are shown in Table 2. All domains except driving showed statistically significant lower values in patients with ADR. Comparison of the sociodemographic and glaucoma treatment parameters among patients with and without ADR are shown in Table 3 and 4. There was no statistically significant difference in terms of age, gender and duration of treatment. However, ADR was more common among patients in the low socioeconomic group ($p=0.001$), rural residence ($p=0.006$) and multiple drug use ($p < 0.001$).

Multivariate analysis of the different variables and vQOL scores are shown in Table 5. Significant relationship was noted between patients with ADR and poor vQOL scores ($P = 0.03$). The rural area of residence, prolonged duration of treatment for glaucoma (more than 5 years), and multiple drug use also showed significant associations with low vQOL scores.

Domains	N	Mean	SD	Minimum	Q1	Median	Q3	Maximum
General Health	111	55.6	18.1	25.0	50.0	50.0	75.0	100.0
General vision	111	64.9	15.8	40.0	60.0	60.0	80.0	80.0
Ocular pain	111	68.7	19.6	37.5	50.0	62.5	87.5	100.0
Near activities	111	57.5	26.7	12.5	41.7	50.0	83.3	100.0
Distant Vision	111	62.8	28.0	12.5	37.5	75.0	87.5	100.0
Social Function	111	70.9	30.4	25.0	37.5	87.5	100.0	100.0
Mental Health	111	74.9	18.6	31.3	62.5	81.3	93.8	100.0
Role Limitation	111	67.5	26.8	25.0	50.0	75.0	100.0	100.0
Dependency	111	77.1	23.2	16.7	66.7	75.0	100.0	100.0
Colour vision	111	78.4	30.1	25.0	50.0	100.0	100.0	100.0
Peripheral Vision	111	66.2	28.9	25.0	50.0	75.0	100.0	100.0
Driving	23	73.6	20.7	25.0	58.3	75.0	91.7	100.0

Table 1. vQOL Scores in Glaucoma Patients

	ADR				T	P
	Absent (N =31)		Present (N =79)			
	Mean	Std	Mean	Std		
General Health	61.3	12.6	53.5	19.5	2.063	.042
General vision	72.3	11.2	62.0	16.5	3.172	.002
Ocular pain	75.0	16.5	66.1	20.3	2.163	.033
Near activities	68.0	21.6	52.8	27.1	2.794	.006
Distant Vision	80.1	17.0	55.8	28.8	4.405	.000
Social Function	92.7	15.4	62.3	30.8	5.237	.000
Mental Health	84.7	12.8	70.9	19.1	3.695	.000
Role Limitation	75.0	22.1	64.1	27.9	1.949	.054
Dependency	87.1	16.6	72.9	24.2	3.000	.003
Colour vision	96.8	10.7	70.9	32.1	4.381	.000
Peripheral Vision	79.0	19.5	60.8	30.4	3.101	.002
Driving	79.2	19.4	70.6	21.3	.950	.353

Table 2. Comparison of vQOL Scores among Patients with and without ADR

ADR	N	Age (Years)		T	p
		Mean	Std		
Absent	31	54.6	11.0	.771	.443
Present	79	52.7	11.8		

Table 3. Comparison of Age between Patients with and without ADR

		ADR				Total		χ ²	df	p
		Absent		Present		N	%			
		N	%	N	%					
Sex	Male	21	67.7	58	73.4	79	71.8	0.354	1	0.552
	Female	10	32.3	21	26.6	31	28.2			
Socio economic status	*APL	27	87.1	41	51.9	68	61.8	11.686	1	0.001
	**BPL	4	12.9	38	48.1	42	38.2			
Place of residence	Urban	22	71	33	41.8	55	50	7.591	1	0.006
	Rural	9	29	46	58.2	55	50			
Treatment Duration	< 1 year	2	6.5	2	2.5	4	3.6	1.206	2	0.547
	1-5 years	8	25.8	25	31.6	33	30			
	>5 year	21	67.7	52	65.8	73	66.4			
No of drugs	Single drug	25	80.6	33	41.8	58	52.7	13.497	1	<0.001
	>1 drug	6	19.4	46	58.2	52	47.3			

Table 4. Comparison between Patients with and without ADR

Above (*) and below (**) Poverty line.

	Univariate Analysis			Multivariate Analysis		
	Beta	T	P	Beta	t	p
(Constant)					12.413	.000
Age in years	-.098	-1.032	.304	-.095	1.260	.211
Sex	-.006	-.062	.950	-.080	1.071	.287
Socioeconomic status	-.536	-6.631	.000	-.042	.491	.625
Place of residence	-.204	-2.179	.031	-.297	3.418	.001
Duration of Treatment	-.405	-4.621	.000	-.260	3.175	.002
No. of drugs	-.538	-6.665	.000	-.231	2.485	.015
ADR	-.363	-4.044	.000	-.175	2.207	.030

Table 5. Linear Regression Model of vQOL Score

DISCUSSION

ADR related to topical anti-glaucoma medications and its implications on the vQOL has not been studied before in South Indian patients. In our study, the incidence of ADR was fairly common with 71% reporting at least one ADR. The three most common ADR reported was burning, blurred vision and bitter taste. However, no lethal or severe adverse effects were reported. In spite of ethnic and geographic differences, our results are comparable to similar studies from different parts of the world, such as Nordmann et al,⁸ Pisella et al¹⁰ and M Alaei¹¹ et al (ADR in 62.4%, 57% and 50% respectively).

Timolol was found to be the most prescribed drug in about half the number of cases followed by Prostaglandin analogues, Brimonidine and Dorzolamide. ADR was reported in nearly all the patients treated with Dorzolamide and Dorzolamide + Timolol combination. This was followed by Timolol, Brimonidine and Prostaglandin analogues. This observation was different from other studies in which ADR related to Dorzolamide was less frequent while Brimonidine (Bhatt et al)¹² and Latanoprost (M Alaei et al)¹¹ were found to be the most frequent offending medications. Since the ADR could also be related to preservatives (Used in the topical drug preparations), it is difficult to make a definite conclusion regarding this observation.

Incidence of ADR was found to be significantly higher in patients of low socioeconomic status, rural residence and on polypharmacy (p value 0.001, 0.006 and <0.001 respectively). This might be related to improper drug storage, handling or compliance, which is difficult to ascertain however.

Within the study population, lower mean scores were noted for the general health and near activities domains of the vQOL, irrespective of ADR. Several previous studies^{4,13,14} have reported visual acuity loss and advanced field loss as the main causes associated with lower vQOL in POAG. However, according to Odberg et al,^{15,16} QOL impairment occurs much earlier; at the time of diagnosis. We could not do a subgroup analysis based on the staging of the disease as our survey based data did not include the clinical staging of glaucoma.

The most remarkable finding in our study was the statistically significant lower composite QOL scores for patients with ADR upon regression analysis (p value 0.03). The rural area of residence, prolonged duration of treatment for glaucoma (More than 5 years) and polypharmacy also showed significant associations with poor vQOL, independent of ADR (p value 0.001, 0.002 and 0.015 respectively).

CONCLUSION

The incidence of ADR is fairly common, affecting nearly three fourth of the patients on topical anti-glaucoma medications. Our study clearly demonstrates an unequivocal negative impact of ADR on the vision-related quality of life, emphasising the integration of proper patient education and counselling in the longterm management of glaucoma.

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