

FREQUENCY OF OCULAR OPACITIES IN CARDIAC PATIENTS TAKING AMIODARONE FOR CARDIAC ARRHYTHMIAS

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ABSTRACT:

BACKGROUND:

Amiodarone acts by modifying the depolarization and repolarization of myocardium. It is therefore very effective in treating the arrhythmias. But it has many side effects which may involve eyes, skin, thyroid or nerves etc. The occurrence of side effects may be related to use of high doses.

AIMS & OBJECTIVE:

To determine the frequency of ocular opacities in cardiac patients taking Amiodarone for cardiac arrhythmias.

MATERIAL & METHODS:

This was a cross sectional observational study performed at Department of Cardiology, Punjab Institute of Cardiology, Lahore in collaboration with Department of Ophthalmology, Services hospital, Lahore from January 2018 to December 2018 after approval from hospital ethical committee. Total 100 patients of age 40-80 years of either gender taking Amiodarone for arrhythmias were selected through consecutive non-probability sampling technique. While patients already diagnosed as diabetic retinopathy or raised intracranial pressure were excluded from study. Patients were referred to Department of Ophthalmology, Services hospital for slit lamp examination and Goldmann Perimetry to confirm the presence of ocular opacities. The data was analysed using SPSS version 21.

RESULTS:

The mean age of patients was 60.55±12.07years. There were 62 (62%) males and 38 (38%) females. The patients had a mean BMI of 24.14±3.23kg/m². The mean duration of taking amiodarone was 14.05±6.64months. Ocular opacities were present in 62 (62%) patients while 38 (38%) did not develop ocular opacities. Among patients who had ocular opacities, 12 (19.4%) had vortex keratopathy, 12 (19.4%) had ocular deposition, 12 (19.4%) had cataract, 10 (16.1%) had glaucoma, 7 (11.3%) macular degeneration while 9 (14.5%) had other ocular opacities.

CONCLUSION:

The frequency of ocular opacities is high in patients taking Amiodarone. So there is a need to screen patients on regular intervals to assess changes in eyes of cardiac patients.

KEY WORDS:

Cardiac Patients, Arrhythmias, Amiodarone, Ocular Opacities

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INTRODUCTION:

In the last two decades, supraventricular arrhythmias like atrial fibrillation (AF) are quite prevalent and is of great public concern. The reported prevalence of cardiac arrhythmias is around 2% in cardiac emergencies.¹

There are four classes of anti-arrhythmic drugs. Class three drugs including Amiodarone acts by modifying cardiac depolarization and repolarization. Thereby, it is very effective in treating arrhythmias. Primarily, it is a potassium channel blocker, but it can also block sodium and calcium channels. It may also has effect on alpha and beta adrenergic receptors.² It has adverse effects on various organs including skin, eyes, lungs, thyroid gland, liver and nerves. These adverse effects has direct relationship with the amount of dose being used.³ The whorl-like pattern described by Fleischer in 1910 in cornea is characterized as powdery, white, yellow, or brown corneal opacities. It is proposed that the drug reaches the cornea via the tear film, aqueous humor, and limbal vasculature. This pharmacological agent and its metabolites enter the lysosomes and bind with cellular lipids, producing drug-induced lipidosis.

It has been reported that about 50% of the patients taking amiodarone can develop ocular opacities.⁴ Other showed that the most common ocular finding is corneal epithelial opacities resembling a cat's whiskers in 70–100% of patients; however, lens opacities have been reported in 50–60% of patients taking Amiodarone.⁵ One more study reported that the deposition could be detected as early as 2 months after the onset of treatment in 83.7% eyes, by slit-lamp and confocal microscopy.⁶

Rationale of this study was to determine the frequency of ocular opacities in cardiac patients taking Amiodarone for arrhythmias. Literature has showed controversial evidence regarding ocular changes with use of amiodarone. But local data is not available in literature which could help us in determining the extent of problem in local population. So we want to conduct to get local evidence and be able to implement the results of this study in future. This will help use to implement the early screening of cardiac patients taking amiodarone for arrhythmias and for early management to prevent the hazardous consequences and can save the patients from developing other complications.

MATERIAL AND METHODS:

This cross sectional study was carried out in Department of Cardiology, Punjab Institute of Cardiology, Lahore in collaboration with

Department of Ophthalmology, Services hospital, Lahore from January 2018 to December 2018. Sample size of 100 cases was calculated with 95% confidence level, 10% margin of error and taking expected percentage of corneal opacities i.e. 50% in patients taking Amiodarone for arrhythmias. Non-probability consecutive sampling technique was used. Patients of age 40-80 years of either gender taking Amiodarone for arrhythmias were included. Arrhythmia was defined as heart rate >100bpm or <60bpm and patient taking amiodarone for more than 2months. Ocular opacity was labeled if there were ocular changes anyone or more (vortex keratopathy (anterior segment shows a whorl-like pattern of corneal epithelial deposits on Slit-lamp examination), ocular deposition (deposition of drug contents in on cornea on optical coherence tomography), cataract (clouding of the lens on ophthalmoscope), glaucoma (IOP>21mmHg on tonometry) and macular degeneration (damage to the macula of retina detected on optical coherence tomography) present in eye after at least 2 months use of amiodarone (on medical record). Patients already diagnosed as diabetic (BSR>186mg/dl) or diabetic retinopathy. Patients having increased intracranial pressure.

STATISTICAL ANALYSIS:

100 patients who fulfilled the selection criteria were enrolled in the study from outpatient Department of Cardiology, Punjab Institute of Cardiology, Lahore. Written informed consent was obtained. Demographic data (age, gender, BMI, duration of taking Amiodarone) was noted. Then patients were referred to Department of Ophthalmology, Services hospital for assessment of ocular investigations. Slit lamp examination and Goldmann Perimetry were done to confirm the presence of ocular opacities. All examinations were done by a single senior ophthalmologist having at least 4 years' experience to control bias. All this information was recorded on proforma. The collected data was analysed statistically by using SPSS version 21. Quantitative variables like age, BMI and duration of taking Amiodarone was presented in form of mean \pm S.D. Qualitative variables like gender and presence of ocular opacities and types were presented in form of frequency and percentage. Data was stratified for age, gender, BMI, duration of taking Amiodarone. Post-stratification, chi-square test was applied to check significance in stratified groups. P-value \leq 0.05 was considered as significant.

RESULTS

The mean age of patients was 60.55 ± 12.07 years. Minimum and maximum age of patients

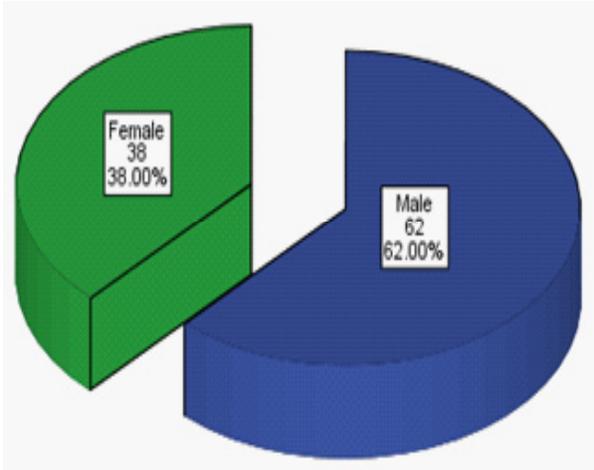


Figure 1: Distribution of gender of patients

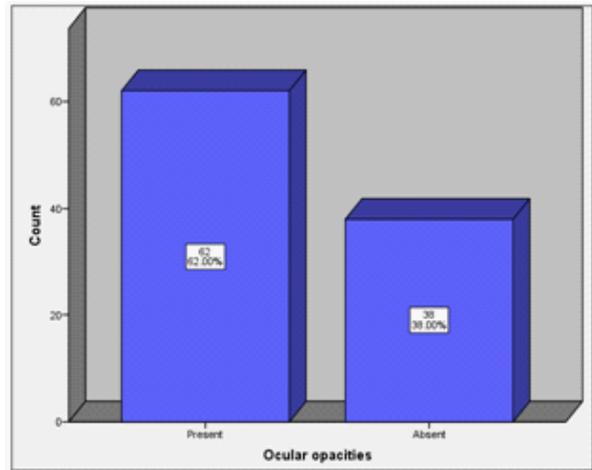


Figure 2: Distribution of presence of ocular opacities

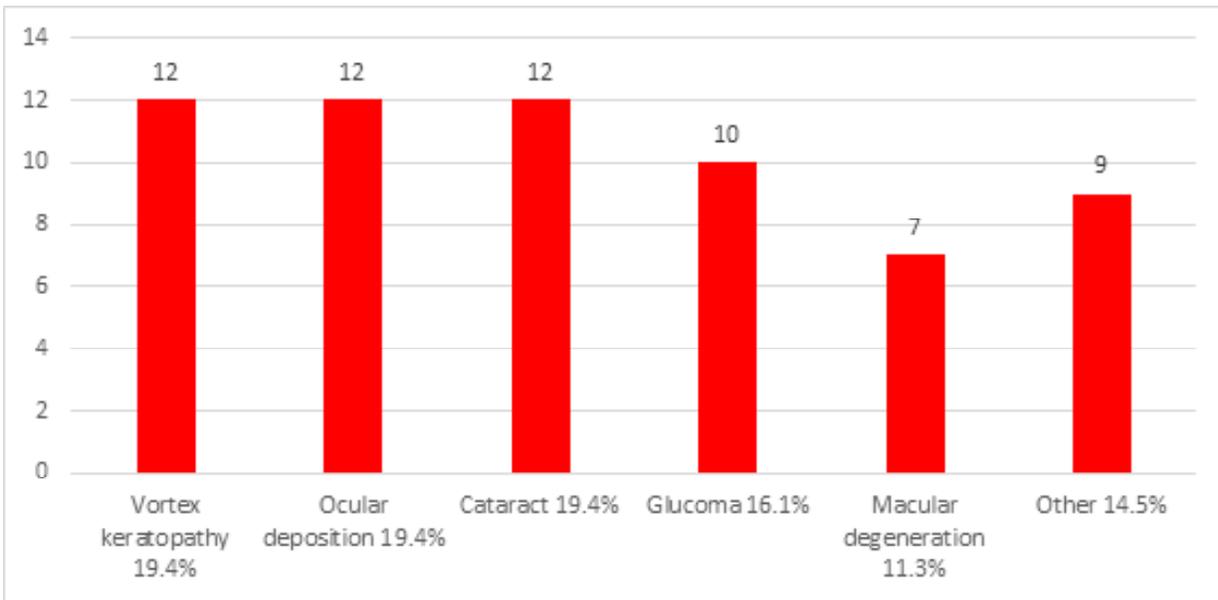


Figure 3: Distribution of type of ocular opacities present

observed were 40 and 80 years, respectively. There were 62 (62%) (figure-1) males and 38 (38%) females. The male-to-female ratio was 1.6:1. The mean BMI of patients was $24.14 \pm 3.23 \text{ kg/m}^2$. Minimum and maximum BMI of patients observed were 19.20 kg/m^2 and 29.68 kg/m^2 , respectively. The mean duration of taking amiodarone was 14.05 ± 6.64 months. Minimum and maximum duration of taking amiodarone were 3 months and 24 months, respectively. Ocular opacities (figure-2) were present in 62 (62%) patients while 38 (38%) did not develop ocular opacities. Among patients who had ocular opacities, 12 (19.4%) had vortex keratopathy, 12 (19.4%) had ocular deposition, 12 (19.4%) had cataract, 10 (16.1%)

had glaucoma, 7 (11.3%) (figure-3) macular degeneration while 9 (14.5%) had other ocular opacities. Data was stratified for age of patients. In age group 40-60 years, 38 (65.5%) (table-1) patients had ocular opacities. In age group 61-80 years, 24 (57.1%) had ocular opacities. The difference was insignificant ($p > 0.05$). In patients who had 40-60 years, 7 (18.4%) had vortex keratopathy, 15 (20.8%) had ocular deposition, 9 (23.7%) had cataract, 6 (15.8%) had glaucoma, 5 (13.2%) macular degeneration while 6 (15.8%) had other ocular opacities. In patients who had 61-80 years, 5 (20.8%) had vortex keratopathy, 7 (18.4%) had ocular deposition, 3 (12.5%) had cataract, 4 (16.7%) had glaucoma, 2 (8.3%)

Table 1: Comparison of type of ocular opacities in age strata

		Age (years)		Total
		40-60	61-80	
Type	Vortex keratopathy	7 (18.4%)	5 (20.8%)	12 (19.4%)
	Ocular deposition	5 (20.8%)	7 (18.4%)	12 (19.4%)
	Cataract	9 (23.7%)	3 (12.5%)	12 (19.4%)
	Glaucoma	6 (15.8%)	4 (16.7%)	10 (16.1%)
	Macular degeneration	5 (13.2%)	2 (8.3%)	7 (11.3%)
	Other	6 (15.8%)	3 (12.5%)	9 (14.5%)
Total		38 (100%)	24 (100%)	62 (100%)

Chi-square test = 3.363 p-value = 0.644 (Insignificant)

Table 2: Comparison of type of ocular opacities in gender strata

		Gender		Total
		Male	Female	
Type	Vortex keratopathy	6 (15.8%)	6 (25.0%)	12 (19.4%)
	Ocular deposition	8 (21.1%)	4 (16.7%)	12 (19.4%)
	Cataract	7 (18.4%)	5 (20.8%)	12 (19.4%)
	Glaucoma	6 (15.8%)	4 (16.7%)	10 (16.1%)
	Macular degeneration	5 (13.2%)	2 (8.3%)	7 (11.3%)
	Other	6 (15.8%)	3 (12.5%)	9 (14.5%)
Total		38 (100%)	24 (100%)	62 (100%)

Chi-square test = 1.255 p-value = 0.939 (Insignificant)

Table 3: Comparison of type of ocular opacities in BMI strata

		BMI		Total
		Normal	Overweight & obese	
Type	Vortex keratopathy	8 (23.5%)	4 (14.3%)	12 (19.4%)
	Ocular deposition	6 (17.6%)	6 (21.4%)	12 (19.4%)
	Cataract	6 (17.6%)	6 (21.4%)	12 (19.4%)
	Glaucoma	4 (11.8%)	6 (21.4%)	10 (16.1%)
	Macular degeneration	5 (14.7%)	2 (7.1%)	7 (11.3%)
	Other	5 (14.7%)	4 (14.3%)	9 (14.5%)
Total		38 (100%)	24 (100%)	62 (100%)

Chi-square test = 2.574 p-value = 0.765 (Insignificant)

macular degeneration while 3 (12.5%) had other ocular opacities. The difference was insignificant ($p > 0.05$). Data was stratified for gender of patients (table-2). In males, 38 (61.3%) patients had ocular opacities. In females, 24 (63.2%) had ocular opacities. The difference was insignificant ($p > 0.05$). In males, 6 (15.8%) had vortex

keratopathy, 8 (21.1%) had ocular deposition, 7 (18.4%) had cataract, 6 (15.8%) had glaucoma, 5 (13.2%) macular degeneration while 6 (15.8%) had other ocular opacities. In females, 6 (25.0%) had vortex keratopathy, 4 (16.7%) had ocular deposition, 5 (20.8%) had cataract, 4 (16.7%) had glaucoma, 2 (8.3%) macular degeneration while 3

Table 4: Comparison of type of ocular opacities in duration strata

		Duration (months)		Total
		3-12	13-24	
Type	Vortex keratopathy	1 (6.3%)	11 (23.9%)	12 (19.4%)
	Ocular deposition	4 (25.0%)	8 (17.4%)	12 (19.4%)
	Cataract	2 (12.5%)	10 (21.7%)	12 (19.4%)
	Glaucoma	3 (18.8%)	7 (15.2%)	10 (16.1%)
	Macular degeneration	2 (12.5%)	5 (10.9%)	7 (11.3%)
	Other	4 (25.0%)	5 (10.9%)	9 (14.5%)
Total		38 (100%)	24 (100%)	62 (100%)
Chi-square test = 4.545 p-value = 0.474 (Insignificant)				

(12.5%) had other ocular opacities. The difference was insignificant ($p > 0.05$). Data was stratified for BMI of patients (table-3). In normal weight patients, 34 (58.6%) patients had ocular opacities. In overweight & obese patients, 28 (66.7%) had ocular opacities. The difference was insignificant ($p > 0.05$). In normal weight patients, 8 (23.5%) had vortex keratopathy, 6 (17.6%) had ocular deposition, 6 (17.6%) had cataract, 4 (11.8%) had glaucoma, 5 (14.7%) macular degeneration while 5 (14.7%) had other ocular opacities. In overweight & obese patients, 4 (14.3%) had vortex keratopathy, 6 (21.4%) had ocular deposition, 6 (21.4%) had cataract, 6 (21.4%) had glaucoma, 2 (7.1%) macular degeneration while 4 (14.3%) had other ocular opacities. The difference was insignificant ($p > 0.05$). Data was stratified for duration of taking amiodarone (table-4). In patients with duration 3-12months, 16 (39.0%) patients had ocular opacities. In patients with duration 13-24months, 46 (78.0%) had ocular opacities. The difference was significant ($p < 0.05$). In patients with duration 3-12 months, 1 (6.3%) had vortex keratopathy, 4 (25.0%) had ocular deposition, 2 (12.5%) had cataract, 3 (18.8%) had glaucoma, 2 (12.5%) macular degeneration while 4 (25.0%) had other ocular opacities. In patients with duration 13-24months, 11 (23.9%) had vortex keratopathy, 8 (17.4%) had ocular deposition, 10 (21.7%) had cataract, 7 (15.2%) had glaucoma, 5 (10.9%) macular degeneration while 5 (10.9%) had other ocular opacities. The difference was insignificant ($p > 0.05$).

DISCUSSION:

Amiodarone is an iodinated benzofuran derivative. It has been associated with toxicity affecting the eyes, thyroid, skin ,lungs, liver and nerves. The daily (400 mg/day) and cumulative dose (100 g

combined with the length of therapy is associated with the toxicity. However, toxic effects may also be observed at lower maintenance doses.³

In our study, we included 100 cardiac patients who were taking amiodarone for cardiac arrhythmias. The mean of age was 60.55 ± 12.07 years. The males were 62 (62%) while females were 38 (38%). The ratio of male to female was 1.6:1. The mean duration of taking amiodarone was 14.05 ± 6.64 months. In our study, ocular opacities were present in 62 (62%) patients while 38 (38%) did not develop ocular opacities. Among patients who had ocular opacities, 12 (19.4%) had vortex keratopathy, 12 (19.4%) had ocular deposition, 12 (19.4%) had cataract, 10 (16.1%) had glaucoma, 7 (11.3%) macular degeneration while 9 (14.5%) had other ocular opacities.

The ocular complications of long-term amiodarone therapy have been recognized for many years. Ingram DV carried out a study of 175 patients on long-term treatment with amiodarone and reported that 98% developed corneal micro deposits with progression over the period of time and changed with the modification of dose of the drug. He also showed that with the withdrawal of the drug, 16 patients showed some recovery and had no permanent damage. In 6% patients visual symptoms developed due to these corneal deposits, 3% complained about photophobia. Halos were present in 2%.⁴

One study showed that 50% patients developed ocular opacities who were taking amiodarone for cardiac arrhythmias.⁵ Ugur Tukr reported that multi organ involvement and toxicity may be present in low doses of amiodarone as well. The toxicity may be noticed in low dose and shorter duration therapy.⁶ Manjot K in his case report found case of amiodarone induced retinal phototoxicity.⁷

Yoon Kin reported that there was higher frequency of adverse effects in patients on amiodarone for a long time which was amenable to reversal by dose lowering or drug discontinuation. Incidence of ocular adverse effects was 15% during first year of amiodarone use increased up to 50% during long-term use. The most common ocular change after long-term use of amiodarone is corneal epithelial opacities in 70% to 100% patients followed by lens opacities in 50% to 60% of patients.⁸

Other studies has showed that cat's whiskers like corneal opacities are present in 70–100% of patients; while lens opacities may be present in 50–60%.⁹ One more study reported that the deposition may be detected even after 2 months after the onset of treatment in 83.7% eyes, by slit-lamp and confocal microscopy.¹⁰ The ocular effect of amiodarone is vortex keratopathy creating a whorl-like pattern by producing lysosomal deposits in the basal epithelial layer.^{11, 12} Ikaheimo et al.,

reported that abnormal blue colour vision test in 2 patients with normal other visual parameters. Corneal deposits were present in 100% and subcapsular lens opacities were present in 22.2% of the patients while 9.1% complained about dryness of eyes. Examination of fundus of eye did not reveal any significant abnormality. It was concluded that colour vision disturbance may be due to mild optic nerve involvement.¹³

Treatment with amiodarone on long term bases and in high doses may cause adverse effects, thereby, needing regular follow-up.

CONCLUSION:

Thus the frequency of ocular opacities is high in patients using amiodarone. So there is a need to screen patients on regular intervals to assess changes in eyes of cardiac patients. It may be recommended that implementing the regular screening of cardiac patients who are taking amiodarone for arrhythmias.

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