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Research Article

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Prevalence of Amiodarone-Induced Vortex Keratopathy at Benghazi National Cardiac Centre

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Abstract

The current study was carried out to determine the prevalence of amiodarone-induced vortex keratopathy and to grade this finding according to dose and duration of use. The study was conducted from the 1st of January to the end of February 2024 at the National Cardiac Center and Benghazi Teaching Eye Hospital. All patients admitted to the cardiac center for a month and received amiodarone were included in this study. Data was collected retrospectively by reviewing medical records. All patients had gone through a complete ophthalmic evaluation. A total of 1056 cases were admitted to cardiac, and 45 (4.3%) cases received amiodarone. Among the cases, 24 were male and 21 were female. Their ages ranged from 20 to 80. Of the 45 cases, 24 (53%) were able to come for ophthalmic assessment. Out of 24 cases, 18 (75%) had vortex keratopathy, most with grade II (33%). Among those with vortex keratopathy, nine had visual complaints such as reduced vision and halos around light. Three of those nine patients had visual complaints but no other findings except for vortex keratopathy. Nine patients showed vortex keratopathy with no other pathology. No other ocular complications of amiodarone use were found among the study group.

Keywords: Vortex Keratopathy, Whorl Keratopathy, Corneal Verticillate Amiodarone, Cordarone, Paceron.

INTRODUCTION

Amiodarone, also known as Cordarone or Pacerone, is a class III antiarrhythmic drug used for treating cardiac conditions such as atrial fibrillation and other life-threatening ventricular arrhythmia such as ventricular fibrillation and ventricular tachycardia. It can be used orally and/or intravenously to return the heart rhythm to normal by blocking signals in the heart. Dosing of the drug is according to the route of use and regimen (initial- loading-maintenance doses) (Mahajan et al., 2020).

Amiodarone has many side effects systemically. Some are common, such as cough, lightheadedness, tingling of toes and fingers, and light sensitivity. Photosensitivity, or photodermatitis, occurs after sun exposure with sunburn, hepatotoxicity, and heart block (Hamilton et al., 2020). Amiodarone rarely can cause thyroid dysfunction, both hyper and hypothyroidism (Cappellani et al., 2023; Gašparini et al., 2023). Ocular side effects include vortex keratopathy and anterior subcapsular cataracts. These effects rarely cause visual impairment, but patients commonly complain of halos around light. Amiodarone rarely causes permanent vision loss due to optic neuropathy (Hamilton et al., 2020; Mäntyjärvi et al., 1998).

Vortex keratopathy, also known as cornea verticillate, whorl keratopathy, or Fleischer vortex, is the most common ocular finding among those using amiodarone, characterized by a basal epithelial lysosomal deposition of golden brownish material, usually at the inferior part of the cornea and usually, bilateral. This effect occurs in most cases using amiodarone at a daily dose of 200 mg or more. Those depositions usually spontaneously resolve after drug cessation (Sahyoun et al., 2022).

There are some other causes of this finding, some of which include drugs such as (NSAID, chloroquine, gentamicin, tamoxifen, meperidine, chlorpromazine, atovaquone, suramin, tilorone, perhexiline maleate, and tyrosine kinase inhibitors vandetanib and Osimertinib) (Astin & Eye, 2001; Maruf et al., 2018; Shah et al., 1995). Fabry disease, which is a life-threatening inherited metabolic disorder (Koh et al., 2019; Lamont et al., 2010), neurotrophic keratopathy, multiple myeloma, and epidemic keratoconjunctivitis, The grading system of amiodarone-induced corneal deposits has been described by Orlando et al (Sahyoun et al., 2022).

Grade I: Appear as microdeposits of golden-brown material just anterior to the bowman layer and look like dust inferior to the pupil and at the mid periphery. They do not take fluorescein stain and are asymptomatic.

Grade II: Appear more linearly aligned with the clear zone between the margin of the deposits and limbus.

Grade III: An increase in the number of filament-like deposits seen in grade II and extending into the visual axis with a whorled pattern seen in the pupillary axis.

Grade IV: Clumping of gold-brown deposits.

This study aims to find out the prevalence of amiodarone-induced vortex keratopathy among patients admitted to Benghazi Cardiac Center, which is the main cardiac center in the eastern part of Libya, and to grade this finding according to dose and duration of use.

MATERIALS AND METHODS

Study design: This descriptive cross-sectional study was conducted from the 1st of January to the end of February 2024 at the National Cardiac Center and Benghazi Teaching Eye Hospital.

Source of data: All patients admitted to the cardiac center during six months (from June to November 2023) and received amiodarone as part of their treatment (45 cases) were included in this study.

Data was collected retrospectively by reviewing medical records of patients filled by resident doctors, using designed Performa, and then refined during patients' visits for ophthalmic evaluation.

Data collected included demographic data such as age, gender, residency, provisional diagnosis, date of admission, causes of admission, other comorbidities, treatment received and doses, and any interventions (catheterizations, stent, coronary artery bypass graft).

All subjects enrolled in this study have given informed consent and gone through a complete ophthalmic evaluation, including a detailed history of any ophthalmic problems such as decreased vision, halos around light, and a history of previous interventions such as investigations or surgeries.

A complete ophthalmic examination was done by the author, including vision and refraction, slit lamp examination of both anterior and posterior segments, intraocular pressure measurement, and sent for investigation (Optical coherence tomography) if needed.

Exclusion criteria: Patients admitted in the same period, but did not receive amiodarone.

RESULTS

A total of 1056 cases were admitted to the cardiac center for different cardiac problems, and 45 (4.3%) cases received amiodarone as part of their treatment and were found eligible for the study. Among the 45 cases, 24 were male, and 21 were female, giving a male-to-female ratio of (1.14:1). Their age ranged from 20 to 80, with a mean age of 58.9. 41 and were Libyan, where 4 were non-Libyan. 39 were from Benghazi. All patients suffered from cardiac arrhythmias due to variable etiologies. (42 cases) had other comorbidities such as diabetes mellitus and hypertension (23 cases) and (29 cases), respectively, with 19 of them with both diabetes and hypertension.

Among them, 3 cases received amiodarone for atrial fibrillation or ventricular arrhythmia alone, with no other health problems. The rest were receiving many drugs for other health problems (anti-hypertensive, antidiabetic, diuretics, anti-hyperlipidemic, etc). of the 45 cases, 24 (53%) were able to come for ophthalmic assessment. 83% received 200mg once daily. None received more than 200 mg, table (1). Treatment duration ranged from one month to nearly three years, with a mean of (3.5 months), the majority of cases took the drug for three months or more (83%), table (2).

Out of 24 cases, 18 (75%) had vortex keratopathy, most with grade II (33%) as shown in the table. Among those with vortex keratopathy, 9 had visual complaints such as reduced vision and halos around light. Six of the nine who had visual complaints had other findings that contributed to reduced vision other than keratopathy (cataracts, posterior capsular opacification, high myopia, and diabetic retinopathy and its complications).Three of those nine patients had visual complaints but no other findings except for vortex keratopathy. Nine patients showed vortex keratopathy with no other pathology and didn't have any complaints, and their visual acuity was 6\6. No other ocular complications of amiodarone use were found among the study group.

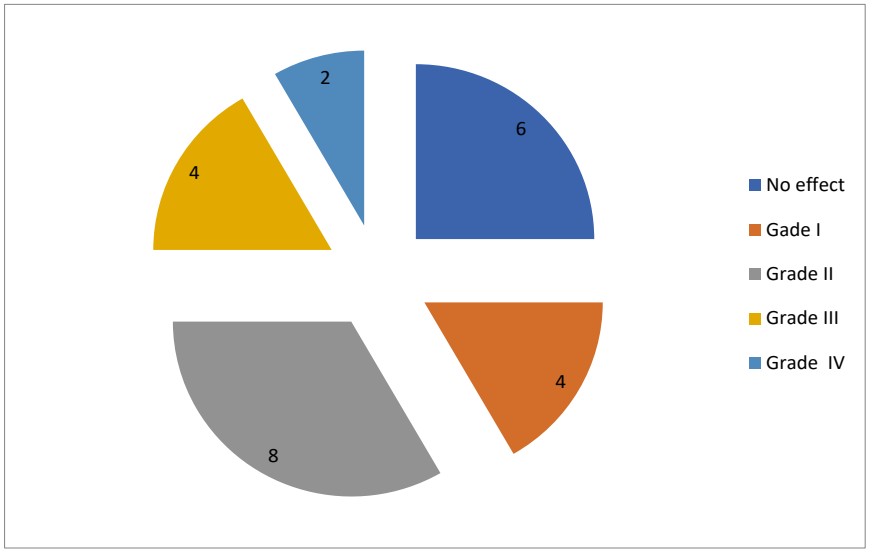

Figure: (1). Patient distribution according to grades.

Table:(1). Correlation between drug dose and grade of vortex keratopathy

Dose (mg)	Grade				
	No finding	I	II	III	IV
100 mg	2	0	2	0	0
200mg	4	4	6	4	2
>200 mg	0	0	0	0	0
Total	6	4	8	4	2

Table (2). Correlation between duration of drug use and grade of vortex keratopathy

Duration	Grades				
	No finding	I	II	III	IV
<3 months	4	0	0	0	0
3-6 months	2	4	6	4	0
6 >months	0	0	2	0	2
Total	6	4	8	4	2

Among the cases that did not show corneal changes, one case gave a history of receiving the drug for one month, six months prior to the examination, another one for two weeks and three months prior to the exam, and the third received amiodarone for 21 days on August 2023. All three received 200 mg once daily, while the other three cases were free of keratopathy, two received a dose of 100 mg for less than two months, and one was still taking the drug with the dose of 100 mg once daily.

DISCUSSION

Amiodarone is an arrhythmic agent used for many types of arrhythmias, both atrial & ventricular, and can be effectively used orally & intravenously (Hamilton et al., 2020). It acts by blocking potassium channels during repolarization, increasing the duration of the refractory period of myocytes and decreasing their excitability.

While in the current study, we found that 18 cases out of 24 (75%) taking amiodarone had vortex keratopathy. The Centre for Adverse Reactions Monitoring claims that 19 cases had corneal deposits in a report of 51 cases having amiodarone-induced corneal complications. Meanwhile, in a study done by Maija Mäntyjärvi, Kaija Tuppurainen, and Kirsi Ikäheimo, cat whiskers like corneal epithelial opacities were seen in 70-100% of patients (Mäntyjärvi et al., 1998).

Vortex keratopathy was seen in 17 out of 18 (94%) cases in at least one eye in the first three months of amiodarone therapy in another study done by Richard G. Orlando, Matthew E. Dangel, and Stephen F. Schaal (Orlando et al., 1984). While Jeffrey B. Florek, Alex Lucas, and Daniel Girzadas considered that the most common ocular side effect, seen in 90% of cases taking amiodarone, is corneal microdeposits of the drug (Florek et al., 2023).

Nine of our cases with vortex keratopathy had visual complaints. Vision is usually not affected by amiodarone, although some might complain of halos around light (Erdurmus et al., 2008). We found that one of the patients reported halos around light, but most of those who complained of reduced vision had other findings more likely to be the cause, such as high myopia, cataracts, and diabetic retinopathies. While the study by The Centre of Adverse Reactions Monitoring had 12 cases with abnormal vision, Jeffrey B. Florek, Alex Lucas, and Daniel Girzadas had 10% of their cases with keratopathy having visual complaints (Florek et al., 2023).

In the current study, the majority of patients (83%) were taking 200 mg once daily. Among the four

cases taking 100 mg, two were evaluated after less than three months of initiation of therapy and showed no deposits, while the other two were taking the drug for a longer time, both showed grade II keratopathy.

Ingram DV, Jaggarao NS, and Chamberlain DA claim that vortex keratopathy can be seen in up to 98% of cases using amiodarone 200-300 mg per day (Ingram et al., 1982). Daily use of amiodarone at 100 mg oral doses can be effective with no side effects (Chokesuwattanaskul et al., 2020). In our study, all patients using amiodarone for longer than three months showed corneal changes. Two patients with grade IV deposits have been using the drug for years, one of them with blurred vision showed dense posterior subcapsular cataracts in both eyes.

We evaluated patients admitted to the cardiac center from June to November 2023. Some were already on amiodarone prior to admission, while others started recently. Our ophthalmic evaluation was in January-February 2024, so the duration of therapy ranged from one month up to three years at evaluation time. Patients who were on amiodarone 200 mg once daily for one month, had not showed corneal changes. While D'Amico DJ, Kenyon KR, and Ruskin JN claim that corneal changes can be seen even after two weeks(D'Amico et al., 1981). 25 vortex keratopathy case reports were systemically reviewed by coauthors Mona Alsheri, MD, and Abdulaziz

In the study of Joury and MD, the time from starting the drug to having those side effects ranged from 2-72 months, with a median of 11.5 months. Amiodarone deposits are usually epithelial in the basal layer (D'Amico et al., 1981; Hollander & Aldave, 2004). However, Mesut Erdurmus, Yusuf Selcoki, Ramazan Yagci, and Ibrahim F Hepsen reported a 65-year-old man with a history of blurred vision and seeing halos around lights had been treated with amiodarone for 6 years. A slit lamp examination of both eyes showed a bilateral, symmetric, whorl-like pattern of brown deposits in the inferocentral corneal epithelium. Severe endothelial deposition was documented with the confocal laser scanning microscope of the HRT II. They concluded that Amiodarone-induced keratopathy with confluent and diffuse endothelial deposition is rare, and it may be indicative of a more severe toxicity associated with amiodarone (Erdurmus et al., 2008).

CONCLUSION

Vortex keratopathy by amiodarone is a common side effect. It's both dose and duration-dependent as its grade increases with larger doses and longer duration of use. It usually doesn't cause visual complaints, but further follow-up for a longer duration and for all patients receiving the drug is recommended, to look for other amiodarone side effects.

Duality of interest: No duality of interest associated with this manuscript.

Author contributions: Sluiman Al Nashad : Drafting the manuscript/revising for important intellectual context, Approval of the final version of the manuscript. Hana Shaheen: Conceived & design of the study, collected the data, contributed data or analysis tools, performed the analysis/ interpretation of data.

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