New Approach in Ocular Involvement of Chronic Treatment with Amiodarone

Teodoru Cosmin Adrian* and Teodoru Minodora
Faculty of Medicine, University Lucian Blaga, Sibiu, România

*Corresponding author: Teodoru Cosmin Adrian, Faculty of Medicine, University Lucian Blaga, Str. Gheorghe Dima, Nr. 3, Sibiu, România, E-Mail: atedoru77@yahoo.com

Received: February 03, 2018; Accepted: April 12, 2018; Published: April 28, 2018

Abstract

Significance: The results of the study will reveal the main risks of ocular alterations in patients treated with Amiodarone, regarding visual acuity, contrast sensitivity, keratometry, visual field, ocular pressure, Schirmer Test, tear break up time (TBUT), OSDI test (Dry Eye Ocular Surface Disease Index).

Purpose: The paper intends to reveal the influence of chronic treatment with Amiodarone especially on the anterior segment of the eye, revealing functional and structural alterations.

Method: The study was a prospective one based on 110 patients with chronic Amiodarone treatment. Studied parameters were: visual acuity, contrast sensitivity, keratometry, visual field, ocular pressure, Schirmer Test, tear break up time (TBUT), OSDI test (Dry Eye Ocular Surface Disease Index). Three groups were considered: 1 (26 patients with initial treatment with Amiodarone), 2 (84 patients on Amiodarone therapy for more than 1 year), 3 (control group – 40 healthy individuals).

Results: 100% of the patients presented cornea verticillata after one year of treatment. There was a statistically significant correlation between the Amiodarone treatment and dry eye disease in the studied patients. Corneal modifications occur during the first year and remain constant the following years.

Conclusions: There was a statistically significant relation between the treatment with Amiodarone and the onset of corneal deposits. There were no alterations of the visual acuity after one year of treatment. There were no significant influences on the visual field, contrast sensitivity, corneal keratometry. There was a statistically significant correlation between the Amiodarone treatment and the TBUT. The OSDI scores showed statistically significant correlations between Amiodarone and dry eye disease.

Keywords: Amiodarone; Cornea verticillata; Dry eye syndrome
Introduction
Amiodarone is used as an antiarrhythmic medication for both ventricular and supraventricular arrhythmias [1]. It has numerous effects on myocardial depolarization and repolarization. It blocks the potassium, the calcium and the sodium channels and the beta and alpha adrenergic receptors [2]. Long-term oral therapies with Amiodarone have been associated with tissue accumulation of the drug. Pigmented whorl-shaped lines can be identified in the corneal epithelium [3]. There have been described especially pulmonary, neurologic, thyroid, skin, ocular and heart side effects of the drug. The most common ocular adverse effect is corneal epithelial opacities (vortex keratopathy). The epithelial deposits originate from a point below the pupil and swirl outwards, sparing the limbus [4]. The pigment lines occurred in a whorl like fashion over the surface of the cornea and are located in the area of the Bowman layer and adjacent stroma. Drug-induced vortex keratopathy is not an indication to stop the drug. The condition is often reversible if the medication is stops [5,6]. In some patients lens opacities have been reported (50%-60%) [7,8]. Retinopathy and optic neuropathy have been rarely observed in patients with Amiodarone treatment without a direct causal relationship [9,10].

Rarely these patients accuse subjective symptoms. Some patients notice colored rings around lights, blurred vision, poor contrast [11]. In medical practice it might happen to find ocular conditions without an apparent cause. A systemic medication should be considered in these cases [12]. The objectives of the study are to reveal the influence of chronic treatment with Amiodarone on the anterior segment of the eye. The study will approach aspects concerning corneal alterations, visual functional modifications and dry eye ocular surface disease related to the use of the drug.

Purpose
The paper intends to reveal the influence of chronic treatment with Amiodarone especially on the anterior segment of the eye, revealing functional and structural alterations.

Materials and Methods
The study is a prospective one based on 110 patients with chronic Amiodarone treatment. Inclusion criteria: Patients on Amiodarone therapy; Cooperative patients; Patients treated for ventricular or supraventricular arrhythmias with 200 mg Amiodarone/day. Exclusion criteria: Pre-existing ocular conditions (cataract, glaucoma, optic neuropathy); Psychical disorders. There were 3 patients groups considered. Group I – 26 patients with initial treatment with Amiodarone; Group II – 84 patients on Amiodarone therapy for more than 1 year; Control group – 40 healthy individuals with similar ages (no local or general treatments, healthy eyes). The study had 1 year duration, with a 3 month follow up examinations. The following parameters were studied: visual acuity, contrast sensitivity, corneal keratometry, visual field, ocular pressure, Schirmer Test, tear break up time (TBUT), OSDI test (Dry Eye Ocular Surface Disease Index). The statistical analysis was performed using SPSS software (Statistical Package for the Social Sciences) (p \leq 0.01% – 99% accuracy for a statistically significant association of the variables; p \leq 0.05% – 95% accuracy for a statistically significant association of the variables; p>0.05 no statistically significant association of the variables). The grading system proposed by Orlando was used: grade 1 – small punctate opacities forming a horizontal line, grade 2 – several, small, curvilinear branches from the initial line, grade 3 –
more increase in the number and extent of the branches with the typical vortex pattern, grade 4 – irregular brown clumps of pigment accompanying the branching pattern [13,14].

**Results**

Group I included 26 patients who started the treatment with Amiodarone after the first ophthalmological evaluation. Group II included 84 patients who were already on chronic treatment with Amiodarone for more than 1 year. The mean age of the patients was 73. 61.81% of them were females. The patients of group I were first evaluated before starting the Amiodarone treatment. They were then examined every 3 month during one year. All patients of this group presented no corneal alteration before the treatment. Most of them (18 patients) presented first corneal signs of vortex keratopathy at 3 month after the beginning of the treatment. At 6 month 24 patients had corneal deposits and all of them had deposits at 12 month.

Grading the deposits into 4 degrees, there were different aspects of the corneal signs during the first year (FIG. 1). Using Likelihood ratio test, Crosstabs showed \( P = .007 \), revealing a statistically significant relation between the general treatment with Amiodarone and the onset of corneal deposits in the first group, compared to the control group. Visual acuity was measured every 3 month. It presented no modifications during the first year of treatment. Contrast sensitivity suffered some modifications during the first year. The patients were tested using Pelli-Robson tests at the presentation, at 3 month, at 6 month, at 9 month and at 12 month after the beginning of the treatment. There were no statistically significant relation between contrast sensibility and the treatment in patients during the first year with Amiodarone treatment. There were performed keratometry measurements at the presentation and at 12 month after the beginning of the treatment. There were found slight differences between these two measurements, but there were no statistically significant results regarding any relation to the Amiodarone treatment.

![FIG. 1. Corneal alteration during the first year – Group 1.](image)

Visual field was performed in the first and last month of the treatment. No significant differences were observed regarding the two examinations. In order to examine the presence of dry eye syndrome there was used the Schirmer Test, (The Tear
Break up Time Test) TBUT and the OSDI test (Dry Eye Ocular Surface Disease Index). There were no significant modifications on Schirmer test in the first year. Using the tear break up time (TBUT) at the presentation of the patients and at 12 month of therapy there was found significant differences. Four patients presented a tear break up time (TBUT) of less than 10 seconds before starting the treatment. After 12 month of treatment 12 of 26 patients (46.15%) presented a TBUT of less than 10 seconds. In the control group there were no modifications on TBUT. There was a statistically significant correlation between the Amiodarone treatment and the TBUT of the studied group (.05) (FIG. 2).

The patients of the first group were asked to answer to the OSDI questionnaire (Ocular Surface Disease Index) in the first month and after 12 month. The OSDI scores in the control group were similar in both examinations (first and last month). There were alterations of the OSDI scores in the Amiodarone group of patients after one year of treatment. The correlation between the chronic treatment and the OSDI alteration was statistically significant ($P=0.005$), meaning that Amiodarone can induce mild to moderate dry eye disease (FIG. 3). The 84 patients of the second group were on Amiodarone therapy for more than 1 year. They were examined two times with a one year interval between these evaluations. All patients of this group presented corneal deposits at the first examination. The patients presented grade 3 and 4 of vortex keratopathy. The aspect of the corneal signs of verticillata keratopathy was similar on the second evaluation (after 12 month). I found no modifications regarding the visual acuity, visual field and contrast sensitivity between the two examinations (after one year). TBUT was altered (less than 10 seconds) in 46.42% of the cases at the first examination and in 48.80% of the cases after one year. The results were similar after one year, similar to the group 1 at the 12 month examination, but different than the control group (17.50% presented less than 10 seconds). The OSDI questionnaire showed no differences between the two examinations and was similar to the OSDI test of the group 1 at one year of treatment. Considering the results on TBUT test and the OSDI questionnaire both on the first group and on the second group, there can be a correlation established between the chronic treatment and the onset of a dry eye disease.

FIG. 2. TBUT – Group 1.
FIG. 3. Ocular surface disease index scores (OSDI) – Group 1.

Discussion
At three month after the beginning of the treatment 18 patients of 26 (69.23%) presented signs of vortex keratopathy. Most authors report the onset of the corneal deposits in the first 2-4 month. In the present study all patients presented corneal signs at 12 month [15,16]. The relation between the general treatment with Amiodarone and the onset of corneal deposits in the first group, compared to the control group was statistically significant. In the first group at 12 month most of the patients presented grade 2 and 3 of keratopathy, while the patients in the 2nd group presented grade 3 and 4. This showed the relationship between the duration of the treatment and the amount of the material in the cornea. Visual acuity presented no modifications in the two groups during one year of follow up. There is no evidence that these deposits can perturb the visual acuity [17-19]. there have been reported halos and photophobia in Amiodarone patients. The current study revealed changes in contrast sensitivity after one year of treatment, but no statistically significant relationship to the drug [11,15,20]. There were no significant changes on the keratometry of the cornea, showing that these deposits do not induce biomechanical changes of the cornea. The visual field measurements were similar in both groups at the beginning of the study and after one year. This can suggest that there were no significant changes of the optic nerve function in the considered patients [20].

TBUT and OSDI tests in both groups showed a significant relation between the drug and the dry eye disease. The study confirms the rapid onset of the corneal deposits after the beginning of the Amiodarone treatment. The novelty of the study consists in revealing the possible risk of inducing symptoms of dry eye disease at these patients. This fact should lead to periodical ophthalmological examination of these patients (including dry eye tests).
Conclusions

- There was a statistically significant relation between the general treatment with Amiodarone and the onset of corneal deposits in the group 1, which started the treatment with Amiodarone.
- There were no alterations of the visual acuity after one year of treatment.
- Amiodarone treatment showed no significant influences on the visual field, contrast sensitivity, corneal keratometry of the studied patients.
- Although there were modifications of the contrast sensitivity in the first year of treatment, there was no statistically significant relation with Amiodarone treatment.
- There was a statistically significant correlation between the Amiodarone treatment and the TBUT (tear break up time) of the studied group.
- The OSDI scores showed statistically significant correlations between Amiodarone and dry eye disease in the studied patients.
- There were no significant modifications of the studied parameters in patients of second group, with chronic treatment for more than one year.
- Studying the two groups showed that the revealed modifications occur during the first year and remain constant the following years.
- Periodical ophthalmological examination (including dry eye tests) should be performed on Amiodarone patients.

Acknowledgement

Project financed from Lucian Blaga University of Sibiu research grants LBUS-IRG-2015-01.

REFERENCES