# Effect of Digoxin on the Color Vision Disorder, A Case-Control Study

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**Abstract:** *Background and Aim*: Digoxin is a drug commonly used in order to treat cardiac failure but its use has got different complications including color vision disorder .Regarding the high prevalence of cardiac failure and the role of taking this drug by patients, it was decided to study color vision disorder in patients who take digoxin.

*Materials and Methods*: The present case-control study was conducted during 2008-2009 in Valli-e-asr hospital in Birjand.The case group consisted of 59 patients having cardiac failure who, at least, had taken oral digoxin for one year. The controls were non-cardiac patients referring to the hospital or were patients' attendants who did not take digoxin. The controls were matched with the cases with respect to age and sex. Both groups were examined regarding whether they had color vision disorder or not by means of Ishihara test. Venous blood was derived from all the cases to assess serum digoxin level.

Then, the obtained data was an encoded and statistically analysed by means of SPSS software at the significant level $\alpha$=0.05.

*Findings*: In this survey, 59 patients with Heart failure who took digoxin and 59 controls were studied. Relative frequency of color vision disorder in the cases was estimated at 6.8%, but in the controls it was estimated at 1.7%; hence the difference was not statistically significant (P=0.36).Frequency of color vision disorder did not reveal a significant difference regarding age and sex. Serum digoxin level was abnormal in 5.1% of the patients. A significant difference was not found between mean serum digoxin and color vision disorder.

*Results*: Using color vision disorder, as a diagnostic measure of Digoxin toxicity, is of no use.

**Keywords:** Digoxin toxicity, color vision disorder, case-control study.

## INTRODUCTION

Cardiovascular diseases are commonly increasing and are still the most prevalent cause of mortality [1]. Digoxin remains a frequently prescribed cardiac glycoside used in the treatment of supraventricular dysrhythmias and congestive cardiac failure [2]. Digoxin is the cardiac glycoside mostly used to treat heart failure and supraventricular arrhythmia. Cardiac glycosides have a narrow therapeutic dose and a significant overlap with the concentration of serum drugs in toxicated and non-toxicated patients (due to taking digoxin). Despite the fact that since about 30 years ago, monitoring digoxin serum level was recommended to prevent toxicosis with it and many of physicians and pharmacists know this point, the most prevalent but preventable cause of patients' hospitalization is digoxin complications [3]. Following taking digoxin, 5%-20% of patients may become intoxicated. Usually, digoxin toxicity has digestive symptoms (e.g. anorexia, nausea, and vomiting). Other symptoms include neurologic, ophthalmic and cardiac complications. However, the most outstanding symptom of intoxication with digoxin is cardiac which will lead to death if not diagnosed and treated timely [4].

Although the clinical diagnosis of digoxin toxicity has fallen substantially over the past 20–30 years [3, 4], it remains a common medical problem, particularly in the elderly, where it is often difficult to diagnose [5].

Various ophthalmic complications of digoxin in the form of color-vision complication have been reported [6-9]. The most prevalent visionary complication is color vision disorder, especially Chromatopsia, in which the perception of colors-particularly yellow or green-is complicated.Perhaps digoxin has other ophthalmic complications such as blurred vision, or photopsia [10].

Regarding chromatopsia relationship with serum level of digoxin, too, some studies have been conducted [10-15]. Since contradictory results have been mentioned in these studies, the present project was conducted.

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**Table 1: Demographic Data of Case and Control**

| P Value | Control<br>Mean (SD) | Case<br>Mean (SD) | |
|---|---|---|---|
| 0.41 | 9.3 ± 64.7 | 10 ± 66.1 | Age(years ) |
| 0.46 | 32(54.2%)<br>28(47.5%) | 27(45.8%)<br>31(52.5%) | Sex male<br>Female |

## METHODS

The present case-control study was conducted in Valli-e-asr hospital of Birjand in 2008-2009.

There were 59 subjects in each of the groups (i.e. cases and controls). The cases were patients who had referred to the cardiology clinic of Valli-e-asr hospital. The age range of them was 50-80 years; they had daily been administered 250 microgram digoxin for 5 days a week at least one year. The controls were selected from patients referring to the clinics of the hospital, but did not take digoxin; besides, both groups were matched with respect to age and sex. Both of them were given Ishihara test by a trained medical student [15]. The test was administered on the day and under fitting light. Since there are different congenital and acquired reasons for color vision disorder for example: diabetics, congenitally color deficient patients, users of drugs like chloroquine, employers in paint industry, those in rubber industry, and individuals working in glue production were excluded from the study [16-20]. Both group members entered the study after the aim of the study was justified to them and their conscious written consent was received.

After getting the consent of the cases, 2cc of blood was extracted from each to test serum digoxin in the lab. Sampling was done at least 6 hours after taking the last dose of the drug. Serum level of digoxin was measured using Eliza method. In the present study, normal digoxin level was taken 2ng/dl. It is noteworthy that the above project had already been approved by the Research Committee of the School of Medicine.

The obtained encoded data was fed into SPSS software and statistical analysis was done using T-test and Fisher exact test. Finally, α=0.05 was taken as the significant level.

## RESULTS

In this survey, color vision disorder in 118 individuals (59 patients who took digoxin and 59 individuals who didn't) was compared. In Table **1**, characteristics of the cases are given. As it is seen, the two groups were matched with respect to age and sex.

As it is evident from Figure **1**, there was not a significant statistical relationship in color vision disorder between the two groups .Relative frequency in the case-group was estimated at 6.8%, but it was 1.7% in the controls. However, the difference between the two groups was not statistically significant; P=0.36.

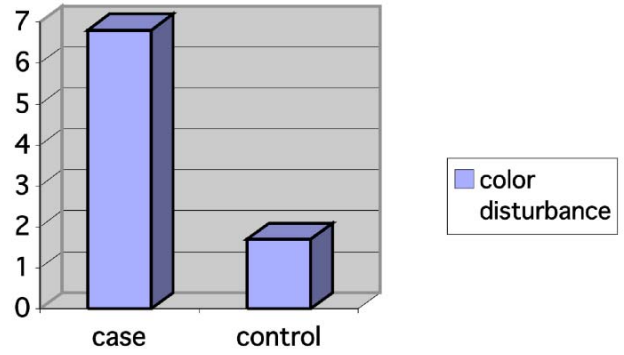


**Figure 1:** Percentage of color vision disorder between two groups.

Based on Table **2**, there was no difference between color vision disorder between sex and age in the case and control.

Digoxin level was high in 5.1% of the patients. We compared dig level in case group with color vision disorder,as was shown in Table **3**, no statistically significant difference was observed between mean serum digoxin level and color vision disorder.

## DISCUSSION

Digoxin is a cardiac drug which is commonly used in treating heart failure and tachyarrhythmia. Digoxin toxicity, if not diagnosed and properly treated on time, can be fatal. Thus, understanding the complications of the drug is very critical.

One of the complications of digoxin is visual problems. The most prevalent visual complication is color vision disorder, which causes abnormalities in distinguishing colors; particularly “yellow” or “green”.

**Table 2: Comparison of Color Vision Disturbance with Age and Sex in Case and Control Groups**

| Color vision Disturbance | | Case | | | Control | | |
|---|---|---|---|---|---|---|---|
| | | Yes N (%) | No N (%) | Fisher Exact Test | Yes N (%) | No N (%) | Fisher Exact Test |
| Sex | Male | 3 (1.1) | 24 (88.9) | 0.3 | 1 (3.2) | 30 (96.8) | 1 |
| | Female | 1 (3.1) | 31 (96.9) | | 0 (0) | 28 (100) | |
| Age | < 60 yr | 0 (0) | 17 (100) | 0.31 | 1 (4) | 24 (96) | 0.42 |
| | ≥ 60 yr | 4 (9.5) | 38 (90.5) | | 0 (0) | 34 (100) | |

**Table 3: Mean Dig Level in Case Group and Color Vision Disturbance**

| Color Vision | N | Dig Level(ng/dl) Mean ±SD | p-Value |
|---|---|---|---|
| Normal | 55 | 1.17 ± 0.75 | 0.53 |
| Abnormal | 4 | 1.24 ± 0.54 | |

Of course, it is probable that digoxin has other ophthalmic complications such as blurred vision, or photopsia. The origin of ophthalmic disorders following digoxin use is not entirely known. Maybe, these disorders are because of hyperactivity of the photoreceptors of the retina. The cells of the retina possess various Sodium and Potassium energy-bound channels. These channels actively pump Sodium out of the cell and Potassium into the cell. This function of these channels prevents from accumulation of additional Potassium outside the cell. These channels are inhibited by digoxin and as a result the electrical activity of retina changes [9].

The relationship between digoxin serum level and chromatopsia has been assessed in various studies. In the present study, such a relationship was not observed.

In a study conducted by Butler, too, no relationship was found. He ophthalmologically examined 6 patients (aged 66-85 yrs) who took digoxin. The results revealed that 5 of them had photopsy and 1 one suffered decreased vision. Patients with photopsia had their symptoms worsened after waking up and during the day. These complications of digoxin have been attributed to the hyperactivity of photoreceptors in the retina. All 6 patients had normal digoxin level. One of them had yellow color perception disorder, which disappeared on ceasing the use of digoxin [9].

Lawrenson studied 30 patients, who daily took digoxin (mean period of taking the drug was 32.4 months), and 30 individuals who didn't use digoxin (mean age of the patients was 81 yrs) with respect to chromatopsia. Based on this study, chromatopsia was significantly more prevalent in the cases. But no significant relationship was observed between digoxin serum level and chromatopsia [10].

The reason why the results of the present study and those of Lawrenson are different is both because of the age difference of the subjects (66.1 yrs vs 81 yrs) and the fact that only Ishihara test was used in the present study but Lawrenson used various tests such as Lathony tritan, City tritan, VEP, HRR, Farnsworth-Munsell-100-Heu Tritan to assess color-vision so that minor changes of color vision would be assessable [10].

In a similar study in Yazd (Iran), 100 patients taking digoxin and 100 healthy individuals were surveyed. According to the results obtained 15% of the cases and 2% of the controls had color vision disorder; thus, the difference was significant, P=0.001. However, digoxin serum level had no relationship with chromatopsia [11].

In several studies, patients have been introduced who developed color vision disorder following taking digoxin e.g. Wolin introduced two patients. One of them had developed shimmering light after taking digoxin. The second patient's vision had weakened. Digoxin serum level in both of them was at normal range, and following abstaining from digoxin, abnormal vision symptoms in both patients disappeared [7]. Madreperlad sequentially followed the condition of a patient, who had been intoxicated with digoxin, from the acute state to complete remedial and ophthalmologically examined him. He was found that in this patient electroretinographic amplitudes were reduced and implicit times were delayed. The above changes gradually decreased after lowering of serum

digoxin level [6]. Duncker conducted study on 57 patients in order to compare ophthalmic complications resulted from using digoxin or digitoxin (29 patients being treated with digoxin and 28 being treated with digitoxin). The results showed that using of both of these glycosides has ophthalmic complications even at therapeutic level [12]. Aronson, after a study on 10 digoxin toxicated patients and the control group, concluded that in intoxicated patients there are more ophthalmic complications [13].

## CONCLUSION

In summary, elderly patients receiving maintenance digoxin therapy showed a high incidence of color vision impairment. Often, this complication occurs when serum digoxin is normal and if digoxin taking decreases or stops it becomes better. Thus, it is recommended that patients who take digoxin should be examined regarding ophthalmic complications, and if necessary, chromatopsia examinations should be done using different tests.

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