



Ocular Surface Findings in Chronic Renal Failure

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ABSTRACT

The purpose of this study was to describe the ocular surface findings in chronic renal failure (CRF). Sixty eyes of 30 patients with CRF group and 70 eyes of 35 healthy subjects were evaluated. Schirmer-I, tear film break-up time tests and conjunctival impression cytology were performed in addition to complete ophthalmologic examination. The presence of dry eye symptoms and conjunctival calcification were noted. The groups were age and gender matched. The mean break-up time was 10.3±3.1 in group-1 and 11.2±1.7 seconds in the group-2 (p=0.03). The mean Schirmer score was 11.2±2.8 mm and 12.0±1.7 mm in the CRF and control group (p=0.095), respectively. In CRF group, conjunctival impression cytology was revealed as grade-0 findings in 16 eyes, grade 1 findings in 41 eyes and grade 2 findings in 3 eyes, in control group, it was revealed grade-0 findings in 48 eyes, grade 1 findings in 22 eyes and showed no changed in grade 2 (p<0.001). In CRF group, conjunctival calcification was regarded as grade 0 findings in 18 eyes, grade 1 findings in 34 eyes and grade 2 findings in 8 eyes. Grade 0 changes were seen in all subjects in group 2 (p<0.001). Itching (45%), redness (95%) and foreign body sensation (83%) were observed more frequently in the CRF group and also in all eyes with conjunctival calcification in both groups (p<0.001). Chronic renal failure patients suffer more than normal subjects from ocular surface complaints because of conjunctival calcifications and tear film instability although they have the same tear production with their contemporaries.

Key words: Calcification, chronic renal failure, impression cytology, lissamine

Kronik Böbrek Yetmezliğinde Oküler Yüzey Bulguları

ÖZET

Çalışmamızdaki amacımız kronik böbrek yetmezliği (KBY)'nde oküler yüzey bulgularını tanımlamaktır. KBY bulunan 30 hastanın 60 gözü ve sağlıklı 35 olgunun 70 gözü değerlendirildi. Tam bir oftalmolojik muayenenin yanında Schirmer I testi, göz yaşı kırılma zamanı ve konjunktival impresyon sitolojisi yapıldı. Konjunktival kalsifikasyon ve kuru göz bulguları kaydedildi. Gruplar yaş ve cinsiyet uyumlu idi. Ortalama göz yaşı kırılma zamanı KBY grubunda 10.3±3.1 ve kontrol grubunda 11.2±1.7 saniye idi (p=0.03). Schirmer skoru KBY grubunda 11.2±2.8 ve kontrol grubunda 12.0±1.7 mm olarak ölçüldü (p=0.095). Impresyon sitolojisi bulguları KBY grubunda 16 gözde grade 0, 41 gözde grade 1 ve 3 gözde grade 2 iken kontrol grubunda 48 gözde grade 0, 22 gözde grade 1 olarak izlendi (p<0.001). Konjunktival kalsifikasyon değişimleri KBY grubunda 18 gözde grade 0, 34 gözde grade 1 ve 8 gözde grade 2 iken kontrol grubunda tüm olgular grade 0 olarak tespit edildi (p<0.001). Kaşıntı (%45), kızarıklık (%95) ve yabancı cisim hissi (%83) KBY grubunda konjunktival kalsifikasyon olan olgularda daha sık olarak görüldü (p<0.001). Kronik böbrek yetmezliğinde göz yaşı üretimi normal olmasına rağmen kalsifikasyonlar ve göz yaşı kalitesinin bozulmasına bağlı olarak normal bireylere göre oküler yüzey şikayetleri daha fazla olmaktadır.

Anahtar kelimeler: Impresyon sitolojisi, kalsifikasyon, kronik böbrek yetmezliği, lisamin

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INTRODUCTION

Chronic renal failure (CRF) causes ocular disorders for many reasons such as uraemia, haemodialysis and hypertension. Common ocular surface findings are corneal and conjunctival calcifications (CCC), which sometimes leads to red eye and squamous metaplasia (1-3).

Squamous metaplasia of the conjunctival epithelium, dialysis-associated fluctuations in the central corneal thickness and in the refractive status, conjunctival or corneal calcium deposits, hypertensive retinopathy and cataracts are widely reported ocular findings of CRF patients (4-6). Rare ocular findings in patients with CRF include ischemic ocular motor nerve palsy and tear function changes (5-7).

Taking specimens from the conjunctival surface by using conjunctival impression cytology (CIC) is a safe, relatively simple and painless method (8). This technique helps us to assess the morphology of epithelial cells, examine cytoplasmic and nuclear characteristics and quantify the goblet cell population in the conjunctiva (8-11).

The purpose of this study was to describe the ocular surface findings in CRF and relationship with ocular complaints.

MATERIALS AND METHODS

Sixty eyes of 30 patients receiving hemodialysis with CRF group and 70 eyes of 35 healthy subjects (control group) were evaluated. Control group consisted of thirty-five age-matched patients without a history of ocular disease and surgery admitted to our clinic for refractive errors. Schirmer-I, tear film break-up time (BUT) tests and CIC, corneal and conjunctival lissamine staining according to the Oxford Classification were performed in addition to complete ophthalmologic examination (12). The presence of itching, foreign body sensation and CCC were noted.

The study was approved by the ethics committee and conducted according to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients.

Impression cytology specimens were collected from both eyes of the patients by the same physician using a cellulose acetate filter paper (11106-47 N Sartorius

AG, Germany) with a pore size of 0.022-0.025 μm cut into 2x3 mm pieces, and applied to the superotemporal conjunctiva by pressing the filter to the eye with the blunt tip of a forceps for five seconds. The filter was then grasped gently with the forceps and placed in fixative 85% alcohol. The samples were stained with periodic acid-Schiff (PAS) and Hematoxylin-Eosin (H&E), and graded according to the Nelson Classification (13).

Calcification of the conjunctiva and cornea was assessed by a slit lamp and was graded according to the criteria of Porter and Crombie (2), as follows:

Grade 0: No deposits in the conjunctiva or cornea

Grade 1: Conjunctival calcium deposits only

Grade 2: Irregular corneal deposits and conjunctival deposits

Grade 3: Single line of corneal deposits and conjunctival deposits

Grade 4: Increased corneal deposits, often as two lines, and conjunctival deposits

Grade 5: Extensive corneal deposits, often as three lines, and conjunctival deposits

Exclusion criteria included the presence of an active ocular infection or serious ocular pathological condition, a history of dry eye syndrome which not due to CRF, blepharitis, ocular surgery within the previous three months, contact lens use, pregnancy and lactation, known hypersensitivity to study medications or their components, use of any kind of topical ocular or systemic medication which causes dry eye during the study and being younger than 18 years old.

Statistical Analysis

Statistical analyses were performed with statistical software package version 15.0 for Windows (SPSS, Chicago, Illinois, USA). The Kolmogorov-Smirnov test was applied to test the distribution pattern of each data. In group comparisons of numerical data, the Student's t test was used for normally distributed data and the Mann Whitney-U tests test was used for not normally distributed data in group comparisons. Categorical data were analyzed with the chi-square test. The data was described as mean \pm standard deviation. A p-value of less than 0.05 was considered statistically significant.

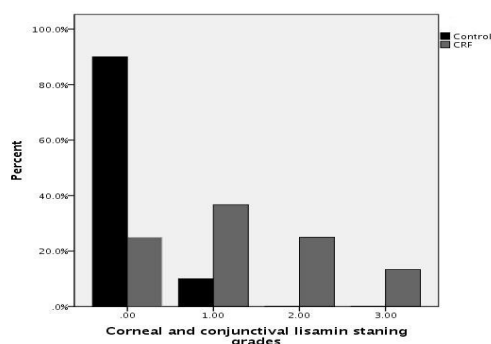


Figure 1. Corneal and conjunctival lissamine staining grades of groups

RESULTS

The mean ages of CFR and control group were 52.4 ± 11.8 and 51.7 ± 13.6 years, respectively ($p=0.836$). Male to female ratio was 32/28 in CRF group and 35/35 in control group ($p=0.705$). The mean duration of haemodialysis was 3.43 ± 1.96 years (range 1-8 years). The mean Schirmer I test score was similar between the groups; 11.2 ± 2.8 mm and 12.0 ± 1.7 mm respectively ($p=0.095$). The mean tear film BUT score was lower in CRF group than control group, at 10.3 ± 3.1 and 11.2 ± 1.7 seconds, respectively ($p=0.03$). Corneal and conjunctival lissamine staining grades were higher in CRF group ($p<0.001$, Figure 1). Itching, redness and foreign body sensation were observed more frequently in CRF group ($p<0.001$, Table 1) and also in all eyes with CCC in both groups ($p<0.001$, Table 2). CIC and CCC grades were higher in CRF group (Table 3,4).

DISCUSSION

Accumulation of calcium salts in cornea and conjunctiva in patients with CRF was first reported by Abrams (14). Interpalpebral accumulation of calcium salts is the most common form of metastatic calcification in patients

with CRF. The reason for this is not yet fully understood. According to the most widely accepted theory on this subject, with the permanent loss of carbon dioxide, tissue pH increases causing the precipitation of hydroxyapatite salts in the alkaline medium. Due to the irritative effect of these calcium salts in the cornea and conjunctiva subjective, complaints such as red eye, itching, burning, foreign body sensation and photophobia were higher in patients with CRF (8,14,15).

The most frequent alterations in the anterior segment of patients undergoing haemodialysis are CCC. Reports of their incidence vary widely in the literature, from 36% to 86%. Generally, the calcifications are located in the perilimbal conjunctiva (2,8,16,17). In our study, we found that CCC's were higher in patients with CRF, as described in the literature. Most of our cases were grade-1 (57%). Aktas et al. reported similar results to our study with only grade-1 calcification in 59% of patients (16). However, Dursun et al. reported higher proportions, in that 63% of patients were grade-3 to 5 (4). This difference among these studies may be associated with the duration of haemodialysis of the patients. The mean duration of haemodialysis was 3.43 years in our study, 3.6 years in Aktas et al.'s study but 5.0 years in Dursun et al.'s study (4,16). Hsiao et al. also reported a significant relationship between the duration of haemodialysis and the degree of calcification (18).

In our study, subjective eye complaints such as redness, itching and foreign body sensation were higher in CRF patients. In the patients group Schirmer test, was found to be similar to the control group however BUT was lower than the control subjects. According to these findings, we thought that in CRF patients, tear quality and stability are more impaired than the tear production.

Red eye is the most common symptom of CRF patients. Perhaps the primary cause of red eye is the irritative effect of calcifications (2, 16). Red eye is the most common symptom in our patient group (83%). Porter and Crombie reported a positive correlation between red eye and abnormal Schirmer's test, but in contrast, some

Table 1. Frequency of subjective complaints according to the groups.

n(%)	Itching	Foreign body sensation	Redness
Control group	5 (7)	8 (11)	8 (11)
CRF group	23 (38)	44 (73)	51 (85)
p value	<0.001	<0.001	<0.001

CRF; chronic renal failure

Table 2. Frequency of subjective complaints according to the presence of calcification

n(%)	Itching	Foreign body sensation	Redness
Calcification (+) patient	19 (45)	35 (83)	40 (95)
Calcification (-) patient	9 (10)	17 (19)	19 (22)
p value	<0.001	<0.001	<0.001

CRF; chronic renal failure

studies have indicated that red eye can be found despite normal tears (2,3).

In conjunctival diseases, a decrease of goblet cells count leads to the loss of secretory function of the conjunctiva and finally dry eye. In dry eye, CIC may change. Dursun et al. reported that CRF patients developed squamous metaplasia and had a decreased number of goblet cells, which produce the mucus component of tear. According to their study, 66% of the patients had grade 2-3 CIC findings. In our study, only 5% of the patients were grade 2-3. This may be due to the short duration of the haemodialysis of the patients, as described in the study of Aktas et al. (4, 16).

A study of Aktas and colleagues found a correlation between CIC and calcification but they did not find any relationship between CIC and decrease in BUT and Schirmer's test (16). In our study, mean disease durations did not differ according to calcification and CIC stages. We only found an increase in subjective eye findings in calcification-positive patients.

Vital staining by fluorescein, rose Bengal or lissamine green has been reported as a useful tool for the diagnosis and assessment of various ocular surface disorders (19-22). Ozdemir et al. found an increase in staining with rose Bengal in the patient group as compared to the control subjects (6). In our study, when we evaluated the staining with lissamine green, we found positive staining in conjunctiva and cornea in 23 of the patients. This was significantly higher in patients than controls ($p < 0.001$).

In the present study, we evaluated the Schirmer's and

BUT tests, lissamine green staining patterns and the CIC and CCC in patients with CRF. We found that the Schirmer's test results were similar among the patients with CRF and controls. However, abnormal BUT test results and lissamine green staining was more common in patients with CRF than in controls. The subjective dry eye symptoms were also more common in patients with CRF. We implied that tear production was not altered; however, tear instability and quality were remarkably effected because of the calcifications and metabolic changes in patients with CRF.

In conclusion, CRF patients suffer more than normal subjects from ocular surface complaints, likely related to corneo-conjunctival calcifications and tear film instability.

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Table 3. Grading of conjunctival impression cytology

	CIC Grades n(%)			p value
	0	1	2	
Control group	48 (69)	22 (31)	0	<0.001
CRF group	16 (27)	41 (68)	3(5)	

CRF; chronic renal failure

Table 4. Grading of corneal and conjunctival calcification

	CCC Grades n (%)			p value
	0	1	2	
Control group	48 (69)	22 (31)	0	<0.001
CRF group	16 (27)	41 (68)	3(5)	

CRF; chronic renal failure

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