A comparison of the occurence of dry eye between arthritic and non-arthritic subjects

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Received 10 December 2012; revised version accepted 28 February 2013

Abstract

Various studies have reported that dry eye is a common occurrence in patients with rheumatoid arthritis but not much has been done to determine its occurrence in other forms of arthritis. This study was designed to compare the symptoms of dry eye, tear film breakup time and tear production respectively in arthritic and non-arthritic subjects and also between rheumatoid arthritic patients and patients with other forms of arthritis. A total of 106 subjects within the age range of 41-90 years were included. Fifty-nine were non-arthritic with mean age and standard deviation (SD) of 58.2 ± 11.9 years, while 47 had arthritis with mean age and SD of 63.4 ± 13.3 years. Of the 47 arthritic patients 34 had osteoarthritis, 10 had rheumatoid arthritis, two had ankylosing spondylitis and one had gout. Subjects were evaluated using a McMonnies and Ho Dry Eye Questionnaire, invasive tear break-up-time test, Schirmer I test and fluorescein staining. The percentage of subjects with dry eye symptoms in both the arthritic and non-arthritic groups was quite small (<10%) however, there was a statistically significant difference in dry eye symptoms between both groups (Mann-Whitney: $U = 1035.5$, $p = 0.025$) even though both groups were largely asymptomatic. There was no significant difference in tear breakup time (Mann-Whitney: $U = 175$, $p > 0.05$), or tear quantity respectively (Unpaired *t*-test: $p > 0.05$) between both groups. Also, there was no statistically significant difference in symptoms of dry eye, tear break up time, or tear quantity respectively between rheumatoid arthritis and other forms of arthritis (Unpaired *t*-test: $p > 0.05$). In conclusion, the occurrence of dry eye is largely independent of the presence of arthritis even though arthritic subjects may be slightly more symptomatic and the presence of dry eye is independent of the form of arthritis. (*S Afr Optom* 2013 **72**(1) 34-40)

Key words: Dry eye, arthritis, rheumatoid arthritis, osteoarthritis, tear break-up time, tear quantity

Introduction

Dry eye syndrome is a multifactorial disease of the tears and underlying ocular surface that produces discomfort, visual disturbance, and tear film instability. Dry eye can cause potential damage to the ocular surface[1]. Dry eye is a complicated condition involving inflammation of the ocular surface and the tear producing glands and it is consequently associated with common symptoms such as ocular discomfort, soreness, irritation, gritty sensation, burning or stinging, dryness, itching, and the presence of stringy mucous discharge[1-3]. There have been major efforts among investigators to quantify the prevalence of dry eye[4-6]. Although the methodologies of such studies vary, overall current knowledge of this condition indicates a prevalence which varies

between 14 and 36%. The development of dry eye disease is significantly associated with several factors such as age and sex. From studies[4, 7-12], it is apparent that ageing and female hormones contribute a great deal to causing dry eye. Systemic diseases like rheumatoid arthritis[4, 13-14], rosacea[11], thyroid disease, diabetes and Sjögren's syndrome[4] amongst others, also pose a risk for dry eye disease. Medications[4-5, 7, 15-16], some ocular surface diseases such as pterygium[10], cornea scar[5, 17-18] and meibomian gland dysfunction[19, 20] environmental factors[7, 10, 15], caffeine use, smoking[4-5, 7, 21], menopause[22] and concentrated visual tasks, have also been identified as possible risk factors for dry eye development. According to the 2011 International Workshop on Meibomian Gland Dysfunction (MGD), MGD is now considered the leading cause of dry eye[20].

Although dry eye is apparently very common in our society, it can be challenging to diagnose. Accurate diagnosis of patients with dry eye syndrome requires a combination of symptoms and clinical signs obtained from dry eye tests. A careful patient history and the use of different dry eye questionnaires have proven to be useful in assessing patients, to identify those with dry eye requiring further tests, to determine the severity of dry eye, possible risk factors, and to judge progress of the condition with treatment given, based on responses to questions asked[23]. In addition to evaluating symptoms of patients, objective tests that could be performed to diagnose dry eye include; Schirmer test, tear thinning test, invasive tear break-up time test (TBUT), phenol red thread test, tear osmolarity measurement and ocular surface staining[24].

Arthritis refers to the inflammation of one or more joints resulting in pain, swelling and limited movement. Arthritis could result from injury, infection, overuse of joints causing degeneration, deposition of crystals in the joint, autoimmunity, or the presence of some systemic diseases. There are over 100 forms of arthritis of which the most common ones include osteoarthritis, rheumatoid arthritis, gout, ankylosing spondylitis, psoriatic arthritis, reactive arthritis, arthritis associated with inflammatory bowel disease and juvenile arthritis[24].

Osteoarthritis is the most common form of arthritis[26-28] and is also known as degenerative joint disease. The condition could occur following an infection of the joint, trauma, or as a result of ageing[28, 29]. The next most common form of arthritis - rheumatoid arthritis, is an autoimmune inflammatory joint disease which occurs when the patient's immune system mistakenly attacks joints in the body. This is the form of arthritis that has been mostly investigated[13, 14]. It is common knowledge that the presence of rheumatoid arthritis in an individual may be linked with the development of dry eye[4, 13, 17, 31]. From previous studies, dry eye does not occur with all such patients and its occurrence may vary with different forms of arthritis. This study is therefore designed to compare the presence of dry eye in arthritic and control subjects, as well as investigate the presence of dry eye in rheumatoid and other forms of arthritis.

Methodology

This prospective case control study was carried out among black subjects diagnosed with arthritis and attending the Rheumatological centre at Olabisi Olabanjo University Teaching Hospital (OOUTH), Nigeria and age and sex matched controls from the general population living near the hospital. This study was done with the aim of comparing the occurrence and pattern of dry eye between the arthritic and non arthritic group, and between the rheumatoid and non-rheumatoid arthritic groups of subjects. Subjects who had other conditions that could possibly cause dry eye such as pterygiae, pinguenculiae, corneal scar, proptosis, chronic blepharitis were excluded. So also were those with systemic conditions like thyroid disease, Sjögren's syndrome; those who were on medications like antihypertensive, antihistamine or hormone replacement therapy (HRT). Chronic smokers and patients wearing contact lens were also excluded. The subjects were classified into arthritic and non-arthritic groups by one examiner while the other examiner carried out the tests without knowing to which group each subject belonged. The right eye only was investigated for each subject.

The study comprised of 47 arthritic patients; 34 had osteoarthritis, 10 had rheumatoid arthritis, two patients had ankylosing spondylitis and one had gout. Data from 59 age and sex matched subjects were used as controls. Each subject was given the computer based McMonnies and Ho Dry Eye Questionnaire[32]. This questionnaire was used because upon completion, the dry eye scores were automatically computed. The questionnaire contains questions on age, gender,

affected daily activities, use of systemic and ocular medications, allergies, self assessment and previous diagnosis of dry eye and other systemic conditions that could affect dry eye. The questionnaire also had questions to elicit the major symptoms of dry eye, namely; grittiness, burning, soreness, itching, and dryness and subjects also indicated their frequency. The scores generated were used to place subjects into those with symptoms and those without based on the cut off point for this questionnaire which was 14.5. Subjects who scored greater than 14.5 were regarded as having symptomatic dry eye.

The diagnostic tests for dry eye performed in this study were; invasive tear film break-up time, Schirmer I test, and fluorescein staining to determine any ocular surface abnormality in these subjects. These tests were chosen because they are easier to carry out than other objective tests for dry eye and because they are readily available for use. For Schirmer's I test, a 35 x 5 mm size filter paper (Whatman no 41) was used to measure the amount of tears produced over five minutes. The strip was placed in the inferior fornix at the junction of the middle and lateral one thirds of the lower eyelids. The patient was instructed to keep their eye closed during the course of the test. The level of tears on the strip was then read off and recorded in millimeters. A value of less than or equal to 5 mm was regarded as an indication for the presence of dry eye.

For the evaluation of tear film break-up time and corneal fluorescein staining, the cornea was observed under cobalt-blue filter colored light of a Burton lamp. Fluorescein strip was wetted with saline water and inserted into the lower fornix taking precaution not to touch the cornea. The patient was asked to blink three times and then look straight ahead without blinking. The tear film break-up time was taken as the time between the last blink and appearance of the first random corneal dry spot. The test was repeated three times and average recorded. A tear film break-up time of less than 10 seconds was regarded as abnormal and an indication for the presence of dry eye.

For the fluorescein staining test, the Burton lamp was used to evaluate the degree of corneal staining. The criteria by Lemp (1995)[2] was used to grade any corneal stain present. The cornea was divided into five sectors (superior, inferior, nasal, temporal and central) with each sector being evaluated individually. By assigning a score from 0-3 (grade 0 represents no staining, 1-mild, 2-moderate and 3-severe staining) to the intensity of staining pattern in each sector, each zone is graded independent of one another to the nearest 0.1 value. All values are added together to give a final cumulative score for that eye. Any subject with a significant cornea stain of greater than 3/15 (20%) was regarded as having dry eye.

Results

The Kolmogorov-Smirnov *Z* test was used to analyse the distribution of data for this study. This test showed that the scores for symptoms of dry eye between the arthritic and non-arthritic groups were not normally distributed, hence it was analysed using the Mann-Whitney *U* test. The values for tear quantity and quality were normally distributed and thus the unpaired *t*-test was therefore used to analyse the data. The symptoms of dry eye between rheumatoid arthritis and other forms of arthritis were analysed with the Mann-Whitney *U,* while tear quality and quantity between the rheumatoid arthritis and non-rheumatoid arthritic group was analysed using the unpaired *t*-test.

The arthritic subjects had a mean age and SD of 63.4 ± 13.3 years and consisted of 41 females and six males. Non-arthritic subjects had a mean age and SD of 58.2 ± 11.9 years consisting of 50 females and nine males.

From evaluation of symptoms with the McMonnies and Ho Dry Eye Questionnaire, most patients in both the arthritic group (93.6%) and the non-arthritic group (91.5%) were asymptomatic (Table 1). However, statistical analysis using the using the Mann-Whitney *U* test showed there was a statistically significant difference between the symptoms of dry eye in the arthritic and non-arthritic groups (U =1035.5, p = 0.025).

Table 2 below indicates that a greater percentage of arthritic subjects had dry eye (12.8%) than non-arthritic subjects (5.1%). The mean tear quantity value in the arthritic group was less than the non-arthritic group. Analysis of their means showed that there was no statistically significant difference in tear quantity between the arthritic and non-arthritic group (t = –0.99, p = 0.67).

Table 1: Subjects with symptomatic dry eyes

Group	Subjects with symptomatic dry eye		Subjects without symptomatic dry eye		Mean McMonnies and Ho score ± SD
	No	%	No	%	
Arthritic (n = 47)	3	6.4	44	93.6	10±3.3
Non-arthritic (n = 59)	4	6.8	55	93.2	8.4±3.9

Table 2: Subjects with reduced tear quantity

Group	Subjects with reduced tear quantity		Subjects with normal tear quantity		Mean tear quantity ±SD (mm)
	No	%	No	%	
Arthritic (n = 47)	6	12.8	41	87.2	14.2±8.7
on-arthritic (n = 59)	3	5.1	56	94.9	15.8±7.1

Data from Table 3 below show a greater percentage of arthritic subjects (25.5%) having poor tear stability as compared to the non-arthritic group (13.6%). However, statistical analysis using the *t*-test showed no statistically significant difference between the mean TBUT of both groups ($t = -0.632$, $p = 0.53$).

Table 3: Subjects with poor tear stability

Group	Subjects with poor tear stability		Subjects with good tear stability		Mean TBUT±SD (seconds)
	No	%	No	%	
Arthritic (n=47)	12	25.5	35	74.5	12.9±5.5
Non-arthritic (n=59)	8	13.6	51	86.4	13.5±4.9

Table 4 indicates the percentage of subjects with rheumatoid arthritis that had symptomatic dry eye (20%) were seven times the non-rheumatoid arthritis group (2.7%). However statistical analysis showed that there was no statistically significant difference between the degree of symptoms of dry eye in both groups of arthritis ($t = -0.43$, $p = 0.65$).

Table 4: Symptomatic dry eye in different arthritic groups

Group	Subjects with Symptomatic dry eye		Subjects without Symptomatic dry eye		Mean McMonnies And Ho score±SD
	No	%	No	%	
Non rheumatoid arthritis (n = 37)	1	2.7	36	97.3	9.8 ±2.8
Rheumatoid arthritis (n = 10)	2	20.0	8	80.0	10.5±0.7

Using the Schirmer I test, a greater percentage of subjects without rheumatoid arthritis had reduced tear quantity (Table 5). Statistical analysis of the results however, showed that there was no statistically significant difference between the tear quantities in both forms of arthritis ($t = -1.51$, $p = 0.15$).

Table 5: Tear quantity in different arthritic groups

Group	Subjects with reduced tear quantity		Subjects with normal tear quantity		Mean tear quantity±SD(mm)
	No	%	No	%	
Non rheumatoid arthritis: n=37	5	13.5	32	86.5	13.24±8.6
Rheumatoid arthritis: n=10	1	10.0	9	90.0	18.2±9.4

As seen in Table 6 below, the percentage of subjects with rheumatoid arthritis who had poor tear stability (40%) based on the TBUT test, were almost double the non rheumatoid arthritis group (21.6%). But, statistical analysis of the results showed that there was no statistically significant difference between the tear break-up-time in both forms of arthritis (t =1.44, $p = 0.17$).

In all subjects seen, only two (one from the control group and the other from the rheumatoid arthritic group) had corneal staining. Out of these two, only the subject with rheumatoid arthritis had a significant corneal stain of 4/15 (26.7%) denoting dry eye surface compromise from chronic dryness.

Table 6: Tear break-up time in different arthritic groups

Group	Subjects with poor tear stability		Subjects with good tear stability		Mean TBUT±SD (seconds)
	No	%	No	%	
Non rheumatoid arthritis (n = 37)	8	21.6	29	78.4	13.44±5.7
Rheumatoid arthritis: (n = 10)	4	40.0	6	60.0	11.52±3.6

Discussion

Results from this study show that out of 47 arthritic subjects, only 6.4% presented with dry eye symptoms while in the non-arthritic 6.8% of the 59 subjects presented with dry eye symptoms. Although both groups were relatively asymptomatic (93.6% and 93.2% respectively) statistical analysis showed that there was a significant difference symptoms in both groups (U = 1035.5, p = 0.025). This may be due to the fact that the mean score of subjects in the arthritic group (10 ± 3.3) was higher than the mean score of the non-arthritic group (8.4 ± 3.9), indicating that the arthritic subjects are perhaps slightly more symptomatic. From the study by Moss *et al*[4], where dry eye was diagnosed using patient symptoms, they found that a history of arthritis was significantly associated with dry eye (odds ratio [OR], 1.91; 95% confidence interval [CI], 1.56 - 2.33).

A comparison of tear quantity between the arthritic and non-arthritic group showed that the mean value of the arthritic group (14.2 ± 8.7 mm) was lower than the non-arthritic group (15.8 ± 7.1 mm), but statistical testing of these means showed that there was no statistically significant difference in tear quantity (t = 0.99, p = 0.33). The finding of this study was also consistent with that of Punjabi *et al*[13] in which their result showed that more rheumatoid arthritic subjects (27.3%) had dry eye than the control group (12%). They found this to be statistically significant (p = 0.003). The difference in these results may be due to their greater number of subjects (n = 168), and their non inclusion of other forms of arthritis.

Although statistical analysis failed to find any difference in TBUT value between both groups, the percentage of arthritic subjects diagnosed as having poor tear stability was almost double that of the non-arthritic subjects. The study by Punjabi *et al*[13] found that 22.6% of rheumatoid arthritic subjects had TBUT of less than 10 seconds when compared to the control group (9.52%), and this was found to be statistically significant (p<0.001). The difference between these results may be due to the fact that their subjects were only those with rheumatoid arthritis while this study included other forms of arthritis.

From this study, the Schirmer and TBUT tests identified a greater percentage of arthritic subjects as having dry eye than the non-arthritic subjects, while with subjective symptoms, the number of subjects identified as having dry eye were similar. This discrepancy in the result may be attributed to the fact that during the course of the examination, some subjects who were symptomatic had normal TBUT and or tear quantity while some others who were not symptomatic had reduced TBUT and or tear quantity. A similar observation was made in other studies[5, 13-14]. They generally observed that individuals varied greatly in their tolerance to dry eye symptoms. In these studies, subjective scores did not correlate significantly with objective measures of dry eye.

Based on the McMonnies and Ho Dry Eye Questionnaire[32] we found a greater percentage of rheumatoid arthritic subjects (20%) were symptomatic compared to 2.7% in other forms of arthritis. Statistical analysis however showed no significant difference between the degree of symptoms of dry eye in both groups of arthritis (t = –0.43, p = 0.65). Rheumatoid arthritis is greatly recognized as a form of arthritis that causes dry eye. It has been stated that patients with rheumatoid arthritis have dry eye because inflammation of the lacrimal gland results from the same autoimmune state that causes inflammation in the joints[25]. The inflammation in the lacrimal glands could translate into various symptoms patients' tolerance to these symptoms may vary greatly due to individual differences.

With the Schirmer test, a greater percentage of subjects without rheumatoid arthritis had dry eye. This result is in contrast with that in the study by Fujita *et al*[14]. In their study, there was a correlation between Lansbury index (used to evaluate rheumatoid activity) and Schirmer's test (p = 0.048), and

erythrocyte sedimentation rate (ESR) and Schirmer's test (p = 0.035). They concluded that dry eye is common in rheumatoid arthritis patients including those with Sjögren's syndrome, stating further that dry eye should be taken into consideration regardless of the rheumatoid arthritis activity. A reason for these discrepancies may be explained by the fact that the Schirmer's test gives variable results and has poor reproducibility and low sensitivity for detecting dry eye. This was reported in the comparative study done by Kallarackai *et al*[33] to assess the clinical use of fluorescein meniscus time with tear break-up-time and Schirmer's test in the diagnosis of dry eye. They concluded that the fluorescein meniscus test is a more sensitive test with good reproducibility compared to the Schirmer's test. This is due to several factors such as the positioning of the filter paper in the eye, confounding effects of reflex tearing due to the irritation caused by the paper and the influence of evaporation, temperature and humidity. In addition, it has been identified by Pflugfelder *et al*[34], that diagnostic tests evaluating tear composition and clearance appear to show stronger correlation with dry eye than the conventional Schirmer test.

A comparison of the tear stability of subjects in both the rheumatoid arthritis and non-rheumatoid arthritis groups showed that a greater number of rheumatoid arthritis subjects had poor tear stability. This result is therefore in line with the study by Punjabi *et al*[13], who had 19 (22.62%) subjects with rheumatoid arthritis having poor TBUT as compared to eight (9.52%) controls, thereby identifying rheumatoid arthritis as a risk factor for having poor tear stability. Although statistics did not show any significant difference in both groups from our study, this may be due to the fact that the number of subjects who had poor tear stability was quite few.

Fluorescein staining was negative in all subjects except two (one from the non-arthritic group and one from the rheumatoid arthritis group). Out of these two subjects, only the subject with rheumatoid arthritis had a significant corneal stain of 4/15 (26.7%) denoting dry eye surface compromise. Lemp, (1995)[2] pointed out that fluorescein will stain denuded areas of the cornea surface caused by a chronic dry eye state. In a study by McCarty *et al*[9], comprising a larger number of subjects, (N=926), 1.5% had dry eye based on fluorescein staining, another 10.8% had dry eye based on rose Bengal staining. These results indicate the necessity for further research using a larger sample size, as the percentage of patients who may test positive for fluorescein stain may be quite small. However, in another study by Lekhanont *et al*[35], there was a significant fluorescein staining in 16.6% of 550 subjects (p = 0.013). The fewer number of subjects who had significant fluorescein staining could be attributed to the small number of subjects in our study.

Conclusion

From this study, clinical tests showed that there was no significant difference in the occurrence of dry eye between arthritic and non-arthritic subjects also since both groups on average were relatively asymptomatic we conclude that dry eye may occur in individuals irrespective of the presence of arthritis. In addition, dry eye symptoms, Schirmer test, TBUT test and fluorescein staining results in rheumatoid arthritis subjects was not different in subjects who has osteoarthritis.

Acknowledgement

Thanks to Professor Femi Adelowo, the Dean of the Faculty of Clinical Sciences, Olabisi Olabanjo University Teaching Hospital (OOUTH) Sagamu, for providing the necessary approval we needed to carry out this research. Dr Edujubin, and all other rheumatology residents at OOUTH, Dr Ojo of University of Benin Teaching Hospital, Afi and Eddy Otirikpen, and Dr Hamzat Amiebenomo. Thank you for your unequalled support.

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