

A comparative study to assess the clinical use of Fluorescein Meniscus Time (FMT) with Tear Break up Time (TBUT) and Schirmer's tests (ST) in the diagnosis of dry eyes

GU Kallarackal¹, EA Ansari², N Amos¹,
JC Martin³, C Lane² and JP Camilleri¹

Abstract

Introduction The clinical diagnosis of dry-eye is confirmed by a suitable test of tear production and the technique commonly used today to diagnose dry eye is the Schirmer's test (ST). Although the ST is easy to perform it gives variable results, poor reproducibility and low sensitivity for detecting dry eyes. Another test, the tear break up time (TBUT) is used to assess the stability of tears which if abnormal may also cause symptomatic dry-eye. We present the results of both these tests and a new test, which shows greater sensitivity than the ST in detecting aqueous tear deficiency. The fluorescein meniscus time (FMT) is a new test developed in conjunction with one of the authors (CL) and the Department of Ophthalmology at the University Hospital of Wales. The FMT is a measure of the rate at which a fluorescent tear meniscus is formed using 2% sodium fluorescein, a stopwatch and suitable illumination with a slit lamp. **Method** An open controlled study in 62 patients and 51 controls was conducted to compare the ability of ST, FMT and TBUT to detect dry-eye in a group of patients diagnosed with rheumatoid arthritis and symptomatic dry eyes for a minimum period of 6 months. A separate control group of 15 subjects was tested on three separate occasions to assess the reproducibility of the FMT test. **Results** All three tests showed a statistically significant difference between the patient

and control populations; Mann–Whitney $P < 0.001$. There was a correlation between the right and left eye for all three tests in the control group (ST $r^2 = 0.77$, FMT $r^2 = 0.98$, TBUT $r^2 = 0.94$). This correlation was markedly reduced for FMT and TBUT in the patient population and was in keeping with the symptoms reported as being worse on one side in a proportion of the patients (FMT $r^2 = 0.52$, TBUT $r^2 = 0.54$, ST $r^2 = 0.75$). A correlation with age was also observed for all the three tests in the control group (ST $r^2 = 0.74$, FMT $r^2 = 0.92$, TBUT $r^2 = 0.51$), but not in the patient population (ST $r^2 = 0.06$, FMT $r^2 = 0.18$, TBUT $r^2 = 0.03$). A significant correlation was observed between the ST and FMT in both the control (ST *vs* FMT $r^2 = 0.65$) and patient population (ST *vs* FMT $r^2 = 0.44$). There was no value greater than 200 seconds for FMT recorded in the control group. Using this value to define an abnormal FMT, 85% of the patients (72% of the eyes tested) had an abnormal result. This was in contrast to 35% of patients (26% of the eyes tested) with abnormal results detected by ST.

Using ANOVA and Student's paired *t*-test, there were no significant differences between the three sets of values recorded serially over 3 months to assess the reproducibility of the FMT. The average standard error of the mean was 2.72% and the average co-efficient of variation 4.07%.

Conclusion Our study suggests that the FMT is a more sensitive test with good

¹Department of Rheumatology University Hospital of Wales Heath Park Cardiff CF14 4XN, UK

²Department of Ophthalmology University Hospital of Wales Heath Park Cardiff CF14 4XN, UK

³Department of Rheumatology The Royal Glamorgan Hospital Llantrisant CF72 8XR, UK

Correspondence: GU Kallarackal Tel: 029 20742626 E-mail: skallarackal@hotmail.com

reproducibility compared to the Schirmer's test. The FMT correlates with the ST and suggests that both tests measure aqueous tear deficiency. The FMT therefore is a better alternative to ST currently being used to test aqueous tear deficiency.

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Keywords: dry eye; Schirmer's test; fluorescein meniscus time; aqueous tear deficiency

Introduction

The clinical diagnosis of dry eye is usually confirmed by a test of measurement of tear production. The technique commonly used today is Schirmer's test (ST) developed by the German ophthalmologist, Otto WA Schirmer in 1903.¹ Although ST is easy to perform, it gives variable results, poor reproducibility and low sensitivity for detecting dry eyes.^{2–4} Attempts to preserve glandular function are now being made with the use of topical immunosuppressants, and initial results from these studies have been encouraging. With such treatments becoming available a more sensitive and easily performed test would be advantageous to detect and monitor the effect of treatment and the progression of the disease.

Abnormalities of mucin and lipid components in tears may alter the quality of the tear film and result in symptomatic dry-eye even if the quantity of aqueous tear production is normal.⁵ The TBUT is used to assess the stability of the tear film.⁶

Colorimetry, using 1% fluorescein and 1% Rose Bengal and the principle of tear dilution, has been used as an alternative method to measure aqueous tear production. The colour intensity of the tear meniscus, 5 min after the introduction of the above combination of dyes, has been shown to correlate with the level of tear production.⁷

The proposed new FMT test measures the rate of tear meniscus formation. After the introduction of 2% sodium fluorescein drops, tears, which are continually being produced, dilute the fluorescein to form a fluorescent meniscus along the lower eye-lid, beginning at the outer canthus. The rate of production of this meniscus reflects the rate of tear production.

The objective of this study is to compare the ST, FMT and TBUT in detection of dry-eye in a group of patients with rheumatoid arthritis and symptomatic dry eyes with a set of age-matched controls.

Methods

Comparative study

Patient population Patients ($n = 62$) with symptomatic dry eyes for a minimum period of 6 months and diagnosed with rheumatoid arthritis were recruited from the Rheumatology clinic at the University Hospital of Wales between June 1997 and June 1999. The symptoms were validated using a standard questionnaire.⁸ The exclusion criteria were a history of conjunctival, scleral or corneal diseases, diabetes mellitus, thyroid disorders, patients taking antidepressant or diuretic medication and present or past use of contact lenses.

Control group The control group ($n = 51$) was recruited from staff at the University Hospital of Wales and patients attending the Optometry clinic for the assessment and management of refractive error. The controls had no symptoms of dry eyes and did not suffer with any other medical or rheumatological disorders. The exclusion criteria for the control group were the same as that for the patient population.

Reproducibility study

A separate group of 15 female subjects with no previous ophthalmic history and taking no medication was used to test the reproducibility of FMT. The exclusion criteria for this group were the same as that for the comparative study patient and control population. The test was performed monthly over 3 months. An average of three measurements was recorded for each eye during each visit.

Ocular assessments

Schirmer's test (ST) The test was performed using a standardised kit containing a strip of filter paper 5 mm \times 30 mm and placed on to the lower lid margin in a temporal position. The patient looks up and blinks normally for 5 min before the strip is removed and the length of wetted paper measured. A value of < 5 mm was taken as abnormal.¹

Fluorescein meniscus time (FMT) A drop of 2% sodium fluorescein is placed in the lateral canthus of the eye. The natural flow of tears towards the lacrimal duct draws the dye along the lower eye-lid in a medial direction as it is diluted with the tears produced by the lacrimal gland. Using a slit lamp and a cobalt-blue light filter and a stop watch, the time taken for the fluorescent meniscus to fill the lateral half of the lower

eyelid was measured in seconds. An average of three measurements was recorded.

Tear break up time test (TBUT) The stability of the tear film over the conjunctiva and cornea was assessed using a Burton's lamp with a cobalt blue filter and sodium fluorescein. A drop of 2% sodium fluorescein was applied to the eye, and the patient is asked to blink five times so that a film is formed over the cornea and bulbar conjunctiva. The patient is then asked to refrain from blinking during which time black spots or lines begin to appear indicating dry spots. The interval between the last blink and the first randomly distributed dry spot was taken as the tear break-up time. An average of three measurements was recorded. A value of < 10 seconds is taken as abnormal.⁶

Procedure All patients and controls were screened for evidence of any disease affecting the cornea and sclera or anterior blepharitis by an ophthalmologist. The tests were carried out in sequence, FMT followed by TBUT followed by Schirmer's test. This sequence was chosen to minimise any error caused due to reflex tearing. A set of three readings of FMT and TBUT were taken from each eye in both groups and the average recorded. The Schirmer's test was then performed in each eye and the results recorded.

Tests for statistical analysis Correlation was calculated using Pearson's correlation test. The significance of the results between the patient and control group was calculated using the non-parametric Mann-Whitney U test. The variation of FMT over 3 months was analysed using ANOVA and Student's paired *t*-test. The reproducibility of FMT was analysed using standard error of mean and the coefficient of variation (SPSS).

Results

Patient demographics The mean age of the patient group was 63.8 yrs (range 13–88) and that of the control group was 58.2 yrs (range 40–86). All the patients were rheumatoid factor positive and had erosive disease of mean duration 13.6 yrs (range 4–36 yrs). Using rank analysis there was no significant difference between the two groups for age; Mann-Whitney U $P = 0.196$. The proportion of females in the patient group was slightly higher than those in the control group (88% vs 72%).

Range of results The ranges of the results for FMT, ST and TBUT in the control group were 20–200 seconds, 9–20 mm and 10–60 seconds, respectively. The ranges

of the results for FMT, ST and TBUT in the patient population were 90–360 seconds, 0–40 mm and 1–13 seconds, respectively (Figure 1).

Correlation with age A strong correlation with age was noted for all the three tests in the control group. However this correlation was not observed in the patient population (Table 1 and Figure 2).

Comparison of patient and control group: the distribution of the data is as shown in Figure 1. The data were non-parametric in nature therefore rank analysis was used to determine the difference between the two groups. The results of the ST in the patient group showed complete overlap with that in the

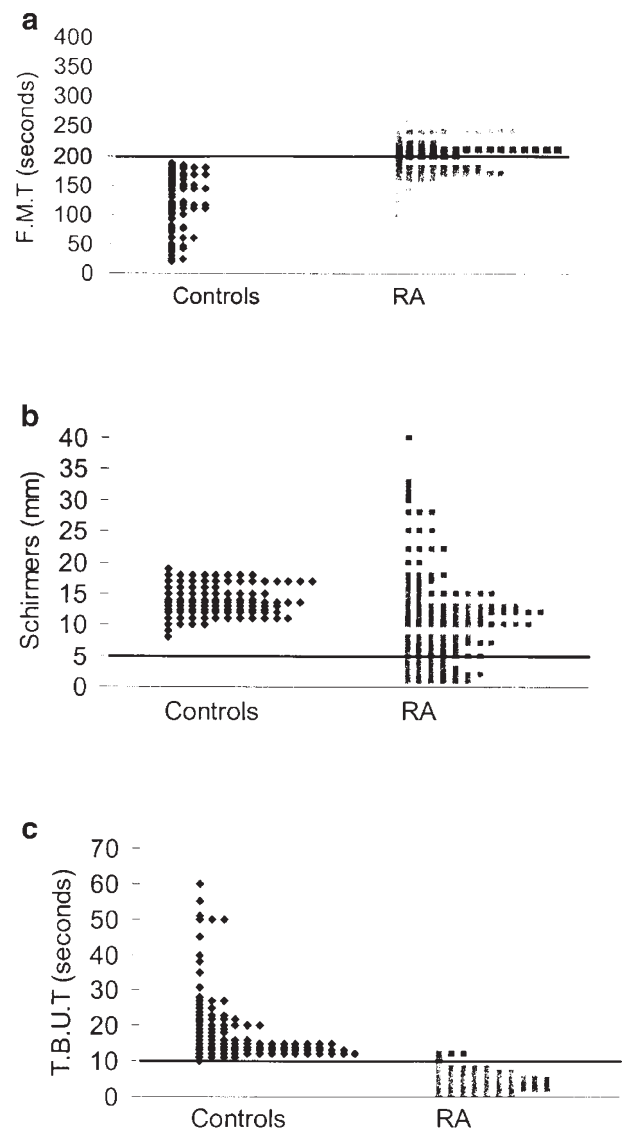


Figure 1 The distribution of (a) Fluorescein Meniscus time; (b) Schirmer Test; and (c) Tear Break Up Time in the control and rheumatoid population.

Table 1 The correlation between age and Fluorescein Meniscus time (FMT), Schirmer's test (ST), and Tear Break-up Time (TBUT)—Comparative study

	Control group r^2	Patient group r^2
Age vs FMT	0.92	0.18
Age vs Schirmer's	0.74	0.06
Age vs TBUT	0.51	0.03

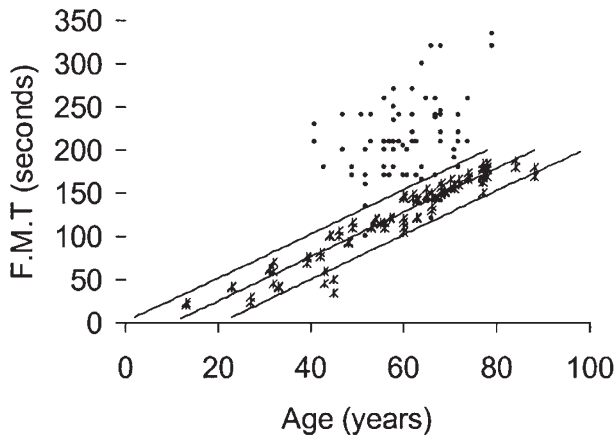


Figure 2 The age correlation of Fluorescein Meniscus time (FMT) with 95% confidence limits in the control (x) and Fluorescein Meniscus time values for rheumatoid patients (●).

control. However a better separation between patients and controls was noted with FMT and TBUT. All three tests showed statistically significant differences between the patient and control population; (absolute values: control vs patient population, $P < 0.001$ for ST, FMT and TBUT).

Comparison of right and left eye The right and left eyes were tested separately for all the three tests in both the patient and control groups. There was a strong correlation between the right and left eye for all three tests in the control group. This correlation was markedly reduced for FMT and TBUT in the patient population and was in keeping with the symptoms reported as being worse on one side in 17% of the patients. Therefore, each eye was considered separately for further analysis (Table 2 and Figure 3).

Table 2 The right and left eye correlation in the patient and control groups—comparative study

	Control group r^2	Patient group r^2
Right FMT vs left FMT	0.98	0.53
Right TBUT vs left TBUT	0.94	0.54
Right Schirmer's vs left Schirmer's	0.77	0.75

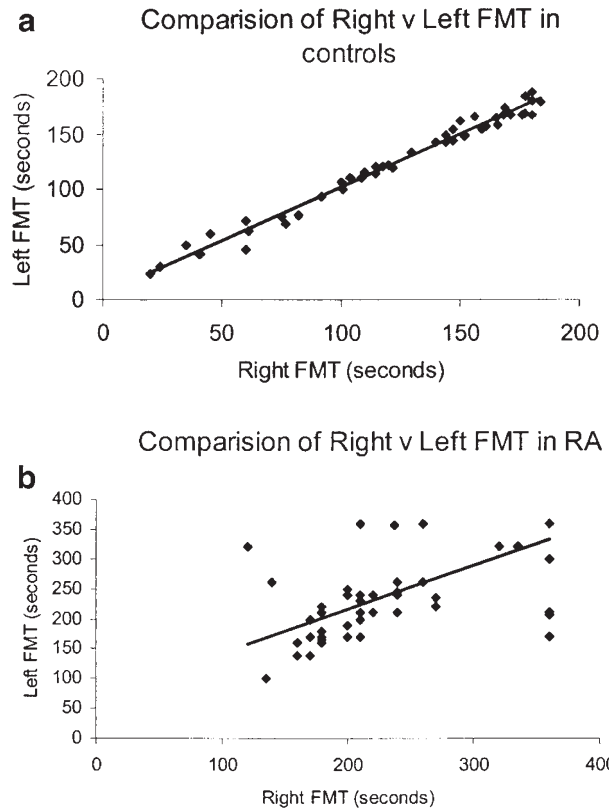


Figure 3 (a) and (b) The comparison of Fluorescein Meniscus time (FMT) between right and left eyes in the control and rheumatoid patients.

Correlation between FMT, Schirmer's & TBUT A significant correlation was observed between the ST and FMT in both the control and patient population. There was a poor correlation between TBUT and ST and between TBUT and FMT in the patient and control group (Table 3). There was no value greater than 200 seconds for FMT recorded in the control group. Using this value to define an abnormal FMT, 85% of the patients (72% of the eyes tested) had an abnormal result. This is in contrast to 35% of patients (26% of the eyes tested) with abnormal results detected by ST (Table 4).

Table 3 The correlation between Fluorescein Meniscus time (FMT), Schirmer's test (ST) and Tear Break-up Time (TBUT)—comparative study

	Control group r^2	Patient group r^2
FMT vs Schirmer's	0.65	0.44
FMT vs TBUT	0.65	0.01
Schirmer's vs TBUT	0.34	0.02

Table 4 The percentage of patients with an abnormal result for FMT Schirmer's and TBUT—comparative study

	% of patients with an abnormal test	% of eyes with an abnormal test
FMT	85	72
Schirmer's Test	35	26
TBUT	97	95

Reproducibility of FMT As seen in the control population of the comparative study, the FMT showed a correlation between the right and left eye ($r^2 = 0.98$) and with age ($r^2 = 0.87$). There were no statistically significant differences between the three sets of values recorded serially over 3 months— $P > 0.05$. The average standard error of the mean for the 15 cases was 2.72%. The average co-efficient of variation was 4.07%.

Discussion

Our study reflects the results of many others showing a poor sensitivity for ST in detecting dry eyes.^{2–4,9} 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.^{4,10}

The correlation co-efficient (r^2) of FMT and TBUT in the right and the left eye in the asymptomatic control group was close to 1 compared to that of ST. This correlation between right and left eye was markedly reduced in the patient population for FMT and TBUT and was in keeping with symptoms reported as being worse on one side in 17% of the patients. The Schirmer's test was unable to detect this difference.

Because FMT measurements increase with increasing age (Figure 2), an age-related normal range would be best suited to define normal limits. However due to the limitation of this study we chose the highest recorded value for FMT in the control population to define normal limits. This cut-off value for 'normal' FMT was <200 seconds. The age-related correlation for ST and FMT seen in the control group was not observed in the patient population. Therefore we observed that the pathological process has a more pronounced effect on tear production than the age-related change within the patients (Figure 2). Because of this effect of the disease on tear production and because the numbers studied were small, we have used 100% confidence limits to define abnormal FMT. Though all patients gave a history of symptoms of dry eye for at least a period of 6 months, ST was able to detect an abnormality in only 35%, while the FMT was able to do so in 85%. By using 100% confidence

intervals to define normal limits of FMT, the test is made 100% specific, however we may have compromised the sensitivity of the test. No patient with an abnormal ST had a normal FMT, however a large number of patients with normal ST had an abnormal FMT. Hence the FMT would be a more sensitive method for assessing tear production compared to ST (Figure 4).

Premature break-up of the tear film is a feature of any form of dry eye. A reference value of <10 seconds for TBUT is used in the diagnosis of dry eyes.¹¹ The TBUT has been shown to be dependent on the reduction of surface tension by mucins and other surface-active agents but not so much on the quantity of aqueous content in tears.^{12,13} Using the above value 97% of the patients had an abnormal TBUT (Figure 5). Though this test seems to be most sensitive, it is a clinical measurement of the stability of the tear film rather than of aqueous tear production, and is more appropriately used in conjunction with measurements of aqueous tear deficiency, in the evaluation of symptoms of dry eye. Rose Bengal staining is another commonly used test to evaluate symptomatic dry eye.¹⁴ This test quantifies the epithelial damage caused by the lack of tears and is not a true measure of tear production at the time of the test.¹⁵ Because of this, the Schirmer test was chosen for comparison with the FMT. Rose Bengal also causes pain on instillation and this pain may outlast by hours or days the duration of topical anaesthesia commonly used.¹⁶ This makes the test extremely unpopular among patients. The currently established criterion for the diagnosis of dry eye uses both tests, ie tests for surface damage and tear secretion to evaluate symptoms.^{17,18}

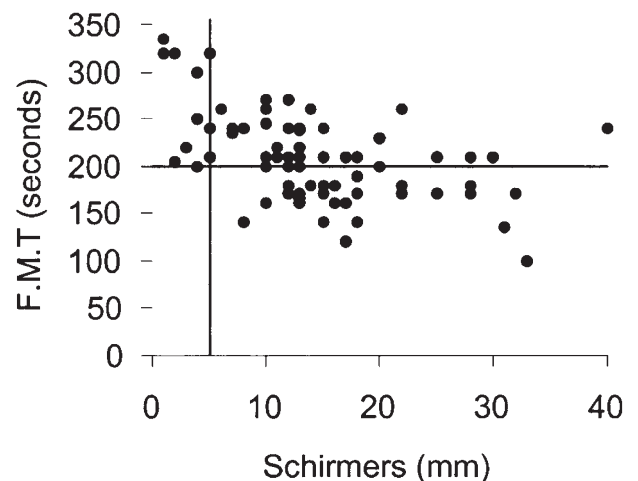


Figure 4 Comparison of Fluorescein Meniscus time (FMT) vs Schirmers Test (ST) in patients with rheumatoid arthritis and dry eye symptoms. (Abnormal ST ≤ 5 mm; Abnormal FMT ≥ 200 seconds.)

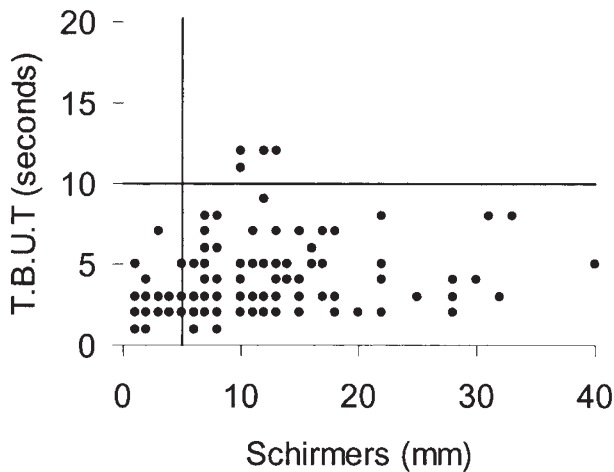


Figure 5 Comparison of Tear Break Up Time (TBUT) vs Schirmer's Test (ST) in patients with rheumatoid arthritis and dry eye symptoms. (Abnormal ST \leq 5 mm; Abnormal TBUT < 10 seconds.)

Attempts to limit the destruction of the lacrimal gland and preserve its function are being made with the use of topical androgens and cyclosporin A, and initial studies have given encouraging results.^{19–21} Such a treatment would help both the pathological process and symptoms of dry eye. If new and more effective treatments become available, a test, such as FMT, that is sensitive and easily performed would be needed to detect and monitor the effect of treatment and the progression of the disease.

A number of methods to assess tear secretion accurately have been proposed and this involves a detailed study of the tear meniscus, which accounts for 75–90% of the tear volume.^{22–24} Although more reliable, these tests need more sophisticated equipment and skill to do and would usually be performed in a specialist ophthalmology/research clinic. The Schirmer's test has been known to be insensitive, but the ease with which the test is performed adds to the popularity of this test. The FMT is similarly easily performed using a slit lamp, stop watch and 2% sodium fluorescein. Although both tests are subjective, our study shows that the FMT is a more sensitive test compared to the Schirmer's test commonly used today.

The FMT also has good reproducibility with a low standard error of mean (2.72%) and co-efficient of variation (4.07%) in a trained observer. This is in contrast to the Schirmer's test with a coefficient of variation greater than 10% as reported in previous studies.² Our study suggests that the FMT is a sensitive test that could replace the Schirmer's test currently being used to test aqueous deficiency in dry eye.

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