THE EFFECT OF MALARIA TREATMENT TYPE ON THE MEAN QUANTITY, QUALITY, AND SPREAD OF THE TEAR FILM BEFORE AND AFTER MALARIA TREATMENT

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ABSTRACT

ports, close-up work and other activities rely on the eyes, which are affected by the quantity, quality and dispersion of the tear film. Several medical disorders, most notably malaria, hypertension, diabetes, and spread, can have an impact on the quantity, quality, and distribution of tear film. At the University of Benin Health Center, a total of 425 outpatients between the ages of 10 and 50 were studied, including 180 men and 245 women. The presence or absence of systemic pathology was determined using case histories, clinical notes and testing. To rule out any eye pathology, a visual acuity (VA) test, external examination, and ophthalmoscopy were performed. The subjects were subjected to a rapid diagnostic test (RDT) kit to check for malaria. Patients who tested positive for malaria had their blood type and genotype examined. Before and after treatment for malaria with antimalarial Artesunate and Amodiaquine (Camosunate), as well as Artemether and Lumefantrin, the amount, quality, and distribution of the tear film (tear film workup) was assessed on them using Schirmer's test, keratometry, and blink rate (Lonart). Generally, treatment with Camosunate produced better result and was a better option compared to Lonart treatment as regard improved tear film quantity and spread in both sexes, especially in females was significant (p < 0.001) with the good association. The quantity, quality, and distribution of tear film production were unaffected by the kind of parasites (Plasmodium falciparum and Plasmodium vivax), either before or after treatment. Additionally, the results show that malaria has a greater impact on both sexes' tear film production and distribution the more parasitaemia there is. Except for the spread of the tear film, which substantially and sufficiently (p 0.001) improved after the incidence of malaria, the quantity and quality outcomes of the tear films were unaffected by the disease.

Keywords: Malaria, Parasitaemia, Tear film, Tear quality, Vision
INTRODUCTION

Malaria is a major public health problem especially in developing and underdeveloped countries of the world. Resistance to anti-malaria drugs as well as the resistance of malaria vectors to insecticides is a major challenge (Crutcher and Hoffman, 1996). According to the World Health Organization (2019), in 2018, there were an estimated 228 million cases of malaria worldwide. The estimated number of malaria deaths stood at 405 000 in 2018. Children aged under 5 years are the most vulnerable group affected by malaria; in 2018, they accounted for 67% (272 000) of all malaria deaths worldwide.

In a typical primary care setting in Benin, Nigeria observation of a 4 - year data (Adeyemo et al., 2014) indicated that there was an upward shift in the occurrence of malaria among the students who visited the health center. There were eleven anti-malaria drugs given for the treatment of malaria at the university of Benin health center in the years under study. Lumarten and Quinine tablets were the most commonly administered drugs to patients with malaria infections during the first year under study, while in the second year under study, there was an increase in the number of drugs dispensed. We look at a case outside Nigeria. Khattak et al. (2013) undertook a study to determine the current prevalence and distribution of Plasmodium species across Pakistan. A malariometric population survey was conducted in 2011 using blood samples collected from 801 febrile patients of all ages in four provinces and the capital city of Islamabad. Microscopically confirmed Plasmodium-positive blood samples were reconfirmed by polymerase chain reaction (PCR). Confirmed parasite-positive samples were subjected to species-specific PCR capable of detecting four species of human malaria. Results showed that of the 707 PCR-positive samples, 128 (18%) were P. falciparum, 536 (76%) were P. vivax, and 43 (6%) were mixed P. falciparum and P. vivax. Ninety-four microscopy-positive samples were PCR-negative and Plasmodium malariae and Plasmodium ovale were not detected. Prevalence of P. vivax ranged from 2.4% in Punjab Province to 10.8% in Sindh Province and prevalence of P. falciparum ranged from 0.1% in Islamabad to 3.8% in Balochistan. They concluded that Plasmodium infections in Pakistan are largely attributed to P. vivax but P. falciparum and mixed species infections are also prevalent. In addition, regional variation in the prevalence and species composition of malaria was high.

Sports, close-up work, and other activities rely on the eyes, which are affected by the quantity, quality, and dispersion of the tear film. Several medical disorders, most notably malaria, hypertension, diabetes, and spread, can have an impact on the quantity, quality, and distribution of tear film. Malaria patients have systemic dehydration, which may have an impact on the eye's tear film. If malaria is not treated, it will advance to impact the quality and spread of the tear film in addition to the number of tears (lina et al., 2011). The standard of human actions, which constitutes human relations, will be impacted by an aberrant tear film. In light of this, the researcher must answer the crucial question, "To what extent does malaria alter the number, quality, and dissemination of the tear film in humans?

The clinical and histopathologic findings of malarial ocular lesions were described by Biswas et al. (1996). Bright field and polarized light microscopy were used to study the eye of a 53-year-old man who passed away from chloroquine-resistant Plasmodium falciparum malaria in 1993. Conjunctiva, episclera, and the tendinous attachment of the medial rectus muscle were all affected by an epibulbar hemorrhage. Mwinyi et al. (2009) studied the fundi of 73 infants with a confirmed diagnosis of cerebral malaria who ranged in age from six months to six years. On admission, 38 patients had normal fundi, 18 had papilloedema, and 17 had retinal hemorrhages. Age, sex, entrance coma score, posture, packed cell volume, parasite density, serum glucose, and serum electrolyte profile did not significantly differ between the three groups.
The study aim is to investigate the effect of malaria treatment type on the mean quantity, quality, and spread of the tear film before and after malaria treatment. This will help to provide vital information on the effects of malaria infection on the tear film. This will be of immense value to eye health care practitioners in the diagnosis and treatment of Eye related problems during the course of malaria infection.

**MATERIALS AND METHOD**

**Study population**
This study was carried out at the medical unit of the Department of Health Services and the Optometry clinic, Ugbowo Campus of the University of Benin, Benin City, Edo State. The subjects consisted of malaria patients visiting the University of Benin Health Centre.

**Approval/ ethical clearance**
Before the study, approval was obtained from the Department of Health Services, the University of Benin, while ethical clearance was obtained from the Department of Optometry, University of Benin, Benin City, and written informed consent was also obtained from individuals and parents of children that constituted the study population of this research after careful explanation of the procedures.

**Sample size determination**
The sample size for this study was 425 males and females outpatients aged between 10 and 50 years. It was determined based on Cochran’s formula \( N = \frac{Z^2pq}{d^2} \) Where

- \( N \) = desired minimum sample size
- \( z \) = standard statistics which is 1.96 for the level of confidence interval, 95%
- \( p \) = proportion of target population estimated to have characteristics being measured on previous studies
- \( q \) = 1 – \( p \)
- \( d \) = 0.05 (level of statistical significance)

**Inclusion Criteria**
- a) Staff, students, and other outpatients that were present at the health center and consented to be part of the study.
- b) The age bracket of 10 – 50yrs
- c) Patients whose blood sample tested positive for malaria parasite the case.

**Exclusion Criteria**
- a) Subjects that come with any pathological eye condition.
- b) Pregnant women.
- c) Those that have symptoms of malaria, but laboratory findings were negative.
- d) Subjects who are on medications for conditions that have similar signs and symptoms with malaria, or have symptoms to malaria
- e) Subjects who are on artificial tears therapy (Dry eye patients)
**Research procedure**

Upon approval, a mobilization and sensitization campaign was carried out with the assistance of the Head of the Department of the Medical Laboratory unit of the Department of Health Services, University of Benin, Benin City, Edo State. Those that were recruited for the study were screened for malaria parasites using Rapid Diagnostic test (RDT) Kits. The RDT determined the subjects that were positive for malaria. Microscopy was also done to determine the level of parasitaemia in the patients. The blood group and genotype of the patients were also determined.

**Rapid Diagnostic Test:** A pair of new gloves was used for each patient. The patient’s name was indicated on the test. The alcohol swap was opened. The patients thumb or fourth finger was swabbed with alcohol. With the aid of the lancet, the patient’s finger was pricked to obtain a drop of blood. Each lancet was discarded after use. The capillary tube was used in collecting and transferring the drop of blood into the square hole of the rapid diagnostic test kit. The capillary tube was then discarded in the sharps box. Romanovsky stain was added into the round hole. After 15mins of adding the buffer, the test result was read. A line near letter ‘C’ and a line near the letter ‘T’ indicated that the test was positive for malaria. The test was also considered as positive even if the line near the ‘T’ is faint. A line near letter the ‘C’ and no line near letter the ‘T’ was interpreted as negative for malarial. No line near letter the ‘C’ and one or no line near letter the ‘T’ was interpreted as invalid results. The test was repeated using a new RDT if no control line appears.

**Microscopy for malaria parasite test:** A blood specimen collected from the patient was spread as a thick or thin blood smear, stained with a Romanovsky stain (most often Giemsa), and examined with a 100X oil immersion objective. Visual criteria are used to detect malaria parasites and to differentiate (when possible) the various species (Adeoye and Nga, 2007). All selected patients were subjected to the following eye procedures: case history collection, test for visual acuity, ophthalmoscopy, Schirmer’s test, keratometry, and blink rate measurement. All findings from the tests were recorded into a case note.

**Case history:** This helped to rule out those with general and eye conditions that were excluded from the study. Patients were asked about the presence of systemic conditions like hypertension, diabetes, pregnancy, any current systemic medications. On ocular conditions, they were asked of presence of eye conditions like the sensation of eye pains, sandy or gritty sensations, and uncomfortable vision of the eyes.

**Visual Acuity:** This was performed using the standard Snellen visual acuity charts (literate and illiterate) at both distance and near. This ascertained the visual capabilities of the patients. The test was performed at 6metres from the chart. They were recorded appropriately.

**Ophthalmoscopy:** This was carried out using the Keeler direct ophthalmoscope. The subject was instructed to look at a distant object while the examiner held the instrument with the right hand in an attempt to examine the subject’s right eye and vice versa. The health of various tissues of the eye was checked for any pathology. This helped to rule out those with eye conditions to be excluded from the study ab initio.
Each participant was seated comfortably on improvised examination chair for all the three standard procedures (Schirmer’s test, Non-invasive Tear Break Up time and the Blink Rate) was performed in that order.

**Schirmer’s test for the quantity of tears:** A calibrated strip was inserted at the outer third of the lower right eyelid. The strip was left in place for 5mins. Thereafter, the length of the wetted part of the strip was noted and recorded. This procedure was carried out before and after malaria treatment between the hours of 8:00 am and 12:00 noon. Wetting of the strip of 15mm and above was considered normal (Guillebaud *et al.*, 2013).

**Non-invasive tear break-up time for the quality of tear film:**
The head and chin of the participant was placed on the head and chin rest of the Keratometer. Keratometer mires were placed at the center of the Cornea. The time taken for the mires to get blurred or distorted was noted and recorded. This procedure was carried out before and after malaria treatment between the hours of 8:00 am and 12:00 noon. A tear break-up time of 20 seconds and above was considered normal (Guillebaud *et al.*, 2013).

**The Blink Rate spread of the tear film**
While the participant was seated comfortably during case history, the number of times the participants blinked in 1min was noted without his or her knowledge. This procedure was carried out before and after treatment between the hours of 8:00 am and 12:00 noon. A blinks rate of 12 times and above in 1 minute was considered normal (Guillebaud *et al.*, 2013). Patients who participated in the research study were given incentives such as anti-malaria drugs for those diagnosed with malaria, vitamin C, and yeast were also provided. Two weeks later these procedures were repeated on those that reported back who complied with the instruction given to them. Findings were documented.

**Data Analysis**
Data were represented in tables and graphs. Percentages were calculated. Analysis was carried out to determine the statistical significance of difference using Chi-square, ANOVA, and Cramer's V. Statistical significance at the level of significance set at p< 0.05 using Statistical Package for Social Sciences (SPSS) Version 22.0.

**RESULTS AND DISCUSSION**
Figure 1 shows the result of the comparism of the mean quantity of the tear film within the males and females after treatment with Artesunate + Amodiaquine (Camosunate) and Artemether + Lumefantrine (Lonart) antimalaria tablets on one hand and the comparism between the males and females treated with these drugs on the other hand. The mean values of the quantity of tear film after treatment was higher with Camosunate than with Lonart in both sexes. A comparison of the effects of these drugs between the male and female participants also shows a higher effect on the mean tear quantity of tear film with camosunate tablets.
Table 1 shows the result of the number of patients and percentages of both sexes with the use of camosunate and lonart treatment of malaria infection with regards to the quantity of tear film. In all male patients, the quantity of tear film produced was sufficient while in the female patients the quantity of tear film was sufficient in all except for 12% that were treated with camosunate. Despite the good association between the use of camosunate and tear film in females, its effect was not significant.

Table 1: Association between type of antimalarial drug used and the post treatment quality of the tear film produced in male and female patients.

<table>
<thead>
<tr>
<th>Antimalaria drugs</th>
<th>Categorization/ classification of tear film quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male No (% examined)</td>
</tr>
<tr>
<td></td>
<td>Insufficient</td>
</tr>
<tr>
<td>Camosunate</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Lonart</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Cramer’s V = 0.199, p = 0.002 Good association

Table 2 shows the result of the comparison of the quality and spread of the tear film within the male and female patients with camosunate and lonart treatment of malaria infection on one hand and the comparison of the quality and spread of the tear film between the males and females on the other hand. The mean values of the quality of tear film were slightly higher with lonart (40.2 s) than with camosunate (40.0s) in the male patients but were the same in the females. Comparison of the effects of both drugs on the participants revealed no significant difference. For the effects of both drugs on the spread of tear film on both participants, the result shows that the mean value of the spread of tear film was slightly higher with camosunate (15X) than with lonart (13X) in the male participants but the reversed was the case in the females (Camosunate 16X, Lonart 18X). A Comparison of the effects of both drugs on the patients revealed that the use of camosunate treatment enhanced the spread of tear film in both sexes significantly (p <0.001).
Table 3 shows the result of the number of patients and percentages of both sexes with the use of camosunate and lonart treatment of malaria infection with regards to the quality of tear film. Tear quality was sufficient in all patients examined of both sexes and there was no association between the use of the drugs and the mean tear film quality of the tear film of Participants. Despite the good association between the use of camosunate and tear film in the females, the effect was not significant. The result of the number of patients and percentages of both sexes with the use of camosunate and lonart treatment of malaria infection with regards to the spread of tear film shows that all the participants had sufficient spread of the tear film. Despite the good association that existed, their effect was not significant (Table 4).

**Table 2:** Distribution of the mean values of the quality, and spread of the tear film in both male and female patients as according to regimens of malaria treatment

<table>
<thead>
<tr>
<th>Malaria treatment type</th>
<th>Male</th>
<th></th>
<th>Female</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>T</td>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Tear quality (seconds)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Camosunate</td>
<td>40.0</td>
<td>-2.250</td>
<td><strong>0.026</strong></td>
<td>40.0</td>
</tr>
<tr>
<td>Lonart</td>
<td>40.2</td>
<td></td>
<td></td>
<td>40.0</td>
</tr>
<tr>
<td>Tear spread (blinks/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Camosunate</td>
<td>15.0</td>
<td>31.972</td>
<td><strong>&lt;0.001</strong></td>
<td>16.0</td>
</tr>
<tr>
<td>Lonart</td>
<td>13.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 3:** Association between the type of antimalarial drug used and the tear film quality in male and female patients after exposure to malaria treatment

<table>
<thead>
<tr>
<th>Drug type</th>
<th>Male</th>
<th></th>
<th>Female</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No(%) examined</td>
<td></td>
<td>No(%) examined</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Insufficient</td>
<td>Sufficient</td>
<td>Total</td>
<td>Insufficient</td>
</tr>
<tr>
<td>Camosunate</td>
<td>0(0.0)</td>
<td>67(100.0)</td>
<td>67(100.0)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Lonart</td>
<td>0(0.0)</td>
<td>113 (100.0)</td>
<td>113 (100.0)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>0(0.0)</td>
<td>180 (100.0)</td>
<td>180 (100.0)</td>
<td>0(0.0)</td>
</tr>
</tbody>
</table>

Cramer’s V = N.A

**Table 4:** Association between the type of antimalarial drug used and tear film spread in male and female patients after exposure to malaria treatment

<table>
<thead>
<tr>
<th>Drug type</th>
<th>Male</th>
<th></th>
<th>Female</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No(%) examined</td>
<td></td>
<td>No(%) examined</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Insufficient</td>
<td>Sufficient</td>
<td>Total</td>
<td>Insufficient</td>
</tr>
<tr>
<td>Camosunate</td>
<td>0(0.0)</td>
<td>67(100.0)</td>
<td>67(100.0)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Lonart</td>
<td>0(0.0)</td>
<td>113 (100.0)</td>
<td>113 (100.0)</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>0(0.0)</td>
<td>180 (100.0)</td>
<td>180 (100.0)</td>
<td>0(0.0)</td>
</tr>
</tbody>
</table>

Cramer’s V = 0.201, p = 0.007; Good association
The study of the effect of the type of malaria treatment on the mean quantity, quality, and spread of the tear film of the study patients as well as the concomitant association tests before and after treatment of malaria infections revealed that the use of Camosunate, was a better treatment option (as the mean tear film quantity was seen to be higher in both sexes) than when Lonart was used for treatment. Tear sufficiency was more in females than males when lonart was the drug of choice. Perhaps biological reasons may account for this. It is not clear how the antimalarial treatment influences blinking as there was no antecedent study to back this. The association test findings of Camosunate and Lonart as it affects the quantity of tear film in both sexes shown in Table 1 was good but insignificant (Cramer's V = 0.199, p = 0.002). This suggests that treatment of malaria infection improves tear film sufficiency probably by the reduction in the inflammation of the skeletal muscles of the eyelid, although there is no study in the literature to support this. Neither treatment option influenced the outcome of the distribution of the mean tear film quality in both sexes.

The use of Camosunate treatment enhanced tear film spread in both male and female patients significantly (p < 0.001), compared to the use of Lonart as a treatment option. Association test for the mean quality of tear film revealed that irrespective of sex, the mean tear quality was not impaired by the incidence of malaria. The use of either Camosunate or Lonart in correcting tear film spread was effective in both sexes as all the counts were sufficient post-treatment. However, results did not show which of the treatment options was better as all patient benefitted from both treatment options. The association test between the spread of tear film and the treatment options revealed a good association in both sexes (Cramer's V = 0.20) but insignificant (p = 0.007).

The effect of age on the Mean quantity, quality and spread of the tear film of the outpatients before and after treatment of malaria infections was studied. The result obtained revealed generally that the mean tear film quantity was greater in female than male patients before and after malaria treatment. This occurred among older patients at the younger age but reduced with advancing age. This result is similar to the findings of Collier in 2015 who in her studies on tears gave the biological reasons as to why women shed more tears than men. Reduced sex hormone levels in women after menopause cause dryness in all mucosal tissues as well as affects their tear production negatively. In men also, the observed reduction in the quantity of tear film in this study correlates with collier’s work that decreasing androgen levels with advancing age may lead to the reduction of tear production. The experimental androgen treatment of mice with Sjogren syndrome to increase tear production also substantiates this idea. In young individuals, the hormone testosterone in men appears to inhibit tearing while the hormone prolactin which is found in higher levels in women promotes it. Tear quantity improved with malaria treatment especially in males aged between 25 and 39. Unlike in males, the effect of age on the quantity of tear film was significant (p <0.001) and with a very strong association (Cramer's V = 0.448) in females.

CONFLICTS OF INTERESTS

The authors declare that there are no conflicts of interest.

REFERENCES


