Alterations in the Tear Film and Ocular Surface in Pediatric Migraine Patients

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Research Article

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Abstract

**Purpose:** To evaluate the ocular surface (OS) parameters in the pediatric migraine patients (PMPs).

**Methods:** This prospective case-control designed study consisted of 51 PMPs (PMP Group) and 55 healthy pediatric patients (HPP Group). In all participants were evaluated of tear function by subjective (Ocular Surface Disease Index (OSDI) questionnaire), objective (Schirmer tear test (STT) and tear film break-up time (TBUT)), clinical and laboratory investigations (conjunctival impression cytology (CIC)). The PMP Group was divided into 2 according to their aura.

**Results:** The mean age and gender distribution of the study groups were almost the same (for both of them: P > 0.05). In the PMP Group, both the STT value and the TBUT value were significantly lower than those determined in the HPP Group (P = 0.021, P = 0.018, respectively). In the PMP Group the OSDI scores of were higher than those in the HPP Group (P = 0.032). In the PMP Group, the goblet cell density (GCD) values were lower than those in the HPP Group (P = 0.01). In regard to the aura, the TBUT and STT values were non-significantly lower in the PMP aura-positive group than in the PMP aura-negative group (for both of them: P > 0.05). The OSDI assessment was similar in both of the groups. In regard to the goblet cell count, it was observed to be less in the PMP aura-positive group than in the PMP aura-negative group (P = 0.01).

**Conclusion:** Influence of the OS in children with migraine was also demonstrated with samples taken from the conjunctiva. These changes were also demonstrated by objective tests such as STT and TBUT. Both clinical objective evaluations and pathological changes were more prominent in the migraine with aura group.

Introduction

Although a throbbing headache is mainly observed in migraine, it is a neurological disease in which nausea, vomiting, mood changes, and a hypersensitivity towards environmental factors are observed [1]. The most common types of headaches in children are usually migraine and tension headaches [2]. As for migraine, the prevalence, reported as 3% during the preschool period, increases over time and reaches 8–23% after secondary school [3–5]. In the 8-year-old patient population, migraine prevalence is nearly equal among females and males, and in older age groups, males have it less than females [6].

In migraine, there are headaches first, sensitivity to light and sound, dizziness, and increased pain while performing physical activity and increased aura [7, 8]. In these patients, bright scotoma and blurred vision are the most predominantly seen visual symptoms, especially with aura, and this is followed by somatosensory symptoms such as slow speech, dyspraxia, and hand numbness [9]. Fatigue, emotional changes, and stiffness in the neck are commonly seen premonitory symptoms in pediatric migraine [10]. At the same time, postdrome symptoms such as thirst, extreme drowsiness, disturbances in vision, cravings, paresthesia, and pain in the eyes are seen in 80–85% of patients in this population [11]. Migraine is a chronic disease that includes both neuronal and vascular mechanisms, the
pathophysiology of which has not been fully elucidated [12]. Another point of view is that there is a basis for neurovascular inflammation in brain vessels [12, 13]. High levels of both interleukin and inflammatory cytokines were detected, especially during interictal periods and acute migraine attacks [14]. Deteriorated tear homeostasis on the ocular surface (OS) may be the cause of dry eye (DrE), which is characterized by symptoms of irritation. Increased evaporation of the tears and ocular as well as systemic pathophysiological mechanisms are responsible for hyperosmolarity [15]. The reason why some researchers have opined that a connection exists between migraine and tear function is that migraine has a complex pathophysiology that includes neuronal and vascular mechanisms. There are no studies on this in the pediatric population in the literature. In our study, histopathological evaluations in pediatric migraine were supported by objective and subjective results.

Methods

Ethics Approval

The current work was a prospective case-control study conducted together in the Department of Pediatric Neurology and Ophthalmology of a tertiary university hospital. All applications made within the scope of this research content adhered to the Declaration of Helsinki. The study protocol was given approval by the institutional committee, which is part of the local ethics committee for the clinic at which the study was performed. All study participants, in addition to their parents, gave the necessary informed consent in written form before being accepted for enrollment into the study.

Inclusion and Exclusion Criteria and Examinations

Pediatric migraine patients (PMPs) with and without aura who were referred from the pediatric neurology clinic and applied to the eye clinic consecutively comprised the PMP Group, and healthy pediatric patients (HPPs) who consecutively applied to the eye clinic comprised the HPP Group, as the controls. Of the 106 subjects, 106 eyes, including 51 eyes of 51 PMPs and 55 eyes of 55 age/sex matched HPPs, were included as the study population.

Migraine severity was determined by a disability questionnaire called the Pediatric Migraine Disability Assessment Score, or the pedMIDAS, was administered to pediatric patients by a pediatric neurologist [20]. The demographic structure and clinical data of the patients were evaluated. Migraine type, disease duration, number, and duration of attacks (every 3 months), accompanying symptoms (nausea, vomiting, photophobia, phonophobia) were recorded. The migraine group consisted of newly diagnosed individuals and those who did not take any medication other than analgesics within 24 hours.

The PMP Group was divided further into 2 sub-groups according to the presence of aura. Those with migraine with aura were designated as the PMP aura-positive group, while those with migraine without aura were designated as the PMP aura-negative group. A control group was formed by matching the same age and gender from healthy children who came to annual routine check-ups (the HPP Group).
Inclusion criteria set for the study participants were given approval by a pediatric neurologist (R.I.) and an ophthalmologist (E.A.). Participants who were aged younger than 6 or older than 18, and those with various systemic diseases, such as hypertension, autoimmune disease, thyroid disease, or heart disease, were excluded from the study. The criteria set for ocular exclusion comprised having a history of any kind of ocular surgery, a corneal pathology, history of trauma, visual acuity determined to be < 20/20, choroidal disease, or an optic disc disorder, refractive error determined to be ≥ ± 1 D, an axial length determined to be > 24 mm, and an intraocular pressure (IOP) determined to be > 21 mm Hg.

In the routine ophthalmological examination of the patients who participated in the study, first, visual acuity (Snellen) measurement was performed, then, IOP was measured using pneumatometer, and an anterior segment as well as a fundus examination was done via slit lamp biomicroscopy, respectively.

Ocular Surface Disease Index score

The Ocular Surface Disease Index (OSDI) questionnaire, with a standardized content of 12 items specified by the Allergan Inc. Outcome Research Group (Irvine, CA, USA), was used to assess both rapidly and reliably the symptoms of irritation on the OS in participants. The pediatric patients accepted for participation in this study were instructed to complete the OSDI form before any ophthalmological examination was performed. Pediatric participants evaluated and filled out the questionnaire without any time limit and without any help from the relevant ophthalmologist. An experienced ophthalmologist (Dr. E.A) explained the questionnaire questions to all pediatric participants. The scores were asked to be graded as 0-1-2-3-4 points: 0 for “never” and 4 points for “always” as answers. After completing the questionnaire, calculation of the OSDI score was done via use of the following formula: \( \left( \frac{\text{the sum of the scores}}{\text{the total number of questions that were answered}} \right) \times 25 \) [16].

Tear film break-up time

At 30 minutes after the ophthalmological evaluation, Schirmer tear test (STT) and tear film break-up time (TBUT) tests were all done with anesthesia. In the TBUT test, fluorescent staining of the cornea of the patients (ERC Medical Products, Ankara, Türkiye) was performed and then, they were instructed to blink 3 times consecutively. After using a fluorescent dye solution on the OS, their tear film was evaluated with slit lamp microscopy. The time was measured from the moment the two eyelids were opened after the third blink until a dry spot first became visible in the cornea. The average of 3 measurements taken consecutively was considered the TBUT. Patients with a TBUT of less than 10 seconds were evaluated in favor of dry eye disease (DrE-D).

Schirmer tear test

A strip of Whatman #41 filter paper (ERC Medical Products, Ankara, Türkiye), standardized for use in the STT was placed in the area close to the lateral canthus, 1/3 of lateral tarsal conjunctiva of the lower lid. It remained there for 5 minutes until wetting of the filter paper, and after the time expired, the amount of wetness on the filter paper was measured in millimeters. This value was recorded as the result of the STT.

Conjunctival impression cytology (CIC)
First, 5 mg (5%) proparacaine HCl (Alcaine; Alcon Laboratories, S.A. Alcon- Covreur N.V. Puurs/ Belgium) drops were applied to the patients for anesthetic purposes. Then, a previously cut 4 × 5-mm piece of cellulose nitrate filter (Whatman; GE Healthcare, Chicago, IL, USA) was placed approximately 4–5 mm from the cornea of the bulbar supero-temporal conjunctiva.

The filter was pressed lightly, and then, after about 5 seconds, it was removed from the conjunctiva via the use of a pair of forceps. Afterwards, the samples were placed in small tubes that contained a solution of 95% ethanol and stained manually using periodic acid Schiff (PAS) stain. In the last step, conjunctival impression cytological specimens stained with PAS were blindly examined by a pathologist (Dr.B.A.T.) with a light microscope. Pathologist microscopic examination was performed on the basis of the Nelson scoring system, which is based on epithelial cell morphology and the goblet cell count and graded from 0 to 3 according to Nelson's classification [17] (Fig. 1).

**Statistical analysis**

IBM SPSS Statistical Statistics program for Windows version 24.0 (IBM Corporation, Armonk, New York, USA) was used to conduct all of the statistical analyses. The participants’ right eyes only were included for use in the statistical analyses. Histograms and probability plots, in addition to analytical methods that included the Kolmogorov-Smirnov test and Shapiro-Wilk test were utilized when testing the normality of the data. The results that were obtained from the descriptive analyses were presented as the mean and standard deviation (SD). For pairwise comparison of the study groups, the student t-test was used in the analysis of the variables determined to be normally distributed, whereas the Mann-Whitney U-test was used for the variables determined to be abnormally distributed. The chi-square test was utilized in the comparison of the categorical variables. Statistical significance was deemed to be $P < 0.05$ in all measurements.

**Results**

The PMP Group comprised 51 participants, while the HPP Group comprised 55 participants. The mean age in the PMP Group was $14.25 \pm 2.35$ (10–17), whereas that in the HPP Group was $13.13 \pm 2.86$ (10–17). In the PMP Group, the ratio of male to females (RM/F) was 21/30, while that in the HPP Group was 21/34. In regard to the demographic characteristics of the PMP and HPP groups, things like the mean age and RM/F were not that different (for both of them: $P > 0.05$). When considering the sample size of the PMP Group subgroups, it was 11 in the PMP aura-positive group and 40 in PMP aura-negative group. The mean ages and RM/Fs were also not that different between the PMP Group subgroups (for both of them: $P > 0.05$).

While the mean TBUT and STT values in the PMP Group were lower in comparison to those in the HPP Group, with statistical significance (for all of them: $P < 0.05$), OSDI scores were non-significantly higher ($P = 0.123$) (Table 1).
Table 1
Details of the clinical and laboratory assessments.

<table>
<thead>
<tr>
<th>Clinical findings</th>
<th>PMP Group (N: 51)</th>
<th>HPP Group (N: 55)</th>
<th>P-value→</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Tf-BUT (s)</td>
<td>11.8 (6–17)</td>
<td>14.8 (9–20)</td>
<td>0.006</td>
</tr>
<tr>
<td>Median Schirmer-1 (mm)</td>
<td>9.6 (5–17)</td>
<td>11.4 (6–19)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Median OSDI score</td>
<td>12.2 (9–23)</td>
<td>9.4 (4–18)</td>
<td>0.123</td>
</tr>
<tr>
<td>Impression cytology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade [categorical (0/1/2/3)]*</td>
<td>40/11/0/0</td>
<td>50/5/0/0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Median grade</td>
<td>0.6 (0–3)</td>
<td>0.3 (0–2)</td>
<td>0.044</td>
</tr>
<tr>
<td>Mean goblet cell count</td>
<td>325.9 ± 180.5 (90–600)</td>
<td>410.3 ± 190.5 (120–850)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Median neutrophil count</td>
<td>0.7 (0–19)</td>
<td>0.3 (0–15)</td>
<td>0.450</td>
</tr>
<tr>
<td>Median lymphocyte count</td>
<td>0.1 (0–2)</td>
<td>0.1 (0–2)</td>
<td>0.897</td>
</tr>
</tbody>
</table>

PMP: Pediatric migraine patients, HPP: healthy pediatric patients
Tf-BUT: tear film break-up time; OSDI: Ocular surface disease index (OSDI)
* Grades 0 and 1 are considered normal, and grades 2 and 3 are considered as abnormal.

± Chi-Square test
→ Independent t test

In the cytologic assessment of the conjunctiva, 7 of the 58 samples in the PMP Group were excluded. And of these, 3 had insufficient cells and 4 were insufficiently stained. Moreover, 51 sufficient samples were assessed and of these, 11 were grade 1 and 40 were grade 0. The mean goblet cell density (GCD) was 238.7 ± 152.5 cells/mm² in the PMP Group. In the HPP Group, 4 of the 59 samples were excluded due to insufficient material. Thus, evaluated were 55 samples: 5 as grade 1 and the rest as grade 0. The mean GCD was 399.2 ± 165.06 cells/mm². The GCD values in the PMP Group were lower in comparison to those in the HPP Group (P < 0.001) (see Table 1). The detailed analysis of the OS parameters of those in the PMP sub-Groups is listed in Table 2.
**Table 2**  
Comparison of clinical and laboratory evaluations between the subgroups

<table>
<thead>
<tr>
<th></th>
<th>PMP aura-positive group (n: 11)</th>
<th>PMP aura-negative group (n: 40)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Tf-BUT (s)</td>
<td>11.6 ± 3.1</td>
<td>12.1 ± 4.2</td>
<td>0.450</td>
</tr>
<tr>
<td>Median Schirmer 1 (mm)</td>
<td>8.9 ± 4.8</td>
<td>10.7 ± 4.1</td>
<td>0.064</td>
</tr>
<tr>
<td>Median OSDI score</td>
<td>13.1 ± 4.3</td>
<td>11.8 ± 3.8</td>
<td>0.530</td>
</tr>
<tr>
<td>Grade [categorical (0/1/2/3)]</td>
<td>7/4/0/0</td>
<td>33/7/0/0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Median grade</td>
<td>0.7 ± 0.86</td>
<td>0.5 ± 0.63</td>
<td>0.072</td>
</tr>
<tr>
<td>Mean goblet cell count</td>
<td>315.9 ± 192.9</td>
<td>370. ± 144.9</td>
<td>0.02</td>
</tr>
<tr>
<td>Median neutrophil count</td>
<td>0.9 ± 2.2</td>
<td>0.5 ± 1.9</td>
<td>0.128</td>
</tr>
<tr>
<td>Median lymphocyte count</td>
<td>0.1 ± 0.9</td>
<td>0.1 ± 0.7</td>
<td>0.890</td>
</tr>
</tbody>
</table>

PMP aura-positive group (pediatric migraine with aura), PMP aura-negative group (pediatric migraine without aura)

Tf-BUT: tear film break-up time; OSDI: Ocular surface disease index (OSDI)

¬ Grades 0 and 1 are considered as normal, and grades 2 and 3 are considered as abnormal.

Results are denoted as the mean ± standard deviation.

*Paired t test

**Discussion**

DrE is a multi-factorial OS disease that is also known to occur with other ocular symptoms, tear film homeostasis imbalance/loss, OS damage as well as inflammation, in addition to neurosensory abnormalities which are involved in its etiology [15]. In ophthalmology, histopathological studies for diagnostic purposes in OS-related diseases have been increasing in recent years. The findings that resulted from this current study might provide important information about the pathogenetic effects of migraine on the OS in pediatric patients diagnosed with migraine.

Currently, within the literature, there is not a high volume of articles evaluating tear function in adult migraine patients [15, 18]. Evaluated in this current study, were the OSDI questionnaire, TBUT, STT, and CIC by dividing pediatric patients with migraine into subtypes as migraine with and without aura to investigate whether or not OS changes developed in children diagnosed with migraine and then compare the results obtained with those of healthy children. With CIC, morphological, cytological, and immunocytochemical changes associated with DrE can be analyzed by taking samples from the conjunctival surface [19]. With this method, it is possible to detect OS changes like squamous metaplasia...
or goblet cell loss during the early stages [20, 21]. When the pathological materials taken were grouped according to the Nelson classification, grades 0–1 was normal; grades 2–3 was considered abnormal [16].

Among the important aspects of our research was our investigation of cytological changes in pediatric patients with migraine by CIC, which has been recommended by some researchers as the gold standard when testing for DrE-D. The findings that resulted from this current study might provide important information about the pathophysiological effects of migraine on tear functions in pediatric participants [15].

Based on the findings obtained in this current study, there were no participants that had abnormal cytology such as grade 2 and grade 3. A decrease that was statistically significant was seen in the GCD in both of the PMP sub-Groups compared to the HPP Group. Some of the patients in the PMP Group exhibited grade-1 cytology, which was characterized by the presence of epithelial cells that were slightly large and polygonal, a nucleus-to-cytoplasm ratio of 1/3, and the GCD which exhibited a slight decrease.

There may be several reasons why the CIC on the OS did not change as morphological grades 2 and 3 in the participants in the PMP Group: 1) Because the study population was made up of pediatric patients, morphological changes on the OS may not have occurred yet, since the disease duration was shorter 2) It may be that the regeneration capacity of the cells in the pediatric population is higher than in the adult population and that the regeneration ability has prevented the changes in the conjunctival morphology. 3) Due to the nature of our study, it may be that we did not choose to include patients diagnosed with DrE who were morphologically grades 2 and 3. Another important finding of this study was that the histopathological abnormalities as well as the GCD, exhibiting a decrease, were strongly associated with migraine with aura. The low TBUT and STT values shown in children with migraine were also supported by histopathological findings in the conjunctival material taken.

In the literature, it has been shown that DrE that is immune-mediated and/or inflammatory can occur in adult patients with migraine [18]. The histopathological abnormalities and decreased goblet count observed in the CIC in this study can be considered as the cause of migraine causing inflammatory pathways, which may in fact play a role in changes seen in clinical manifestations related to tear function in children.

Mucin, water, and lipid are the main constituents making up the tear film. Pediatric patients with migraine are at risk of adverse effects on these components. The low STT results in our study may be related to lacrimal gland dysfunction (GD), which is the gland in control of secreting the watery parts of tear film. The cornea is densely packed with nerves, which transverse along the path of the ophthalmic section of the trigeminal nerve. Some animal studies have suggested the reason for the decreased tear secretion may have a connection with decreased trophic effect from the trigeminal sensory nerves that are located on the cornea and conjunctiva [22]. In another study, it was shown that the length as well as the density of the trigeminal nerve fiber decreased in patients diagnosed with migraine [23]. The reason for the low
STT results in our study may be the effect of a reduction in the excitatory signals coming from the OS and going to the lacrimal gland as a result of decreased corneal sensation.

The TBUT test shows any instability that is present in the tear film. This test is not just for the absence of the film's aqueous layer, it is also for the deficiency of the mucin and/or lipid component of the film which is produced via the meibomian glands as well as the conjunctival goblet cells. The low detection of the TBUT test may be related to the decreased mucin content together with the decreased goblet cells. Another possible mechanism for the low TBUT values in these patients may be the effects of lipid metabolism detected in patients with migraine [24]. The lipid layer protects against premature film evaporation and ensures its continuity. Another possible mechanism for the low TBUT values in these patients is thought to be associated with an accompanying lipid layer disorder and meibomian GD in pediatric patients with migraine [24].

Meibomian GD should be taken into consideration as possibly being a mechanism for these changes in the OS associated with pediatric migraine patients and DrE. However, the validity of this hypothesis should be tested with further investigations such as meibography, with further studies investigating the association with pediatric migraine patients and DrE at longer follow-up.

According to the consensus in both the literature and ophthalmology practice, the detection of TBUT results < 10 s and STT results < 5 mm is considered to be in favor of DrE. According to the results obtained this current study, although the measurements for the STT and TBUT were not as high in the children diagnosed with migraine, the median values obtained for these groups were not considered to be low enough to be seen as abnormal for either test or to diagnose DrE-D.

However, it is of high importance to detect early changes in objective clinical examinations related to tear function, especially when taking into consideration the chronic course of DrE-D starting from the point of diagnosis until the end of the patient's life.

Köktekir et al. with 33 adult migraine patients and 33 control patients, and also Saraç et al. with 46 adult migraine patients and 50 control patients, found statistically significantly lower TBUT and STT values in adult patients with migraine. Similarly, Çelikbilek et al. found lower TBUT and STT values in adult patients with migraine, although it was not statistically significant. In this context, the findings obtained in this current study, which comprised pediatric participants, are quite consistent with reported results in the literature. Another important outcome determined in our study was that worse STT and TBUT values were seen in the PMP aura-positive group. These results are in agreement with previous studies. Although all these studies were performed on adult participants, our results in this study have indicated that one should expect to see effects that are similar to this in pediatric participants with migraine. The strength of this study is that it evaluates DrE parameters in pediatric participants diagnosed with migraine and is the first study on this subject.

When OSDI scores are evaluated, there are 2 possible outcomes: first, values of 0–25 are normal; Second, values > 25 are considered in favor of DrE-D. The OSDI is a clinician's quantitative measure of the effects
of DrE-related ocular irritation symptoms, consisting of subjective assessments of the patient to assess how severe the DrE is. Schiffman et al.\textsuperscript{16} reported a specificity of 79% and a sensitivity of 60% for the OSDI questionnaire. The sample of this current research did not include DrE patients. Moreover, the OSDI scores recorded in both of the groups were well within a normal range. In this study, the results of the OSDI scores and the objective test results, like the TBUT and STT, which were determined to be worse in the participants diagnosed with migraine, were not combined. There could be several reasons for this situation. The first reason may be that the patients in the study group consisted of a pediatric population. A study done by Han et al.\textsuperscript{26} showed that children diagnosed with DrE may not exhibit the same number of symptoms of as adults diagnosed with similar DrE conditions. A possible explanation for this might possibly be that children may not have the same level of discomfort or pain, and therefore they may describe the discomfort caused by OS disorder less [26]. Second, it may have something to do with the method in OSDI scoring having a subjective nature and the fact that the sample was not made up of actual DrE patients. Also, this is not that unusual, because in previous studies, some researchers likewise reported a discrepancy similar to this between the OSDI score and tests like the TBUT and STT [16].

Although the pathogenesis of migraine has not been clarified, it is thought to be a type of neurovascular headache [18]. Neural events have an effect on blood vessels by causing them to dilate, exacerbating pain, and leading to greater activation of the nerves [27]. Trigeminovascular input coming from the meningeal vessels is the main pain pathway. However, the exact mechanism by which migraines are triggered and the sequence of events after being activated have not yet been fully understood. The cornea is made up of very densely packed trigeminal nerve endings that are believed to have involvement in the process of headaches with pain [28]. Kinard et al. conducted an investigation of the structural differences occurring in corneal nerve plexuses in patients diagnosed with chronic migraine via in vivo corneal confocal microscopy [23]. The density and length of nerve fibers were found to be lower in the patients diagnosed with migraine than in the healthy individuals in their study. These results are supportive of the hypothesis that the trigeminal system has a vital role in the way in which migraines develop [18]. These findings showed consistency with the results obtained for the CIC, STT and TBUT, which were determined to be more significant in the aura-positive migraine patients in our study. Future studies with focus on treatments for objective DrE in patients diagnosed with migraine, and especially with aura-positive migraine patients, may be able to reveal clearer insight regarding this connection.

Compared to the literature, the patient population was pediatric, and the patients were grouped as aura-positive migraine patients and aura-negative migraine patients, which were strengths of this research. This study expands our knowledge on this subject and makes two important contributions to the literature: 1) Although there is no DrE in patients diagnosed with migraine, DrE may start in the pediatric period, especially in the aura-positive migraine patients. 2) Contrary to the previous studies, it is important to remember that patients with migraine may have DrEs, not only in the adult population but also in the pediatric population. Based on this information, possible DrE findings should be considered, especially in pediatric patients with migraine resistant to conventional treatments.
The limitations of our study are as follows: meibography, in vivo confocal microscopy, and the absence of tear film osmolarity were not used. In addition, whether the diseases are acute or chronic does not have the same effect on tear function. Conducting a sub-group analysis with the aim of determining the duration of migraine in patients could provide important insight regarding the risk that is associated with OS damage. As far as we have been able to determine, this study represents the first research to have evaluated tear function parameters in pediatric patients with migraine and divided and evaluated pediatric patients based on whether they were aura-positive or aura-negative. Examination of tear function by subjective (OSDI questionnaire), objective (STT and TBUT), clinical and laboratory investigations (CIC), and then reporting these results comprise the important strengths of this work.

In summary, changes occur in the OS in children diagnosed with migraine. These changes are also demonstrated by the STT, TBUT measurements, and histopathological evaluation from the conjunctiva. Significant changes in the histopathological as well as the clinical findings are seen more prominently, especially in aura-positive migraine patients.

Declarations

Author contributions All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by AA and EA. The manuscript was written by AA, EA, and GA, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Conflict of interest None declared

Ethical approval Approval for the study was given by the clinical research ethics committee of Adıyaman University (decision no: 2022/12).

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Presentation at a meeting: It will not be presented at a meeting.

References


Figures

Figure 1

A) Control group (higher goblet cell number); Grade 0. Conjunctival epithelium and goblet cells took on cellulose paper by impression cytology.
B) Pediatric migraine patients without aura; Grade 0. Conjunctival epithelium and goblet cells took on cellulose paper by impression cytology.

C) Pediatric migraine patients with aura; Grade 1, Conjunctival surface epithelial cells with a nucleus: cytoplasm ratio of 1:2 to 3 with decreased number of goblet cells