Risk of dry eye in headache patients: a systematic review and meta-analysis

Shuyi Liu, He Dong, Shifeng Fang and Lijun Zhang

OBJECTIVES: The objective of this meta-analysis was to identify whether headache increase the risk of dry eye disease (DED).

METHODS: PubMed, Web of Science, Cochrane Library and EMBASE databases were searched for relevant studies. The odds ratio (OR) of DED in all-cause headache was calculated via Stata software. To explore the source of heterogeneity, subgroup and sensitivity analyses were conducted. Funnel plots and Egger’s test were performed to assess publication bias.

RESULTS: This meta-analysis included 11 studies. Pooled analysis indicated that all-cause headache was related to a higher risk of DED (OR = 1.586, 95% CI: 1.409–1.785, I² = 89.3%, p < .001). Migraine headache, tension headache and cluster headache were all related to a higher risk of DED (OR = 1.503, 95% CI: 1.369–1.650, I² = 81.8%, p < .001; OR = 1.610, 95% CI: 1.585–1.635, p < .001; OR = 2.120, 95% CI: 1.104–4.073, p = .024), respectively. The risk of DED in case–control studies was slightly higher than in cross-sectional studies and cohort study (OR = 1.707, 95% CI: 1.291–2.258, I² = 85.0%, p < .001; OR = 1.600, 95% CI: 1.590–1.610, I² = 0.0%, p < .001; OR = 1.440, 95% CI: 1.096–1.893, p = .009), respectively. Subgroup analysis in territory type showed that all-cause headache in America, Europe, Asia and Oceania were all related to a higher risk of DED.

Conclusions: This study indicates that headache is related to a higher risk of DED, especially in the migraine patients. These results suggest that headaches should be regarded as an independent risk factor for DED.

KEY MESSAGES

- In this meta-analysis, 11 studies (one cohort study, four case–control studies and six cross-sectional studies) covering 3,575,957 individuals were included.
- Pooled analysis indicated that all-cause headache was related to a higher risk of dry eye (OR = 1.586, 95% CI: 1.409–1.785, I² = 89.3%, p < .001).
- These results suggest that headaches should be regarded as an independent risk factor for dry eye.

Introduction

Dry eye disease (DED) is the most prevalent chronic ocular surface disorder in clinical practice, with constant or intermittent symptoms of ocular dryness or pain, foreign body or burning sensation, photophobia and visual impairment [1–3]. The incidence of DED ranged from 5% to 50%, significantly in association with public health and financial burden worldwide [4,5]. The pathogenesis of DED is complex and multifactorial, but typically involves the production reduction or excessive evaporation loss from the tear film [6]. In recent years, there has been a rising awareness of the prevention strategy in DED, such as risk factor management, may be more cost-effective than disease treatment at the population level [7]. Several previous studies have explored the risk factors, such as gender, age, smoking, diabetes, contact lens use, ocular surgery history, psychiatric disorders [8–12]. The impact of headache on DED is easily neglected in clinical practice.

Headache has arisen as a public health burden, ranked as the second leading cause of disability worldwide. Headache is characterized as a lower life quality, reduced productivity and increased economic expenses [13,14]. Several observational studies have...
explored the risk for DED in headache that patients with headache are more prone to have DED than those without [15,16]. However, the precise nature is still unknown. Therefore, we carried out a study to identify whether headache is related to a higher risk of DED.

**Methods**

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards [17], and the protocol was preregistered in the International Prospective Register of Systematic Reviews (PROSPERO) platform (CRD42022333038).

**Data sources and searches**

We systematically searched the databases including PubMed, Cochrane Library, EMBASE and Web of Science until 12 May 2022. The literature searches were restricted to English language publications and without restriction of countries or study type. The search strategy utilized both medical subject headings (MeSH) and keywords. The terms included ‘Dry Eye Syndromes’, ‘Headache’ and ‘Migraine Disorders’. We manually reviewed the references of the included studies as well as other published systematic reviews for seeking additional relevant studies. The detailed search strategy was presented in Supplementary Materials 1.

**Inclusion criteria**

The eligible studies had to meet the criteria as follows: (1) case-control, cross-sectional or cohort study; (2) investigations of the association of all-cause headache with the risk of DED; (3) the risk of DED as the outcome, and presented as an adjusted odds ratio (OR) and its corresponding 95% confidence interval (CI). In our study, ‘all-cause headache’ was characterized as ‘patients suffered from any form of primary headache in the history’, such as migraine, cluster headache or tension headache and others. We selected the study with the longest follow-up or the largest number of individuals when more than one study reported data based on the same population.

**Exclusion criteria**

Exclusion criteria was as follows: conference abstract, study protocol, duplicate publication or study without interested outcomes.

**Study selection**

Based on predefined criteria, two authors (SY Liu and LJ Zhang) independently selected the titles and abstracts of all records. After the initial screening, duplicate records and unrelated articles were excluded. Following that, we downloaded the full texts of these articles and conducted a thorough review to identify all eligible articles. Discussions were performed with SF Fang if there was a divergence.

**Data extraction**

SY Liu and LJ Zhang independently extracted the relevant data as follows: first author, publication year, country or region, study type, sample size, study period, age, diagnosis of DED and headache, headache type and confounders adjusted. SF Fang checked the data. Discussions were performed with SF Fang if there was a divergence.

**Risk of bias assessment**

We assessed the quality of a cohort or a case-control study with the Newcastle-Ottawa Quality Assessment Scale (NOS) [18] from three aspects: selection, comparability and outcome (cohort study) or exposure (case–control study). And we scored according to the following criteria: low quality (0–3), moderate quality (4–6) and high quality (7–9).

We assessed the quality of a cross-sectional study with the American Agency for Health Care Quality and Research’s (AHRQ) cross-sectional study quality evaluation items [19]. We assessed an item as ‘1’ if the answer was ‘YES’, or as ‘0’ if the answer was ‘UNCLEAR’ or ‘NO’. And we scored according to the following criteria: low quality (0–3), moderate quality (4–7) and high quality (8–11).

**Statistical analysis**

We used the Stata software (version 14.0) to perform the analysis. The adjusted OR and its 95% CI were extracted from the included studies to calculate the relation between headache and the risk of DED. Heterogeneity was calculated via the Chi-square test and $I^2$ value and a random-effects model was used considering the clinical heterogeneity. The sensitivity analysis was conducted to ascertain the reliability of the overall effects. The funnel plots and egger’s regression test was conducted to explore the bias of publication [20,21]. Finally, we performed subgroup
analyses according to the headache type, study type and territory type.

Results

Search results

We collected 2605 articles before 12 May 2022 from the systematic search, and 100 duplicate articles were first excluded. A total of 2488 articles were also excluded after screening the title and abstract. Then six articles were excluded after reading the full-text, of which three conference abstracts, and three articles without interested outcomes \[22–24\]. Eleven studies \[25–35\] were finally included in this systematic review. The selection strategy is shown in Figure 1.

Study characteristics

This meta-analysis included 11 studies \[25–35\] covering 3,575,957 individuals. Of these studies, one study \[26\] was cohort study, four studies \[25,30,32,33\] were case–control studies and six studies \[27–29,31,34,35\] were cross-sectional studies. The publication year of these studies was 2010–2020. The sample size of the included studies was ranged from 99 to 3,265,894 participants. The diagnostic criteria for DED or headache in four studies \[25,31–33\] was the International Classification of Diseases-9 or 10 (ICD-9 or 10) diagnostic codes. The adjusted estimates were presented in most studies except two studies \[31,34\], and the adjusted confounders in the included studies were slightly distinct. The characteristics of the 11 studies are presented in Table 1.

Risk of bias assessment

We assessed the quality of the eleven studies via the NOS and AHRQ, and the scores are presented in Table 1. And the details are presented in Supplementary Tables 2 and 3, respectively. Four studies \[25,26,32,33\]
### Table 1. Characteristics of studies included in the review.

| Author                  | Year | Country | Study type        | Sample Size                                                                 | Study period | Age (years) | Diagnosis of DED | Diagnosis of headache |
|-------------------------|------|---------|-------------------|-----------------------------------------------------------------------------|--------------|--------------|-------------------|-----------------------|
| Tsung-Jen Wang          | 2010 | China (Taiwan) | Case-control | Total: 48,028; DED: 12,007; No DED: 36,021 | 2005–2006    | 52.4 ± 17.5  | ICD-9-CM          | ICD-9-CM               |
| Adam J. Paulsen         | 2014 | America | Cohort            | Total: 3275; DED: 475; No DED: 2800                                      | 2005–2008    | 49 (range 21–84)| Questionnaire     | Questionnaire          |
| Jelle Vehof             | 2014 | England | Cross-sectional   | Total: 3353; DED: 367; No DED: 3171                                    | 2012         | 57.1 ± 13.1  | Questionnaire     | Structured postal questionnaire |
| Asuman Celikbilek       | 2014 | Turkey  | Cross-sectional   | Total: 99; DED: 42; No DED: 57                                        | 2013         | 18–50       | A complete ophthalmologic examination | International Classification of Headache Disorders II diagnostic criteria |
| Soonwon Yang            | 2016 | Korea   | Cross-sectional   | Total: 14,329; DED: 1390; No DED: 12,939                               | 2010–2012    | Over 19     | Questionnaire     | Questionnaire          |
| Victoria S. Chang       | 2018 | America | Case-control      | Total: 233; DED: 94; No DED: 139                                       | 2016         | 46.3 ± 13.0  | DED questionnaire  | A numerical rating scale questionnaire |
| Charity J. Lee          | 2017 | America | Cross-sectional   | Total: 3,265,894; DED (tear film dysfunction, ocular pain): 959,881; No DED: 2,306,013 | 2010–2014    | DED: 69.4 ± 12.9, 63.4 ± 15.3, respectively; No DED: 64.5 ± 14.3 | ICD-9-CM          | ICD-9-CM               |
| Omar M. Ismail          | 2019 | America | Case-control      | Total: 72,969; DED: 9638; No DED: 63,331                                | 2008–2018    | Over 18     | ICD-9 and10       | ICD-9 and 10            |
| Karel Kostev            | 2019 | Germany | Case-control      | Total: 87,354; DED: 102; No DED: 87,252                                 | 2018         | Over 18     | ICD-10            | ICD-10                 |
| Michael T.M. Wang       | 2020 | New Zealand | Cross-sectional | Total: 372; DED: 109; No DED: 263                                      | 2018–2019    | 39 ± 22 (21–85)| TFOS DEWS II      | Not reported            |
| Jelle Vehof             | 2020 | England | Cross-sectional   | Total: 79,866; DED: 7230; No DED: 72,636                                | 2014–2017    | 50.4 (20–94) | Women’s Health Study dry eye questionnaire | A self-administered questionnaire |

### Table 2. Headache type, Confounders adjusted, Adjusted OR Scores.

| Author                  | Headache type       | Confounders adjusted                                                                 | Adjusted OR    | Scores |
|-------------------------|---------------------|-----------------------------------------------------------------------------------|----------------|--------|
| Tsung-Jen Wang          | Headache            | Gender, age, monthly income and level of the community                             | Headsaches: 1.30 (1.24–1.36) | 9      |
| Adam J. Paulsen         | Migraine            | Sex and age                                                                        | Migraine: 1.76 (1.57–1.98)    | 7      |
| Jelle Vehof             | Migraine            | Sex and age                                                                        | Migraine: 1.47 (1.15–1.88)    | 6      |
| Asuman Celikbilek       | Migraine            | Sex and age                                                                        | Migraine: 1.56 (0.69–3.50)    | 8      |
| Soonwon Yang            | Migraine            | Age, sex, BMI, current smoking, heavy drinking, regular exercise, metabolic syndrome, dyslipidemia, stress perception, and diagnosis of depression | Migraine: 1.58 (1.34–1.86)    | 9      |
| Victoria S. Chang       | Headache            | Diet, environmental factors                                                        | Headsaches: 2.14 (1.16–3.95) | 6      |
| Charity J. Lee          | Headaches           | Not reported                                                                       | Headsaches: 1.70 (0.84–3.45) | 6      |
| Michael T.M. Wang       | Tension headache    | Not reported                                                                       | Headsaches: 1.60 (1.59–1.61) | 6      |
| Omar M. Ismail          | Migraine headache   | Age, sex, use of specific medications, a history of rheumatoid arthritis, Sjögren disease or lupus, a history of cataract or refractive surgery | Migraine headache: 1.42 (1.20–1.68) | 8      |
| Karel Kostev            | Migraine            | Age, sex and relevant co-diagnoses (rheumatoid arthritis, Sjögren syndrome, lupus and cataract) | Migraine headache: 3.45 (2.16–5.47) | 8      |
| Michael T.M. Wang       | Migraine headaches  | Not reported                                                                       | Migraine headache: 2.96 (1.38–6.37) | 6      |
| Jelle Vehof             | Cluster headache    | Sex and age                                                                        | Cluster headache: 2.12 (1.10–4.06) | 8      |
|                        | Migraine            |                                                                                   | Migraine: 1.27 (1.20–1.34)     |        |
were scored as ≥7 (high quality) and one study [30] was scored as 6 (moderate quality) according to the NOS criteria. The average score of these five studies was 7.6, representing an overall high quality. Three studies [28,29,35] were scored as ≥7 (high quality) and three studies [27,31,34] were scored as 6 (moderate quality) according to the AHRQ criteria. The average score of these six studies was 7.2, representing an overall high quality.

All-cause headache and risk of DED

Eleven studies [25–35] assessed the relation between all-cause headache history and the risk of DED. The pooling analysis indicated that all-cause headache was related with a higher risk of DED (OR = 1.586, 95% CI: 1.409–1.785, I² = 89.3%, p < .001; Figure 2). Owing to the significant heterogeneity, we also performed a sensitivity analysis to identify the heterogeneity source. Sensitivity analysis revealed that none of the included studies altered the pooled-effect size, demonstrating the robustness of the overall findings and the result is shown in Supplementary Figure A. A visual examination of the funnel plot revealed that there was no evidence of a significant publication bias (Figure 3). And the Egger’s regression tests (p = .714) revealed that the bias of publication was negligible in analysis.

Types of headache and risk of DED

Eleven studies [25–35] assessed the relation between migraine and the risk of DED and found that migraine had a higher risk of DED (OR = 1.503, 95% CI: 1.369–1.650, I² = 81.8%, p < .001; Figure 4). One included study (P29392243) showed that tension headache was associated with an increased risk of DED (OR = 1.610, 95% CI: 1.585–1.635, p < .001; Figure 4); and another included study (P32376389) showed that cluster headache was related to a higher risk of DED (OR = 2.120, 95% CI: 1.104–4.073, p = .024; Figure 4).

Study type and risk of DED

Subgroup analysis in the study type indicated that the risk of DED in case–control studies was slightly higher.
than in the cross-sectional studies and the cohort study (OR = 1.707, 95% CI: 1.291–2.258, I² = 85.0%, p < .001; OR = 1.600, 95% CI: 1.590–1.610, I² = 0.0%, p < .001; OR = 1.440, 95% CI: 1.096–1.893, p = .009; respectively; Figure 5).

**Types of territory and risk of DED**

Subgroup analysis in the territory type showed that the all-cause headache in America, Europe, Asia and Oceania were all related to a higher risk of DED (OR = 1.579, 95% CI: 1.493–1.669, I² = 10.9%, p < .001; OR = 2.158, 95% CI: 1.214–3.836, I² = 80.7%, p = .009; OR = 1.410, 95% CI: 1.196–1.663, I² = 61.6%, p < .001; OR = 2.960, 95% CI: 1.378–6.359, p = .005, respectively; Figure 6).

**Discussion**

**Main findings**

In this study, we investigated the relation between headache and the risk of DED in 3,575,957 individuals...
from eleven studies [25–35]. We discovered that compared with the controls without all-cause headache, there was a 1.586-fold increased incidence of DED among individuals with all-cause headache. Subgroup analyses showed that headache type (migraine, tension headache or cluster headache), study type (case–control, cohort or cross-sectional) and territory type (America, Europe, Asia or Oceania) were all related to a higher risk of DED. These results suggest that headaches should be regarded as an independent risk factor for DED.

**Findings interpretation**

Consistent with the findings of previous review [36], our study revealed that headache might increase the risk of DED. Chen et al. showed that migraine was related to a 1.55-fold increased incidence of DED [36], which was similar that observed in our study. Furthermore, subgroup analysis indicated that the incidence of DED was higher in hospital-based studies (OR = 1.97, p = .036) compared with population-based studies (OR = 1.42, p < .001). However, it did not mean that any type of the headache was related to a higher risk of DED. Moreover, their study showed that there was no relation between geographic location and DED, which may be reasonably associated with only seven published studies included. In our current analysis, we included more relevant and recent published studies and performed subgroup analysis according to the headache type, study type and territory type, providing reliable evidence regarding the relationship between headache and the risk of DED.

Several studies have been reported that headache was related to the inflammatory connective tissue diseases (Sjögren’s syndrome, systemic lupus erythematosus, etc.) [37–40]. So far, the exact pathophysiological mechanism of the relation between headache and DED was not yet fully understood. However, it is well established that the underlying inflammatory
processes may play a major role in the pathophysiology of headache and DED [23]. The density of corneal nerve fibre was markedly lower in the patients with migraine than the controls, which indicates that cornea was a preferred target for neurogenic inflammation and structural changes in the trigeminal nerve might participate the pathophysiology of headache [2,15]. Since there was a close relation between the trigeminal nerve and the secretion of lacrimal gland, neurogenic inflammation might provide an environment that accelerates DED development [41,42]. Neurogenic inflammatory mediators and cytokines (neuropeptides, C-reactive protein, etc.) have been thought to trigger the process of plasma extravasation and trigeminal ganglion hypersensitivity in headache development [43–46]. Meanwhile, the inflammatory changes and hyperosmolarity environment in ocular surface also led to the development and propagation of headache [23,47,48].

We noticed that the heterogeneity of the eleven studies was significant, which could be related to the following factors. First, the sample size in three included studies were relatively small, which may have affected the results accuracy [28,30,34]. Therefore, more studies with larger sample sizes are required to identify the relation. Second, there were discrepancies in the diagnostic standards for headache and DED in the included studies, such as ICD-9/10, examination or questionnaire. Additionally, the diagnosis was mainly according to electronic health records in most included studies, which may also have affected the outcomes. Third, the included studies were performed in the America, Europe, Asia and Oceania, where regional bias is a valid possibility. As the subgroup analysis in the territory type showed that the risk of DED varied in different areas, more studies with the same area were required to identify the relation. Last, study design of the included studies was different, which may also have affected the
outcomes. As the subgroup analysis in the study type indicated that the risk of DED in the case–control studies was slightly higher than in the cross-sectional studies and the cohort study, more studies with the same study design are needed to clarify the association.

**Implications and limitations**

Our study reviewed the research findings concerning the relation between all-cause headache history and the risk of DED, demonstrating that headache should be regarded as an independent risk factor for DED. It emphasizes that we should pay greater attention to the incidence of DED among headache patients.

However, our study also has some limitations. First, there were only 11 relevant studies included. So, we could not conduct subgroup analysis on more types of headache. Second, we did not conduct co-variate analysis in our study. However, most of the included studies mentioned their adjusted confounders, making the confounding bias well-controlled. So, the results of our study were convincing and of clinical value. Finally, and most importantly, since the diagnostic criteria of DED varied in the included studies, we cannot deny the possibility of misdiagnosing neuropathic corneal pain (NCP) to DED. Particularly, in two included studies, the diagnosis of DED was determined by self-report, which might increase the misdiagnosis rate [26,27]. Therefore, ophthalmologists should pay more attention to differentiate the patients presenting with dry eye-like symptoms into DED or NCP and select the appropriate treatment strategies [49,50].

**Conclusions**

Our study indicates that headache increases the risk of DED, especially in migraine patients. However, more relevant studies are still required to identify the exact pathophysiological process behind this clinical phenomenon. The findings of our study can be meaningful in the prevention and treatment of DED.

**Author contributions**

L.J.Z. conceived the study. L.J.Z., S.Y.L. and S.F.F. collected the data. S.Y.L. conducted analysis and drafted the manuscript. S.F.F. and H.D. contributed to data interpretation and revised the manuscript. All authors have read and approved the manuscript.

**Disclosure statement**

No potential conflict of interest was reported by the author(s).

**Data availability statement**

The data sets in the study are presented in the article or supplementary material, and further information can be directed to the authors.

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**References**

[1] Belmonte C, Nichols JJ, Cox SM, et al. TFOS DEWS II pain and sensation report. Ocul Surf. 2017;15(3):404–37.
[2] Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II definition and classification report. Ocul Surf. 2017;15(3):276–83.
[3] Shimazaki J. Definition and diagnostic criteria of dry eye disease: historical overview and future directions. Invest Ophthalmol Vis Sci. 2018;59(14):DE57–12.
[4] Gayton JL. Etiology, prevalence, and treatment of dry eye disease. Clin Ophthalmol. 2009;3:405–12.
[5] Stapleton F, Alves M, Bunya VY, et al. TFOS DEWS II epidemiology report. Ocul Surf. 2017;15(3):334–65.
[6] Bron AJ, de Paiva CS, Chauhan SK, et al. TFOS DEWS II pathophysiology report. Ocul Surf. 2017;15(3):438–510.
[7] Wolffsohn JS, Wang MTM, Vidal-Rohr M, et al. Demographic and lifestyle risk factors of dry eye disease subtypes: a cross-sectional study. Ocul Surf. 2021;21:58–63.
[8] Xu L, Zhang W, Zhu X-Y, et al. Smoking and the risk of dry eye: a meta-analysis. Int J Ophthalmol. 2016;9(10):1480–86.
[9] Yoo TK, Oh E. Diabetes mellitus is associated with dry eye syndrome: a meta-analysis. Int Ophthalmol. 2019;39(11):2611–20.
[10] Almutairi AH, Alalawi BS, Badr GH, et al. Prevalence of dry eye syndrome in association with the use of contact lenses in Saudi Arabia. BMC Ophthalmol. 2021;21:147.
[11] Fogagnolo P, Favuzza E, Marchina D, et al. New therapeutic strategy and innovative lubricating ophthalmic solution in minimizing dry eye disease associated with cataract surgery: a randomized, prospective study. Adv Ther. 2020;37(4):1664–74.
[12] Basilious Amy, Xu Cathy Y, Malvankar-Mehta Monali S. Dry eye disease and psychiatric disorders: A systematic review and meta-analysis. Eur J Ophthalmol. 2022;32:1872–89.
[13] Saylor D, Steiner TJ. The global burden of headache. Semin Neurol. 2018;38(2):182–90.
[14] Yao C, Wang Y, Wang L, et al. Burden of headache disorders in China, 1990–2017: findings from the Global Burden of Disease Study 2017. J Headache Pain. 2019;20(1):102.
[15] Kinard KI, Smith AG, Singleton JR, et al. Chronic migraine is associated with reduced corneal nerve
fiber density and symptoms of dry eye. Headache. 2015;55(4):543–49.

[16] Ozudogru S, Neufeld A, Katz BJ, et al. Reduced visual quality of life associated with migraine is most closely correlated with symptoms of dry eye. Headache. 2019;59(10):1714–21.

[17] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.

[18] Stang A. Critical evaluation of the Newcombe-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25(9):603–05.

[19] Hu J, Dong Y, Chen X, et al. Prevalence of suicide attempts among Chinese adolescents: a meta-analysis of cross-sectional studies. Compr Psychiatry. 2015;61:78–89.

[20] Qu H, Yang S, Yao Z, et al. Association of headache disorders and the risk of dementia: meta-analysis of cohort studies. Front Aging Neurosci. 2022;14:804341.

[21] Lei S, Li X, Zhao H, et al. Risk of dementia or cognitive impairment in sepsis survivors: a systematic review and meta-analysis. Front Aging Neurosci. 2022;14:839472.

[22] Lee CJ, Felix ER, Levitt RC, et al. Traumatic brain injury, dry eye and comorbid pain diagnoses in US veterans. Br J Ophthalmol. 2018;102(5):667–73.

[23] Wang T-J, Wang IJ, Hu CC, et al. Comorbidities of dry eye disease: a nationwide population-based study. Acta Ophthalmol. 2012;90(7):663–68.

[24] Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry eye in the Beaver Dam Offspring study: prevalence, risk factors, and health-related quality of life. Am J Ophthalmol. 2014;157(4):299–306.

[25] Vehof J, Kozareva D, Hysi PG, et al. Prevalence and risk factors of dry eye disease in a British female cohort. Br J Ophthalmol. 2014;98(12):1712–17.

[26] Celikbilek A, Adam M. The relationship between dry eye and migraine. Acta Neurol Belg. 2015;115(3):329–33.

[27] Yang S, Kim W, Kim HS, et al. Association between migraine and dry eye disease: a nationwide population-based study. Curr Eye Res. 2017;42(6):837–41.

[28] Chang VS, Rose TP, Karp CL, et al. Neuropathic-like ocular pain and nonocular comorbidities correlate with dry eye symptoms. Eye Contact Lenses. 2018;44:5307–513.

[29] Lee CJ, Levitt RC, Felix ER, et al. Evidence that dry eye is a comorbid pain condition in a U.S. veteran population. Pain Rep. 2017;2(6):e629.

[30] Ismail OM, Poole ZB, Bierly SL, et al. Association between dry eye disease and migraine headaches in a large population-based study. JAMA Ophthalmol. 2019;137(5):532–36.

[31] Kostev K. Association between migraine headaches and dry eye disease in patients studied in general practices in Germany. JAMA Ophthalmol. 2020;138(2):223.

[32] Wang MTM, Vidal-Rohr M, Muntz A, et al. Systemic risk factors of dry eye disease subtypes: a New Zealand cross-sectional study. Ocul Surf. 2020;18(3):374–80.

[33] Vehof J, Snieder H, Jansonius N, et al. Prevalence and risk factors of dry eye in 79,866 participants of the population-based lifelines cohort study in The Netherlands. Ocul Surf. 2021;19:83–93.

[34] Chen H, Chen A, Wang S, et al. Association between migraine and dry eye: a systematic review and meta-analysis. Cornea. 2022;41(6):740–45.

[35] Tjensvoll AB, Gøransson LG, Harboe E, et al. High headache-related disability in patients with systemic lupus erythematosus and primary Sjogren’s syndrome. Eur J Neurol. 2014;21(8):1124–30.

[36] Zhao J, Chen Q, Zhu Y, et al. Nephrological disorders and neurological involvement in pediatric primary Sjogren syndrome: a case report and review of literature. Pediatr Rheumatol Online J. 2020;18(1):39.

[37] Vargas-Hitos JA, Sabio JM, Martinez-Egea I, et al. Influence of psychological stress on headache in patients with systemic lupus erythematosus. J Rheumatol. 2014;41(3):453–57.

[38] Santos FPST, Nascimento BR, Calderaro DC, et al. Neuropsychiatric syndromes in childhood-onset systemic lupus erythematosus: a systematic review and meta-analysis. J Clin Rheumatol. 2021;27(5):206–14.

[39] Sutris T, Simpson TL, Fonn D, et al. Conjunctival and corneal sensory sensitivities are associated with signs and symptoms of ocular dryness. Invest Ophthalmol Vis Sci. 2008;49(7):2971–76.

[40] Pflugfelder SC. Tear dysfunction and the cornea: LXVIII Edward Jackson Memorial Lecture. Am J Ophthalmol. 2011;152(6):900–90.e1.

[41] Capuano A, De Corato A, Lisi L, et al. Proinflammatory-activated trigeminal satellite cells promote neuronal sensitization: relevance for migraine pathology. Mol Pain. 2009;5:43.

[42] Russo A, Tessitore A, Giordano A, et al. The pain in migraine beyond the pain of migraine. Neurol Sci. 2012;33:S103–S06.

[43] Edvinsson L, Warfvinge K. Does inflammation have a role in migraine? Nat Rev Neurol. 2019;15(8):483–90.

[44] Mantelli F, Micera A, Sacchetti M, et al. Neurogenic inflammation of the ocular surface. Curr Opin Allergy Clin Immunol. 2010;10(5):498–504.

[45] Beuerman RW, Stern ME. Neurogenic inflammation: a first line of defense for the ocular surface. Ocul Surf. 2005;3(Suppl 4):S203–06.

[46] Forristal Mark T, Stephenson Kirk A J. Differentiating primary dry eye disease from ocular neuropathic pain: implications for symptom management. Clin Exp Optom. 2022;undefined:1–7.

[47] Chen Q K, Liang Q F. Research progress of diagnosis in neuropathic corneal pain. Zhonghua Yan Ke Za Zhi. 2022;58(8):629–34.