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Assessment of pranoprofen ophthalmic solution 0.1% application for non-infectious conjunctivitis in patients with symptoms of dry eye disease

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ABSTRACT

Introduction: Dry eye disease (DED) can be caused by many factors and conditions. It is a multifactorial disease, in which ocular surface inflammation plays an important role in the pathogenesis.

Aim of the study: To assess efficacy of pranoprofen ophthalmic solution 0.1% applied for treatment of non-infectious conjunctivitis in patients with symptoms of dry eye disease.

Material and methods: Prospective, single-arm, open, non-interventional study. Near and distant best corrected visual acuity, intraocular pressure measurement with air-puff tonometer as well as Schirmer I test, bulbar hyperemia, conjunctival edema, tear break-up time (TBUT), cornea and conjunctival staining score and lid-parallel conjunctival folds (LIPCOF) were assessed. Slit lamp examination included anterior segment and fundus examination. Patients were treated with pranoprofen ophthalmic solution 0.1% 4 times a day for 2-4 weeks.

Results: 13 patients were screened, and 12 fulfilled inclusion criteria. The most significant improvement was observed in the change of subjective dry eye symptoms reported by the patients (equal for all OSDI sections). Improvement was observed in conjunctival hyperemia as well as degree of conjunctival and corneal staining (Oxford scale). There was no change in TBUT and LIPCOF. There were two non-serious adverse events reported during the course of the study.

Conclusions: Pranoprofen ophthalmic solution 0.1% is an effective and safe treatment for non-infectious conjunctivitis with mild to moderate dry eye symptoms. Add-on treatment with pranoprofen ophthalmic solution 0.1% greatly improved the patient's subjective symptoms (OSDI score).

KEY WORDS: pranoprofen, non-steroidal anti-inflammatory drugs (NSAIDs), dry eye disease, DED, non-infectious conjunctivitis.

INTRODUCTION

Dry eye disease (DED) can be caused by many factors and conditions. It affects the patient's quality of life, reading ability, ocular comfort and ocular surface condition. In the last decades there has been a rising number of patients seeing an ophthalmologist with dry eye signs and symptoms [1, 2]. Prevalence of disease for studies involving symptoms with or without signs ranges from approximately 5% to 50% [3].

According to the report of the Tear Film and Ocular Surface Society International Dry Eye Workshop II (TFOS DEWS II) the newest definition of dry eye disease is as follows: it is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles [4, 5].

First choice treatment for dry eye disease is artificial tears, preferably preservative-free; in the case of severe symptoms anti-inflammatory agents such as corticosteroids, tetracyclines or cyclosporin can be added [6, 7].

Numerous anti-inflammatory agents are being developed as treatment for DED. Their way of action is to reduce the intensity of inflammation on the ocular surface and in the lacrimal system and therefore to break the vicious circle of DED [8]. There are some reports on non-steroidal anti-

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inflammatory drugs (NSAIDs) – bromfenac sodium ophthalmic solution use in patients with moderate to severe dry eye [9]. The mode of action of NSAID is inhibition of cyclooxygenases and thereby prostaglandin production is decreased [10]. Ophthalmologists in China have demonstrated the efficacy and safety of pranoprofen ophthalmic solution 0.1% for mild to moderate dry eye disease. In addition, it is suggested that the drug efficacy may be associated with the reduction of inflammatory factors in conjunctival epithelial cells [11, 12].

AIM OF THE STUDY

The aim of this study was to assess the efficacy of pranoprofen ophthalmic solution 0.1% used for treatment of non-infectious conjunctivitis in patients with symptoms of dry eye disease.

MATERIAL AND METHODS

The study was a prospective, single-arm, open, non-interventional study to assess the efficacy of pranoprofen ophthalmic solution 0.1% in treatment of non-infectious conjunctivitis with dry eye disease symptoms. The study was conducted in the Department of Ophthalmology Poznan University of Medical Sciences between 26th June 2018 and 27th February 2019 and was approved by Ethics Committee at Poznan University of Medical Sciences (Ethics Committee Approval no. 63/2018).

The study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council for Harmonisation (ICH)/Good Clinical Practice (GCP) and applicable regulatory requirements.

Table I shows inclusion and exclusion criteria of the study. Patients who fulfilled inclusion criteria and signed the informed consent form were enrolled in the study. Past ophthalmic history including duration of DED, and past medical history was taken from all patients on the baseline visit. Ophthalmic examination included near and distant best corrected visual acuity, intraocular pressure measurement with air-puff tonometer and Schirmer's test; slit lamp examination included anterior segment and fundus examination. To define the degree of DED the following parameters were assessed at the slit lamp: bulbar hyperemia, conjunctival edema, tear break-up time (TBUT), cornea and conjunctival staining scores as well as lid-parallel conjunctival folds (LIPCOF). Schirmer's test I was measured in each eye. Bulbar hyperemia was graded 0-5 (0 – normal; 1 – trace; 2 – mild; 3 – moderate; 4 – severe). TBUT was measured 3 times and the average score was taken. Corneal and conjunctival fluorescein staining were assessed in the temporal conjunctiva, nasal conjunctiva and cornea of the study eye according to the Modified Oxford Grading Scale (point 0 – absent, to 5 – severe) by 0.5 intervals in the study. The sum of conjunctival and corneal score was also calculated.

Each patient was interviewed for main ocular symptom of dry eye (watery eyes, foreign body sensation, eye fatigue, irritation, blurred vision, dryness and burning) and its change at Week 2 and Week 4 compared to baseline.

Subjective symptoms were measured using the Ocular Surface Disease Index (OSDI) questionnaire. The 12 items of the OSDI questionnaire were divided into 3 subscales representing ocular symptoms (5 questions), vision-related function (4 questions) and environmental triggers (3 questions). All the OSDI items were graded on a scale of 0 to 4, where 0 indicates none of the time and 4 means all of the time and 1, 2, 3 are between those two margin values. The total OSDI score was calculated based on the following formula:

$$\text{OSDI} = [(\text{sum of scores for all questions answered}) \times 100] / [(\text{total number of questions answered}) \times 4].$$

Thus, OSDI was scored on a scale of 0 to 100, with higher scores representing greater disability.

At the baseline visit, "the study eye" – that is the eye under observation of enrolled patients –was determined in accordance with the following:

- the eye which met all of the inclusion and none of the exclusion criteria,
- the eye with the greater score of conjunctival hyperemia,
- the eye with the greater score of fluorescein ocular surface staining (sum of corneal and conjunctival staining).

If both eyes met all of the inclusion and none of the exclusion criteria and the scores of conjunctival hyperemia and fluorescein ocular surface staining were equal, the right eye was selected to be observed.

Patients were treated with pranoprofen ophthalmic solution 0.1% (PRATTACK, Senju Poland Sp. z o.o., Poland) 4 times a day for 2 weeks, but treatment could be prolonged to the next 2 weeks if the treatment benefit was demonstrated but the treatment effect was not satisfactory after 2 weeks of therapy in the investigator's opinion. Patients were using the moisturizing treatment as usual, but to minimize study bias the eye lubricant was expected to be stable within a minimum of 1 month before initiation of pranoprofen ophthalmic solution 0.1% treatment. For whole observation period patients were using artificial tears as previously and additionally pranoprofen ophthalmic solution 0.1%. Efficacy of pranoprofen ophthalmic solution 0.1% was measured by the following assessments:

- change of conjunctival hyperemia and edema at Week 2 at the last observation,
- change of grade of fluorescein staining score (cornea and conjunctiva) at Week 2 at the last observation,
- change of subjective symptoms at Week 2 at the last observation.

All statistical analyses were performed using the R statistical software package (Version 3.5).

Table I. Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
1. 18 years of age or older, male and female who were able to provide their own consent and complete the study 2. Had sign(s) of non-infectious conjunctivitis (e.g. conjunctival hyperemia and/or edema) 3. Corneal surface staining (fluorescein) score 2 to 3 on the modified Oxford scale 4. Conjunctival surface staining (fluorescein) total score (nasal + temporal) 3 to 6 on the modified Oxford scale 5. Subjective symptoms of Ocular Surface Disease Index (OSDI) score of > 20 6. Had dry eye symptoms which had not been improved with 1 month or longer treatment of ocular lubricant(s) before baseline visit 7. Qualified to be treated with pranoprofen ophthalmic solution 0.1% in addition to the therapy of ocular lubricant(s) and to be followed up according to the study schedule as usual care	1. Have allergic conjunctivitis within the past 1 year of baseline 2. Have severe corneal disorder and/or Sjögren syndrome 3. Apparent eye diseases which need to be treated other than conjunctivitis 4. Have treatment history within past 2 weeks of baseline or treatment plans of the following treatment(s) (systemic or ophthalmic medications) during the study: corticosteroids, NSAIDs, anticholinergics, immunosuppressants, moisturizing treatment other than ocular lubricant(s)currently in use, including moisturizing treatment planned to be changed within next 4 weeks after the baseline visit. 5. Patients who have worn contact lenses in the past 1 month before baseline visit or wish to wear contact lenses during the study period

RESULTS

Thirteen patients were screened with 12 persons fulfilling inclusion criteria. The first visit of the first patient took place on 26th June 2018, while the last visit of the last patient occurred on 27th February 2019. Out of 12 participants, 1 patient was terminated early with the patient's decision given as a reason for withdrawal and 11 participants completed the study. The mean duration of pranoprofen treatment was 23.5 ±7.7 days. The shortest treatment time was 8 days (consent withdrawal due to patient's decision). Three patients had their treatments stopped after Week 2; the remaining 8 continued until Week 4 due to expected benefit. Out of 3 patients who concluded stopping pranoprofen ophthalmic solution 0.1% at Week 2, two of them discontinued treatment due to an adverse event (eye pain) while in the case of the third an insufficient treatment result was noted.

Baseline characteristics of the study group are shown in Table II.

During baseline disease assessment none of the dry eye symptoms was indicated as markedly more frequent than the others as the main one. Watery eyes affected 3 patients, while dryness, irritation and foreign body sensation were the main symptoms in 2 patients each. Duration of main ocular symptoms varied widely, with half of the patients suffering for at least 25.2 months (median value). The shortest duration reported was 2.2 months while the longest was nearly 20 years (238.1 months). Schirmer's test at baseline was for the left and right eye respectively: 11.9 ±8.8 and 12.1 ±7.5 in the right and left eye.

Baseline mean bulbar conjunctival hyperemia value was 1.4 ±0.5; it decreased to 1.1 ±0.5 after Week 2 and a further decrease to 0.9 ±0.4 occurred after Week 4. Six out of 7 patients with a trace of conjunctival hyperemia (grade 1) at baseline remained stable and presented grade 1 at the last observation. In 1 of those 7 patients the conjunctival hyperemia completely resolved. Five patients presented mild conjunctival hyperemia (grade 2) at baseline. Three of them improved to grade 1 (trace) and 2 of them became stable with grade 2 (mild hyperemia). None of the patients worsened in terms of conjunctival hyperemia during their pranoprofen therapy.

One case of bulbar conjunctival edema was detected during the baseline visit but it subsided by the Week 2 assessment and the resolution was stable until Week 4 assessment.

Results of Modified Oxford Scale assessment are presented in Table III. A graphical presentation of the median total Oxford score is presented in Figure 1. The Total Oxford Scale score measured in the study population decreased during the course of the study from a mean baseline value of 6.3 ±0.9 to 5.3 ±2.5 (Week 2 visit) and finally 3.9 ±2.3 (Week 4 visit). The improvement grade was the most expressed for cornea score (from 2.2 ±0.3 to 1.8 ±1.0 up to 1.1 ±1.0). In 8 out of 11 patients who completed Week 2 assessment, the improvement was observed in at least one sub-scoring. Three patients demonstrated either stable scoring and/or worsening in 1 sub-scoring. In 8 patients cornea scoring demonstrated improvement, in 1 case it was stable and in 2 cases it slightly worsened (from 3 to 3.5 and from 2 to 3). One of the patients who worsened in cornea scoring was one of the 2 who experienced eye pain, reported as an adverse event (AE). Conjunctiva scoring (either temporal or nasal) demonstrated improvement in 5 cases, in 5 it was stable and it worsened in 1 patient. The patient with conjunctiva score worsening was the second patient with eye pain reported as an AE. The total Modified Oxford scoring demonstrated improvement in 8 cases, and 3 demonstrated minor worsening (0.5 to 1 point compared to the baseline value). The 3 study subjects demonstrating worsening experienced worsening in either cornea score or temporal conjunctiva. In none of these patients did all the sub-scores worsen.

Mean baseline total score of OSDI was 53.8 ±14.3 (n = 12) with the lowest reported result of 36.4 and the highest of 79.5. This total score decreased during Week 2 visit assessment to an average value of 39.9 ±31.3 (n = 11). It

Table II. Baseline characteristics of study group

Variable/Parameter	Study group ($n = 12$)
Age	
Mean (SD)	63.4 (12.6)
Median (min.–max.)	64 (38–85)
Sex	
Female	12 (100%)
Pregnancy status	
Not pregnant	5 (41.7%)
Pregnant	0 (0%)
Post-menopausal	7 (58.3%)
Current smoker	
Yes	1 (8.3%)
No	11 (91.7%)
Computer use	
None	7 (58.3%)
0–2 h/day	1 (8.3%)
2–4 h/day	1 (8.3%)
4–8 h/day	2 (16.7%)
≥ 8 h/day	1 (8.3%)
Environment influence	
Yes	0 (0%)
No	11 (91.7%)
Unknown	1 (8.3%)
Contact lenses use	
Yes	1 (8.3%)
No	11 (91.7%)
Ophthalmic surgery history	
Yes	3 (25%)
No	9 (75%)
Diabetes	
Yes	1 (8.3%)
No	11 (91.7%)

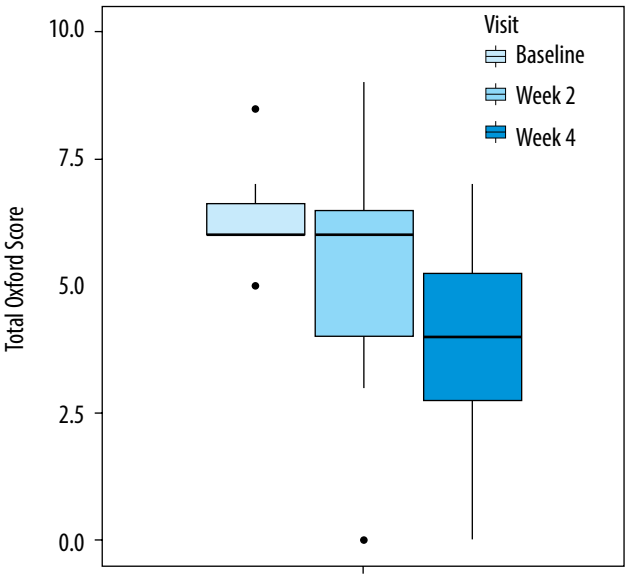

Figure 1. Results of Modified Oxford Scale assessment

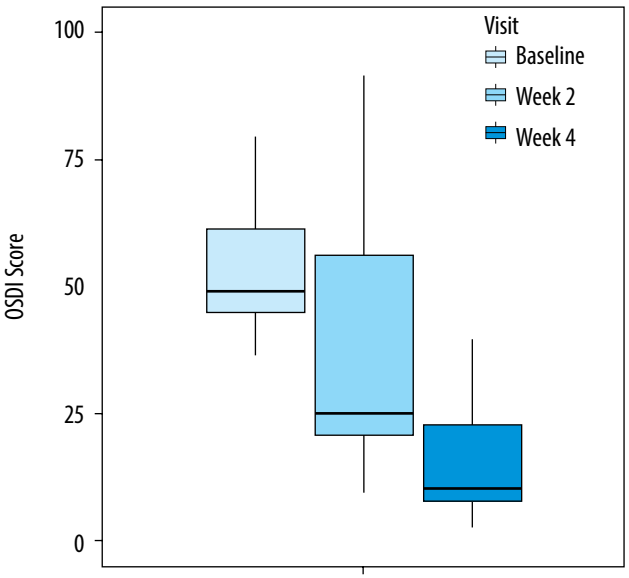

Figure 2. Ocular Surface Disease Index Score change

reached a final value of 15.2 ±12.9 (n = 8) during final assessment in the Safety population (Week 4 visit), which was a substantial decrease, more than a threefold drop compared to the Baseline visit (Figure 2). Seven patients demonstrated improvement of their overall ocular surface disease, while 2 became stable and 2 got worse. The improvement of the OSDI was noticeable in particular sub-scales, with the biggest improvement in the first part, related to the ocular symptoms (Table IV).

During Week 2 and Week 4 visits patients were asked to assess change in the main ocular symptom of dry eye since baseline (watery eyes, foreign body sensation, eye fatigue, irritation, blurred vision, dryness and burning). This was done on a five-point scale from 1 – extremely improved to 5 – extremely worsened. 7 patients reported improvement (including 1 extreme improvement), 2 patients reported a stable result and 2 reported worsening of the main ocular symptom.

TBUT value at the baseline was 9.9 ±5.6. No change was observed at the Week 2 visit (10.4 ±5.4). This increased, however, by Week 4 – the mean tear break-up time was 13 ±7.9.

Mean LIPCOF score during the baseline visit was 2.1 ±0.3 and remained unchanged over the course of the study. Eleven out of 12 patients had baseline LIPCOF Grade 2, while in 9 patients it remained stable (Grade 2) during

Table III. Modified Oxford scale corneal and conjunctival score for study eye

Parameter	Baseline ($n = 12$)	Week 2 ($n = 11$)	Week 4 ($n = 8$)
Cornea Score			
Mean (SD)	2.2 (0.3)	1.8 (1.0)	1.1 (1.0)
Median (min.–max.)	2.0 (2.0–3.0)	2.0 (0.0–3.5)	1.0 (0.0–3.0)
Conjunctiva Score			
Nasal			
Mean (SD)	2.2 (0.4)	1.7 (0.8)	1.4 (0.7)
Median (min.–max.)	2.0 (2.0–3.0)	2.0 (0.0–3.0)	1.5 (0.0-2.0)
Temporal			
Mean (SD)	2.0 (0.6)	1.8 (0.9)	1.4 (0.7)
Median (min.–max.)	2.0 (1.0–3.0)	2.0 (0.0–3.0)	1.5 (0.0-2.0)
Total Oxford Score			
Mean (SD)	6.3 (0.9)	5.3 (2.5)	3.9 (2.3)
Median (min.–max.)	6.0 (5.0–8.5)	6.0 (0.0–9.0)	4.0 (0.0–7.0)

Table IV. OSDI subtotal scores

Parameter	Baseline ($n = 12$)	Week 2 ($n = 11$)	Week 4 ($n = 8$)
OSDI Q1-Q5 Ocular symptoms			
Mean (SD)	9.6 (3.8)	7.3 (6.5)	2.1 (2.5)
Median (min.–max.)	9.0 (6.0–19.0)	5.0 (1.0–18.0)	1.0 (0.0–7.0)
OSDI Q6-Q9 Vision function			
Mean (SD)	6.6 (3.8)	5.5 (4.8)	1.6 (1.6)
Median (min.–max.)	7.5 (0.0–14.0)	4.0 (1.0–14.0)	1.0 (0.0–4.0)
OSDI Q10-Q12 Environmental triggers			
Mean (SD)	6.9 (3.1)	5.1 (4.6)	2.4 (2.3)
Median (min.–max.)	7.0 (3.0–12.0)	3.0 (0.0–12.0)	1.5 (0.0–6.0)

treatment. One patient had LIPCOF decreased to Grade 1 after Week 4 and 1 patient experienced LIPCOF worsening to Grade 3. All patients had the ability to read letters from the chart. Baseline assessment yielded average visual acuity of 0.8 ±0.1 and it increased somewhat on the following visit (0.9 ±0.1) with the same mean value during Week 4 assessment. The mean baseline value of intraocular pressure was 12.4 ±2.2 mmHg. It decreased to 11.9 ±2.1 mmHg after 2 weeks and decreased further at 4 weeks after baseline, reaching a mean value of 11 ±1.7 mmHg.

Two adverse events were reported during the course of the study – in both cases it was eye pain that was classified as a non-serious, treatment emergent adverse event leading to the patients' discontinuation from the study

DISCUSSION

This study was performed to investigate the efficacy of anti-inflammatory treatment with pranoprofen ophthalmic solution 0.1% in non-infectious conjunctivitis with dry eye symptoms, considering that inflammation plays an important role in the pathogenesis and pathophysiology of dry eye. The dry eye vicious cycle includes tear film instability, tear hyperosmolarity, apoptosis of corneal and conjunctival cells, inflammation of the ocular surface and alteration of conjunctival homoeostasis, perpetuating a chronic inflammatory process and dry eye symptoms [13].

Pranoprofen ophthalmic solution 0.1% is an effective anti-inflammatory agent based on belonging to the non-steroidal anti-inflammatory drugs (NSAID). Its mechanism of action is the inhibition of cyclooxygenase 1 and 2 (COX-1, COX-2) responsible for inflammatory prostaglandin synthesis. Prostaglandins are types of lipids, autacoids which are produced at the site of injury or damaged tissue as a part of the body's response to the injury. They are responsible for inflammation induction. Pranoprofen, by blocking the formation of prostaglandins, can alleviate eye inflammation caused by a variety of ophthalmic conditions. It is also given after eye surgery to prevent the occurrence of eye inflammation [14, 15].

The most significant improvement was observed in the change of subjective dry eye symptoms reported by the patient. Significant gradual improvement was recorded particularly in OSDI and it was equal for all OSDI sections. OSDI changes during pranoprofen ophthalmic solution 0.1% treatment confirmed the consistency of the overall result and demonstrated how the resolution of subjective symptoms improved the quality of life of the study patients. The positive change of dry eye symptoms was also confirmed by the subjective assessments of the main ocular complains reported by the patients during the baseline visit, and an overall treatment outcome reported by the investigators was assessed as an improvement (data not shown). Subjective ocular symptoms improvement is consistent with the results presented in previous scientific reports, as was also demonstrated in other pranoprofen studies such as observations by Jing-yao *et al.* [11]. The Chinese researchers Zhang *et al.* in their research concluded that the preoperative administration of pranoprofen eye drops reduced the perceived pain during second-eye cataract surgery, especially when performed after 1-week and 6-week intervals between the first eye and second eye surgery. MCP-1, a pain-related cytokine, was associated with the pain-relief mechanism of pranoprofen when second-eye surgery was performed 1 week after first-eye surgery. The study suggested that an MCP-1-associated inflammatory response occurs in the second eye 1 week after first-eye surgery, which induces greater pain during second-eye surgery, and that this pain can be reduced by the administration of pranoprofen

[16]. The improvement of patients' quality of life thanks to treatment related relief in subjective ocular symptoms is from the practical point of view the most important result. Gomes *et al*. in their review concluded that patient-reported symptoms of DED are generally improved after treatment with topical formulations for tear replacement, tear stimulation or anti-inflammatory therapy compared with baseline or a control treatment [17].

Less improvement was reported in objective outcome measures. Hyperemia and edema are the typical signs of inflammation. The chronic inflammatory response is now thought to be one of the most important mechanisms in DED pathogenesis. The grade of hyperemia is dependent on the severity of the inflammation component [18]. Thus, hyperemia is a hallmark of DED, the observed change in bulbar conjunctival hyperemia while the study was small or even non-significant. However, it is worth highlighting that the baseline status of bulbar conjunctival hyperemia in study patients was either trace or mild.

Safety analysis showed 2 mild side effects of pranoprofen treatment (eye pain), which is less than 20% of the population. This safety result, despite it coming from a small sample size, seems to be in accordance with Chinese research of Chen JingYao [11]. Corticosteroid can cause a moderate response of IOP increase (6 to 15 mmHg) in 33% of the normal population, and 4-6% of the normal population is highly responsive to corticosteroids (IOP elevation > 15 mmHg) [19]. In the present study we did not observe elevation of intraocular pressure. During observation mean IOP in the study group was stable. The prospective study of Simin Zhu confirmed these data, showing that in patients with primary open angle glaucoma treated with latanoprost, the combination with pranoprofen can not only significantly enhance the latanoprost-induced IOP-lowering effect, but also relieve the uncomfortable ocular syndromes caused by latanoprost [20]. The other results such as change in TBUT and visual acuity presented no significant change. As the visual acuity was not bad at baseline, a significant change of this measurement corelated with treatment should not be expected. From the clinical point of view lack of worsening in TBUT, visual acuity and IOP is a satisfactory result.

There were two major limitations of the study. First, the study was single-center with a limited number of patients. A less representative group might have lowered the statistical power of the observation, but since the study was a non-interventional one, in principle it was planned to use descriptive statistics. The smaller number of patients covered with the observation was caused by the lower availability of the targeted population at the study site during the time period of the study conduct. The majority of patients consulted and treated were using other ocular or systemic medications, so they fulfilled exclusion criteria.

The second limitation was study design choice of an open-label, non-randomized and single arm, which can be considered to be a potential source of bias of the assessment.

Taking into account the time-limited and rather short-term pranoprofen ophthalmic solution 0.1% treatment (14-28 days) it might be a solution for dry eye patients. However, further research would be useful with inclusion of a bigger sample size and control arm to investigate pranoprofen's role in eye surface damage recovery and restoration in the ocular surface epithelial integrity thanks to its anti-inflammatory mechanism of action.

CONCLUSIONS

1. Pranoprofen ophthalmic solution 0.1% is an effective and safe treatment for non-infectious conjunctivitis with mild to moderate dry eye symptoms. Add-on treatment with pranoprofen ophthalmic solution 0.1% greatly improved the patient's subjective symptoms (OSDI score), which were not improved with 1 month or longer treatment of ocular lubricant(s).

2. It is suggested that the anti-inflammatory effect of pranoprofen ophthalmic solution 0.1% could contribute to the improvement of the subjective symptoms in this study, considering the results of clinical studies of the drug in China.

3. Further research would be needed with inclusion of a bigger sample size and control arm to investigate pranoprofen's role in eye surface damage recovery.

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DISCLOSURE

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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: 404-437.
2. Mathews PM, Ramulu PY, Swenor BS, et al. Functional impairment of reading in patients with dry eye. Br J Ophthalmol 2017; 101: 481-486.
3. Stapleton F, Alves M, Bunya VY, et al. TFOS DEWS II Epidemiology Report. Ocul Surf 2017; 15: 334-365.
4. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II Definition and Classification Report. Ocul Surf 2017; 15: 276-283.
5. Dastjerdi MH, Dana R. Corneal nerve alterations in dry eye-associated ocular surface disease. Int Ophthalmol Clin 2009; 49: 11-20.
6. Jones L, Downie LE, Korb D, et al. TFOS DEWS II Management and Therapy Report. Ocul Surf 2017; 15: 575-628.
7. Brignole F, Pisella PJ, De Saint Jean M, et al. Flow cytometric analysis of inflammatory markers in KCS: 6-month treatment with topical cyclosporin A. Invest Ophthalmol Vis Sci 2001; 42: 90-95.

8. Baudouin C, Irkec M, Messmer EM, et al. ODISSEY European Consensus Group Members. Clinical impact of inflammation in dry eye disease: proceedings of the ODISSEY group meeting. Acta Ophthalmol 2018; 96: 111-119.
9. Fujishima H, Fuseya M, Ogata M, et al. Efficacy of Bromfenac Sodium Ophthalmic Solution for Treatment of Dry Eye Disease. Asia Pac J Ophthalmol 2015; 4: 9-13
10. Waterbury L, Kunysz EA, Beuerman R. Effects of steroidal and non-steroidal anti-inflammatory agents on corneal wound healing. J Ocul Pharmacol 1987; 3: 43-45.
11. Chen JY, Dong F, Chen W, et al. Clinical efficacy of 0.1% pranoprofen in treatment of dry eye patients: a multi-center, randomized, controlled clinical trial. Chin Med J 2014; 127: 2407-2412.
12. Li Z, Mu G, Chen W, Gao L, et al. Comparative evaluation of topical pranoprofen and fluorometholone in cases with chronic allergic conjunctivitis. Cornea 2013; 32: 579-582.
13. Wei Y, Asbell PA. The core mechanism of dry eye disease is inflammation. Eye Contact Lens 2014; 40: 248-256.
14. Notivol R, Martinez M, Bergamini MV. Treatment of chronic nonbacterial conjunctivitis with a cyclo-oxygenase inhibitor or a corticosteroid. Pranoprofen Study Group. Am J Ophthalmol 1994; 117: 651-656.
15. Akyol-Salman I, Lece-Sertoz D, Baykal O. Topical pranoprofen 0.1% is as effective anti-inflammatory and analgesic agent as diclofenac sodium 0.1% after strabismus surgery. J Ocul Pharmacol Ther 2007; 23: 280-283.
16. Zhang Y, Du Y, Jiang Y, et al. Effects of Pranoprofen on Aqueous Humor Monocyte Chemoattractant Protein-1 Level and Pain Relief During Second-Eye Cataract Surgery. Front Pharmacology 2018; 9: 783.
17. Gomes JAP, Santo RM. The impact of dry eye disease treatment on patient satisfaction and quality of life: A review. Ocul Surf 2019; 17: 9-19.
18. Zhang X, M VJ, Qu Y, et al. Dry Eye Management: Targeting the Ocular Surface Microenvironment. Int J Mol Sci 2017; 18: 1398.
19. Roberti G, Oddone F, Agnifili L i wsp. Steroid-induced glaucoma: Epidemiology, pathophysiology, and clinical management. Surv Ophthalmol 2020; 65: 458-472.
20. Zhu S, Wang D, Han J. Effect of a Topical Combination of Latanoprost and Pranoprofen on Intraocular Pressure and the Ocular Surface in Open-Angle Glaucoma Patients. J Ophthalmol 2018; 2018: 7474086.