Research Article

Pilot Study of the Efficacy of Oral Sodium Diclofenac in the Management of Postoperative Pain after Transepithelial Photorefractive Keratectomy

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Received: 10-04-2019; **Revised:** 24-05-2019; **Accepted:** 02-06-2019.

ABSTRACT

Purpose of this study is to study the efficacy of oral sodium diclofenac in the management of postoperative pain after transepithelial photorefractive keratectomy (tPRK). In this pilot study, 60 patients were included. They were divided into two equal groups. The patients in the control group did not get oral sodium diclofenac in their prescriptions. However, the patients in the diclofenac group got sodium diclofenac 50 mg tab as an addition to the ordinary prescription. Patients were asked to assess their level of pain, photophobia, their functional activity restriction and to specify the number of oral analgesic combi-nation pills, and the number of midazolam pills they have taken till the third day after surgery. Pain intensity in the diclofenac group was significantly less than that in the control group on the day of surgery and on the first day after surgery (p-value=0.01, p-value=0.03 respectively). The functional activity restriction after surgery was remarkably less in the diclofenac group than it was in the control group (p-value=0.01). There was no statistically significant difference between the two groups in terms of photophobia after the surgery (p-value=0.3). There was no important difference between the two groups in terms of the mean number of oral analgesic combination pills consumed by patients (p-value>0.05), and so for the mean number of midazolam pills (p-value>0.05). Oral sodium diclofenac is significantly effective in the management of postoperative pain after tPRK. It also decreases the degree of functional activity restriction. There is no significant effect of oral sodium diclofenac on post-operative photophobia.

Keywords: Tprk, refractive surgery, oral sodium diclofenac, pain management.

INTRODUCTION

Transepithelial photorefractive keratectomy (tPRK), where both the epithelium and stroma are removed in a single step, is a relatively new procedure of laser refractive error correction that provides very similar results with conventional PRK 3 months postoperatively.[1] Excimer laser photorefractive keratectomy (PRK) reshapes the anterior corneal surface and modifies corneal power.[2] The occurrence of severe postoperative pain is consistently reported by excimer laser surgeons as one of the most significant short-term adverse effects of this procedure. Inadequate control of pain after PRK can be a significant source of distress to patients and also interfere with their willingness to undergo a second PRK procedure. Pain usually begins within 1 hour after PRK, increases during the next 3 to 4 hours to reach the peak of pain at around 24 hours after the surgery, and the pain subsides once corneal re epithelialization is complete, ~72 hours after surgery.[3,4] The majority of patients experience significant discomfort after PRK, with most patients reporting a score of 8 or 9 on a 10-point pain scale.[5] Topical forms of NSAIDs are the most widely used approach for achieving post-PRK analgesia.[6] However, topical NSAIDs are associated with many disadvantages, including a delay in epithelial healing and possibility of corneal melting.[7] The effectiveness of oral nonsteroidal anti-inflammatory drugs (NSAIDS) as painkillers is well documented for many acute pain settings although not studied specifically for post-PRK pain.[8] Diclofenac is a well-known nonsteroidal anti-inflammatory drug; the absorption of which is rapid and complete when given orally.[9] This study aimed at determining the efficacy of oral sodium diclofenac in the management of postoperative pain after transepithelial photorefractive keratectomy.

MATERIALS AND METHODS

In this pilot study, we studied 60 patients who were listed to undergo (tPRK) at the ophthalmology department in Tishreen university hospital. The period of our study extended from April 2018 till January 2019. Written informed consents had been obtained from all of the participants (the informed consent form was created by the scientific research ethical committee of the faculty of medicine in Tishreen university). We have also obtained the approval of both the faculty of medicine and the university board in Tishreen university to conduct this study (decision number /1688/ date 28/3/2018).

The selected patients for the study met the following inclusion criteria: age 19 – 35 years, scheduled to undergo transepithelial PRK, documented refraction stability of approximately 1-year, spherical equivalent refractive error ≤6.5 diopters, and central corneal thickness ≥ 460 µm.

Exclusion criteria were: any present ocular disease or previous ocular surgery; keratoconus, including clinical, subclinical; history of allergic reaction to diclofenac or

other NSAIDs; any bleeding disorder; and a history of peptic ulcer, glaucoma, collagen vascular disease, hypertension, diabetes mellitus, or heart disease (including congenital, ischemic, or chest pain); patients with renal failure and any other contraindication for oral sodium diclofenac were excluded from our study.

In this study, patients were divided into two equal groups (30 patients in each). The assignment to either group was done by the ophthalmologist at the eye clinic. The patients in the first group (control group) did not get oral sodium diclofenac in their prescriptions. However, the patients in the second group (diclofenac group) got sodium diclofenac 50mg tab in their prescriptions (starting two hours before surgery) as an addition to the ordinary prescription.

The ordinary postoperative drugs for all patients were:

1. Levofloxacin hemihydrate 1.5% eye drop 4 times daily.
2. Fluorometholone 0.1% eye drop 4 times daily.
3. Eye lubricant (glycerin 2mg/ml, hypromellose 2mg/ml, polyethylene glycol 400:10 mg/ml) eye drop 5 times daily.
4. Combination of Paracetamol 500mg + Codeine phosphate 10mg tab (just in case of severe pain).
5. Midazolam 15 mg tab once daily at bedtime (just in case of severe pain and anxiety).

The patients in the second group had an addition to their prescription; oral sodium diclofenac 50 mg tab TID starting 2 hours before surgery.

The surgeon and the ophthalmologist who evaluated the patients and completed the questionnaire were both masked. Patients hadn't been informed about the difference in prescriptions between the groups and they considered using the routine analgesic regimen of our clinic. An ophthalmologist masked to the treatment groups, filled out the questionnaire.

Patients were asked to assess their level of pain, photophobia, their functional activity restriction and to specify the number of oral analgesic combination pills (combination of paracetamol 500 mg + codeine phosphate 10 mg tab), and the number of midazolam pills (midazolam 15 mg tab) they have taken (pill per day) till the third day after surgery.

We used numerical pain rating scale (NPRS) to measure pain intensity. (NPRS) is an easy, simple and effective subjective way to measure pain that is widely used in research settings.[10,11]

The numerical pain rating scale - consists of integers from 0 through 10- was explained as: "0" means no pain, "5" means moderate pain, and "10" means the worst imaginable pain.[11]

The photophobia degrees were explained in the questionnaire as follows: "0" was assigned if there had been no photophobia, "1" was assigned if there had been photophobia in daylight without sunglasses, "2" was assigned if there had been photophobia in dim light without sunglasses, "3" was assigned if there had been photophobia in daylight with sunglasses, and "4" was assigned if there had been photophobia in dim light with sunglasses.[8]

The functional activity restriction score was explained as "0" means no restriction i.e. the patient's activity was unrestricted by pain, "1" means mild restriction, "2" means moderate restriction and "3" means severe restriction.[8]

The excimer laser device in our hospital is SCHWIND AMARIS® 500E.

Statistical study:

All data were collected in an Excel database and transferred to SPSS (SPSS for Windows, version 15.0, SPSS Inc., Chicago, IL, USA) for data analysis. We used descriptive statistics related to the sample; percentages, central tendency, measures of dispersion and frequencies. Kolmogorov-Smirnov test was used to study data distribution. Mann–Whitney U test was used to compare the means of two independent groups. Spearman correlation analyses were used to measure the strength and direction of association between two ranked variables. A P-value<0.05 was considered statistically significant. The power of the study = 90%. α=5%.

RESULTS AND DISCUSSION

The study sample included 60 patients (19 males, 41 females). The patients' age range was 19-35 year; the mean age was 26.3 ± 3.9 year. The first group (control group); 30 patients (7 males, 23 females), the mean age was 26.3±4 year, the median=25 year. Whereas, the second group (diclofenac group): 30 patients (12 males, 18 females), the mean age was 26.2±3.9 year, the median=25.5 year. (figures 1 and 2).

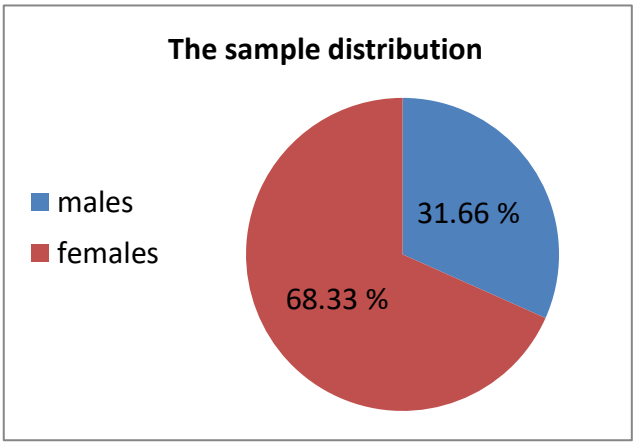

Figure 1: The distribution of the sample between the two sexes.

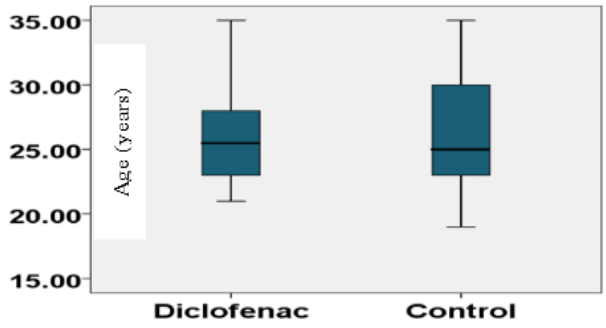

Figure 2: Age distribution of the sample.

The mean post-operative pain intensity

The mean pain intensity on the day of surgery was: 6.3 out of 10 in the control group and 4.7 out of 10 in the diclofenac group. The pain intensity has decreased gradually throughout the next 3 days after surgery in both groups (figure 3). These results are close to the results found by < Alireza Eslampour, et al > as their results were: 6.5 out of 10 in the control group and 4.3 out of 10 in the diclofenac group, though they studied the extended release diclofenac.[8] So, we may be able to conclude that both normal and extended release oral diclofenac are effective in the management of post photorefractive keratectomy pain. The diclofenac has anti-inflammatory effect as it inhibits COX enzyme and consequently inhibits the formation of the inflammatory prostaglandins, not only that but also there is another (not fully understood) central analgesic effect of diclofenac independent of its anti-inflammatory effects.[12]

We compared our results with the results of <Mohammadpour M, et al> who studied the effect of preemptive topical diclofenac on post-operative pain relief after photorefractive keratectomy. In their study; the mean pain intensity on the day of surgery in the control group was 9 out of 10 and in the topical diclofenac group was 8 out of 10.[13] Therefor, we think the topical diclofenac is less effective than oral diclofenac in the management of post photorefractive keratectomy pain. The reason may be that topical diclofenac lacks the systemic central analgesic effects of oral diclofenac (as we previously mentioned).

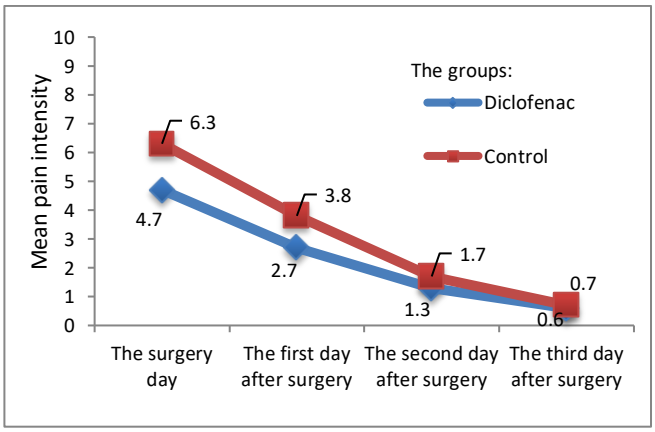

Figure 3: The mean post-operative pain intensity on pain numeric rating scale.

The difference in pain intensity between the study groups:

The analysis of our results -using Mann-Whitney test- showed statistically significant differences in pain intensity between the two groups on the day of surgery (p-value=0.01) and so on the first day after surgery (p-value=0.03) as the pain in the diclofenac group was significantly lesser than that in the control group (table 1). There for, our study supports the results found by < Mohebbi M, et al> and also provides additional clue on the important pathophysiologic role of inflammation in the occurrence of corneal pain after (tPRK).[14]

We didn't find statistically significant differences in pain intensity between the two groups on the second and third day after surgery (p-value=0.3, p-value=0.7 respectively) (table 1, figure 3). These results are compatible with the results found by <Alireza Eslampour, et al> [8] and < Mohammadpour M, et al> in their studies.[13] Which can be explained by the fact the pain subsides as the corneal re-epithelialization progresses.[3]

Table 1: The results of Mann-Whitney test to compare the difference in pain intensity between the two groups up to the third day after surgery.

	U-Value	p-value
The day of surgery	291	0.01
The first day after surgery	316	0.03
The second day after surgery	388	0.3
The third day after surgery	436	0.7

Comparing the photophobia between the two study groups:

The comparison was done by using Mann-Whitney test, the test results were: U=385, P-value=0.3 . So, there was no statistically significant difference between the two groups in terms of photophobia after surgery. On the contrary to our results, <Alireza Eslampour, et al> [8] found that the photophobia was lesser in the diclofenac group than it was in the control group. These conflicting results may be due to the subjective estimating of the degree of photophobia by the patients themselves. As a result, more studies should be conducted to find out whether the oral diclofenac has an effect on the photophobia after (tPRK) or not.

Comparing the functional activity restriction between the two study groups:

The comparison was done using Mann-Whitney test, the test results were: U=304, P-value=0.01. So, there was a statistically significant difference in favor of the diclofenac group i.e. the functional activity restriction in the diclofenac group was significantly lesser than it was in the control group. Similar results were found by <Alireza Eslampour, et al>[8] which is totally logical as the reduced

pain intensity in the diclofenac group leads to less functional activity restriction.

The use of oral analgesic combination pills and midazolam pills:

There was no statistically significant difference in the amount of analgesic combination pills that had been consumed by patients between the two groups (P-value>0.05), though the mean number of consumed oral analgesic combination pills was slightly lesser in the diclofenac group than that in the control group (table 2). The reason could be that some patients may have taken analgesics combination pills because they were afraid of pain rather than in real pain.

Table 2: The mean number of consumed analgesic combination pills in each group (pill per patient) till the third day after surgery.

	Control group	Diclofenac group
The day of surgery	3	3
The first day after surgery	2.5	2
The second day after surgery	1	0
The third day after surgery	0	0

we also didn't find statistically significant difference in the amount of midazolam pills that had been consumed by patients between the two groups (P-value>0.05), though the mean number of consumed midazolam pills was slightly less in the diclofenac group than it was in the control group (table 3). Psychological factors may have played a role in the consumption of midazolam pills by the patients in the two groups, but we couldn't be certain about that. So, more studies should be done to reach a definite answer as the available studies provides contradictory results.[7]

Table 3: The mean number of consumed midazolam pills in each group (pill per patient) till the third day after surgery.

	Control group	Diclofenac group
The day of surgery	1	1
The first day after surgery	1	0
The second day after surgery	0	0
The third day after surgery	0	0

We realize that the most important limitations of this study were that the tolerance of the patients was not equal and the assessment of pain relief and functional deficit was done subjectively as the difference in these issues could not be proven by objective measurements.

CONCLUSION

Oral sodium diclofenac (starting 2 hours before surgery) is significantly effective in the management of postoperative pain after transepithelial photorefractive keratectomy. It also decreases the degree of functional activity restriction in the first few days after surgery. We found no significant effect of oral sodium diclofenac on post-operative photophobia.

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Source of Support: Nil, **Conflict of Interest:** None.

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