

Original Research Article

Comparison of the mean total loss of mydriasis with topical ketorolac tromethamine 0.5% and nepafenac 0.1% during phacoemulsification

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Abstract

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Phacoemulsification with intraocular-lens implantation is the current surgical treatment of choice for cataract extraction. To prevent complications during surgery, there should be adequate pupillary dilation for better visualization of the posterior chamber. The objective of this study is to compare mean total loss of mydriasis with topical ketorolac tromethamine 0.5% and nepafenac 0.1% during phacoemulsification. The study design is randomized controlled trial and it was carried out in Department of Ophthalmology, Shaikh Zayed Hospital Lahore. The duration for this process is six months (August 2019 to January 2020). A total of 100 patients were selected from Ophthalmology Outdoor of Shaikh Zayed Hospital Lahore. The patients were randomly divided into two groups by lottery method, 50 patients in group A (Nepafenac 0.1%) and 50 patients in group B (Ketorolac tromethamine 0.5%). Five minutes later, tropicamide 0.5%, 1 drop every 15 minutes for 4 doses were instilled in both treatment groups. The two groups were compared with diameters of pupil was measured at different stages of cataract surgery and the mean values were compared across the two groups. The mean age of the patients in group A was 55.6±5.6 years and in group B was 54.6±5.7 years. The mean pupil diameter before surgery in group A was 7.9±0.4 and in group B was 8.0±0.5. The mean pupil diameter after surgery in group A was 6.4±0.6 and in group B was 5.7±0.5. The mean total loss of mydriasis in group A was 1.4±0.6 and in group B was 2.1±0.4. It is concluded from this study that Topical nepafenac has been shown to be a more effective inhibitor of miosis during phacoemulsification and provides a more stable mydriatic effect throughout the surgical procedure compared to topical ketorolac.

Keywords: Ketorolac Tromethamine 0.5%, Nepafenac 0.1%, Phacoemulsification, Total loss of mydriasis

INTRODUCTION

Phacoemulsification with intraocular-lens (IOL) implantation is the current surgical treatment of choice for cataract extraction (Garg et al., 2004). To prevent complications during surgery, there should be adequate pupillary dilation for better visualization of the posterior chamber (Guzek et al., 1987). Evidence has shown that intraocular manipulation can trigger the inflammatory

andins within the eye causing miosis (Rowen, 1999). During cataract surgery, maintenance of mydriasis is necessary to facilitate proper incision of the anterior capsule, safe removal of the cataract, and implantation of intraocular lens (Guzek et al., 1987). Mydriatics and antiprostaglandins are routinely applied preoperatively to cascade, releasing cyclooxygenase (COX) and prostagl-

Table 1. Distribution of patients by age

Age (Years)	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
40-50	12	24.0	13	26.0
51-60	23	46.0	26	52.0
61-70	15	30.0	11	22.0
Mean±SD	55.6±5.6		54.6±5.7	

Table 2. Distribution of patients by sex

Sex	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
Male	25	50.0	21	42.0
Female	25	50.0	29	58.0
Total	50	100.0	50	100.0

demonstrated the effectiveness of various topical nonsteroidal anti-inflammatory drugs (NSAIDs) (indomethacin, flurbiprofen, suprofen) in preventing miosis during cataract surgery compared to placebo (Podos, 1976). Podos (1976) compared the effects of topical 0.5% ketorolac tromethamine ophthalmic solution with topical 0.03% flurbiprofen sodium on the inhibition of surgically induced miosis during phacoemulsification. Ketorolac provided a more stable mydriatic effect throughout the surgical procedure. Newer topical NSAIDs also showed similar favourable effects. Coste (Muhtaseb et al., 2004) showed that nepafenac given 3 times a day 1 day before cataract surgery was superior to tobramycin dexamethasone eye drops in maintaining intraoperative mydriasis measured at 4 different stages of the surgery. Nepafenac has been shown to penetrate the cornea rapidly and provides a complete and longer-lasting inhibition of prostaglandin synthesis and vascular permeability (Solomon et al., 1997). Perhaps, this advantage in absorption and bioavailability was the reason behind its superiority in maintenance of mydriasis seen in the study. A study conducted by Abdel and Mahdy (2011) found baseline mean vertical diameter of pupil to be 8.28 ± 1.19 and 8.25 ± 0.80 ketorolac and nepafenac group respectively. At the end of surgery mean pupil diameter was found to be 5.92 ± 0.91 in ketorolac group with total loss of mydriasis of 2.36 ± 1.07 and percent total loss of 27.89%. In nepafenac group mean pupil diameter at the end of surgery was 6.82 ± 1.05 , total loss of mydriasis of 1.43 ± 0.83 and percent total loss of 17.32%. While one study conducted by Zanetti et al showed no statistical difference between Nepafenac and Ketorolac in maintenance of intraoperative mydriasis with p value of 0.791 (Lane, 2006). This study is designed to compare the mean total loss of mydriasis with two newer topical NSAIDs widely available ketorolac 0.5% and nepafenac 0.1% during phacoemulsification. Previously studies have been done

between ketorolac 0.5% and nepafenac 0.1% but on very small sample size of less than 50. Moreover no local study is available in Pakistan. I want to conduct this study on large sample size so that the management strategy can be adopted to find out the superior drug in maintaining mydriasis during phacoemulsification in our population (Ke et al., 2007).

MATERIALS AND METHODS

A total of 100 patients were selected from Ophthalmology Outdoor of Shaikh Zayed Hospital Lahore. The patients were randomly divided into two groups by lottery method, 50 patients in group A (Nepafenac 0.1%) and 50 patients in group B (Ketorolac tromethamine 0.5%). Five minutes later, tropicamide 0.5%, 1 drop every 15 minutes for 4 doses were instilled in both treatment groups. The two groups were compared with diameters of pupil was measured at different stages of cataract surgery and the mean values were compared across the two groups.

RESULTS

The mean age of the patients in group A was 55.6 ± 5.6 years and in group B was 54.6 ± 5.7 years. In group A, there were 12 (24.0%) patients in age range of 40-50 years, 23 (46.0%) patients in the age range of 51-60 years and 15 (30.0%) patients in the age range of 61-70 years. In group B, there were 13 (26.0%) patients in age range of 40-50 years, 26 (52.0%) patients in the age range of 51-60 years and 11 (22.0%) patients in the age range of 61-70 years (Table 1). In group A, there were 25 (50.0%) male and 25 (50.0%) female patients. In group B, there were 21 (42.0%) male and 29 (58.0%) female patients (Table 2). The mean pupil diameter before surgery in group A was 7.9 ± 0.4 and in group B was

Table 3. Distribution of patients by pupil diameter before surgery

Pupil diameter before surgery	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
6.1-7.0	4	8.0	5	10.0
7.1-8.0	37	74.0	34	68.0
8.1-9.0	9	18.0	11	22.0
Mean±SD	7.9±0.4		8.0±0.5	

Table 4. Distribution of patients by pupil diameter after surgery

Pupil diameter after surgery	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
5.1-6.0	22	44.0	47	94.0
6.1-7.0	24	48.0	3	6.0
7.1-8.0	4	8.0	0	0
Mean±SD	6.4±0.6		5.7±0.5	

Table 5. Distribution of patients by total loss of mydriasis

Total loss of mydriasis	Group A (n=50)		Group B (n=50)	
	No.	Percentage	No.	Percentage
Upto 1.0	15	30.0	0	0
1.1-2.0	31	62.0	32	64.0
2.1-3.0	4	8.0	18	36.0
Mean±SD	1.4±0.6		2.1±0.4	

Table 6. Stratification of total loss of mydriasis with age

Age (Years)	Group A (n=50)			Group B (n=50)		
	Total loss of mydriasis			Total loss of mydriasis		
	Upto 1.0	1.1-2.0	2.1-3.0	Upto 1.0	1.1-2.0	2.1-3.0
40-50	2	9	1	0	6	7
51-60	8	13	2	0	20	6
61-70	5	9	1	0	7	4
Total	15	31	4	0	33	17
p-value	0.001			0.001		

Table 7. Stratification of total loss of mydriasis with sex

Sex	Group A (n=50)			Group B (n=50)		
	Total loss of mydriasis			Total loss of mydriasis		
	Upto 1.0	1.1-2.0	2.1-3.0	Upto 1.0	1.1-2.0	2.1-3.0
Male	5	17	3	0	15	6
Female	10	14	1	0	17	12
Total	15	31	4	0	32	18
p-value	0.07			0.3		

8.0±0.5. In group A, there were 4 (8.0%) patients in the pupil diameter range of 6.1-7.0, 37 (74.0%) patients in the pupil diameter range of 7.1-8.0, and 9 (18.0%) patients in the pupil diameter range of 8.1-9.0. In group

B, there were 5 (10.0%) patients in the pupil diameter range of 6.1-7.0, 34 (68.0%) patients in the pupil diameter range of 7.1-8.0 and 11 (22.0%) patients in the pupil diameter range of 8.1-9.0 (Table 3). The mean pupil

diameter after surgery in group A was 6.4 ± 0.6 and in group B was 5.7 ± 0.5 . In group A, there were 22 (44.0%) patients in the pupil diameter range of 5.1-6.0, 24 (48.0%) patients in the pupil diameter range of 6.1-7.0, and 4 (8.0%) patients in the pupil diameter range of 7.1-8.0. In group B, there were 47 (94.0%) patients in the pupil diameter range of 5.1-6.0, and 3 (6.0%) patients in the pupil diameter range of 6.1-7.0 (Table 4). The mean total loss of mydriasis in group A was 1.4 ± 0.6 and in group B was 2.1 ± 0.4 . In group A, there were 15 (30.0%) patients in the total loss of mydriasis range of upto 1.0, 31 (62.0%) patients in the total loss of mydriasis range of 1.1-2.0 and 4 (8.0%) patients in the total loss of mydriasis range of 2.1-3.0. In group B, there were 32 (64.0%) patients in the total loss of mydriasis range of 1.1-2.0, and 18 (36.0%) patients in the total loss of mydriasis range of 2.1-3.0 (Table 5). The stratification of total loss of mydriasis with age and sex are described in table 6 and table 7.

DISCUSSION

Phacoemulsification with intraocular lens (IOL) implantation is the current surgical treatment of choice for cataract extraction. To prevent complications during surgery, there should be adequate pupillary dilation for better visualization of the posterior chamber. Evidence has shown that intraocular manipulation can trigger the inflammatory cascade, releasing cyclooxygenase (COX) and prostaglandins within the eye causing miosis (Lindstrom and Kim, 2006). During cataract surgery, maintenance of mydriasis is necessary to facilitate proper incision of the anterior capsule, safe removal of the cataract, and implantation of intraocular lens. Mydriatics and antiprostaglandins are routinely applied preoperatively to facilitate cataract extraction and prevent intraoperative miosis. Previous studies have demonstrated the effectiveness of various topical non-steroidal anti-inflammatory drugs (NSAIDs) (indomethacin, flurbiprofen, suprofen) in preventing miosis during cataract surgery compared to placebo. Newer topical NSAIDs also showed similar favorable effects (Cervantes-Coste et al., 2009). Coste showed that nepafenac given 3 times a day 1 day before cataract surgery was superior to tobramycin dexamethasone eye drops in maintaining intraoperative mydriasis measured at 4 different stages of the surgery. Solomon compared the effects of topical 0.5% ketorolac tromethamine ophthalmic solution with topical 0.03% flurbiprofen sodium on the inhibition of surgically induced miosis during phacoemulsification (Flach, 1992). Ketorolac provided a more stable mydriatic effect throughout the surgical procedure. Mechanical ocular trauma from phacoemulsification can cause various ocular changes, such as conjunctival hyperemia, inflammation, pain, cystoid macular edema, breakdown of the blood-

aqueous barrier, rise in intraocular pressure, and most especially surgically-induced miosis creating access for cataract removal difficult (Gamache et al., 2000). Prostaglandins play an important role in these changes. NSAIDs inhibit COX enzymes that promote prostaglandin production; hence, providing both analgesic and anti-inflammatory activities. Ophthalmic NSAIDs are used to decrease the various changes brought about by intraocular surgeries. Due to the topical nature of this drug class, systemic absorption is minimal. Nepafenac 0.1%, after topical dosing, is subsequently converted by ocular tissue hydrolases to amfenac, which is thought to inhibit the action of the cyclooxygenase prostaglandin H synthase. Nepafenac 0.1% met its primary objective by showing advantage over the control group in terms of maintaining mydriasis during phacoemulsification (Flach, 2000). In addition, nepafenac 0.1% has also shown to be more effective than placebo at maintaining mydriasis at every stage of the surgery.

Most interesting, however, is the comparison between nepafenac 0.1% and ketorolac 0.5%. Previous studies have established the effectiveness of ketorolac 0.5% for the treatment of both pain and inflammation following cataract surgery. Consequently, ketorolac 0.5% was used as a standard against which the efficacy of nepafenac 0.1% was measured (McColgin and Raizman, 1999). In the study of Antanis et al, nepafenac 0.1% reached statistical superiority compared to ketorolac 0.5% in all four stages of phacoemulsification. Nepafenac has been shown to penetrate the cornea rapidly and provides a complete and longer-lasting inhibition of prostaglandin synthesis and vascular permeability.^{55,56 (Provide)} Perhaps, this advantage in absorption and bioavailability was the reason behind its superiority in maintenance of mydriasis (Shaikh et al., 2003; Gimbel et al., 1996). In our study the mean age of the patients in group A was 55.6 ± 5.6 years and in group B was 54.6 ± 5.7 years. As compared with the study of Antanis et al the mean age in Nepafenac group was 66.3 ± 5.0 years and in Ketorolac group was 64.4 ± 7.9 years, which is comparable with our study. In our study in group A, 50% male and 50% female patients. In group B, 42% male and 58% female patients. As compared with the study of Antanis et al in Nepafenac group 28% male and 72% female patients and in Ketorolac group 29% male and 71% female patients, which is comparable with our study. In our study the mean pupil diameter before surgery in group A was 7.9 ± 0.4 and in group B was 8.0 ± 0.5 . As compared with the study of Abdel and Mahdy (2011) the mean pupil diameter before surgery in Nepafenac group was 8.2 ± 0.9 and in Ketorolac group was 8.3 ± 1.2 , which is comparable with our study. In our study the mean pupil diameter after surgery in group A was 6.4 ± 0.6 and in group B was 5.7 ± 0.5 . As compared with the study of Abdel and Mahdy (2011) the mean pupil diameter before surgery in Nepafenac group was 6.8 ± 1.0 and in Ketorolac group was 5.9 ± 0.9 , which is comparable with our study (Mahdy, 2011). In our study, the mean total

loss of mydriasis in group A was 1.4 ± 0.6 and in group B was 2.1 ± 0.4 . As compared with the study of Abdel and Mahdy (2011) in Nepafenac group the total loss of mydriasis was 1.4 ± 0.8 and in Ketorolac group was 2.4 ± 1.1 , which is comparable with our study.

CONCLUSION

On the above discussion it is concluded that topical nepafenac 0.1% has been shown to be a more effective inhibitor of miosis during phacoemulsification with IOL implantation compared with topical ketorolac (Atanis et al., 2011).

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