Original Article

Assessing the analgesic benefit of phacoemulsification under topical anesthesia using pre-operative nepafenac 0.1%

Matthew Fenech, Thomas Fenech

Abstract

Background: To compare the intra-operative analgesic benefit of cataract surgery under topical anesthesia with and without pre-operative NSAIDs, namely nepafenac 0.1% (Alcon Laboratories Inc, Nevanec®, Fort Worth, TX, USA)

Method: In a study carried out at Mater Dei Hospital, Ophthalmic department, Malta, 199 patients with a cataract were divided into two groups. 100 eyes received nepafenac 0.1% pre-operatively while 99 eyes did not. Intra-operative discomfort was judged by assessing facial grimacing, restlessness, irritability and distress and the results were noted. Patients were divided into refractive error groups, namely myopic, hypermetropic and emmetropic.

Results: Pre-operative nepafenac 0.1% produced significantly more pain free cataract surgeries, resulting in a discomfort rate of 9% vs 28% in the group where pre-operative nepafenac 0.1% was not used. Pain was also most evidently observed on insertion of the phaco handpiece. This may be said for patients in all refractive errors groups.

Conclusions: The analgesic efficacy of nepafenac 0.1% pre-operatively is significant in reduced intra-operative discomfort during cataract surgery repair under topical analgesia.

Matthew Fenech MD, MSc*
Department of Ophthalmic
Mater Dei Hospital
Msida, Malta
fenech.mat@gmail.com

Thomas Fenech MBBS, FRCS, FRCOphth.
Department of Ophthalmic
Mater Dei Hospital
Msida, Malta

**Corresponding Author*

Keywords

NSAIDs, Nevanac®, nepafenac 0.1%, topical anesthesia, myopia, phacoemulsification

Introduction

Nepafenac 0.1% (Alcon Laboratories Inc, Nevanac®, Fort Worth, TX, USA) is an ophthalmic NSAID. It has a prodrug structure, making it a neutral molecule. This property allows it to penetrate the cornea, after which it is converted by intraocular hydrolases to its more active moiety amfenac.[1] Nepafenac is unique, in that its bioconversion to amfenac is targeted to the iris and ciliary body and, to an even greater extent, the retina and choroid.

Like other NSAIDs, nepafenac works by inhibiting the synthesis of prostaglandins. While we are aware of the beneficial implications of NSAIDs in reducing post-operative inflammation and its sequelae such as cystoid macular oedema, not much is yet known about how pre-operative NSAIDs possibly have an effect in reducing intra-operative discomfort.

The primary objective of this study was to assess the effect of pre-operative nepafenac 0.1% on the effects of intra-operative discomfort in cataract surgery performed under local anaesthetic. Secondary outcomes included defining the stage at which discomfort was most likely to be experienced and the impact of refractive error on the degree of discomfort experienced.

Materials and Methods

This observational study was performed at Mater Dei Hospital Malta between January 2014 and January 2016. The study included 196 patients (199 eyes) who underwent phacoemulsification surgery by the same consultant surgeon. 100 eyes were operated on after application of pre-operative topical anesthesia using oxybuprocaine 0.4% while 99 eyes were operated on after application of pre-

operative oxybuprocaine 0.4% and nepafenac 0.1%. All procedures were performed by the same consultant surgeon.

The study was approved by the appropriate patient safety and ethics approval boards. All patients underwent an extensive pre-operative assessment.

Strict inclusion and exclusion criteria were established. Patients being unfit for surgery were excluded from the study cohort. Patients with contra-indications to non-steroidal anti-inflammatory medication or who were already on regular pain relief were not considered for the purpose of the study. Patients, who had communication problems, were unable to co-operate during pre-operative assessment or who were deemed excessively photophobic or expected to endure excessive discomfort due to prolonged surgery or pupils which were difficult to dilate were excluded from the study, necessitating surgery under general anesthesia.

All patients were advised on the steps of the procedure, the expected duration and the importance of relaxing throughout the procedure. Patients were advised to keep their eyes open throughout the procedure, avoiding excessive eye movement at all times. Patients were consented before the procedure and all patients who failed to provide their consent were excluded from the study.

All patients were brought in the morning of the procedure. 100 eyes were instilled with 2 drops of oxybuprocaine 0.4% 5 minutes before the procedure. 99 eyes were also given 2 drops of nepafenac 0.1% 1 hour before the procedure. Patients who were excessively anxious or suffered severe pain during the procedure were given retrobulbar blocks. Top-up topical anaesthetic was also used. Such patients were considered as clear failures to the success of both pre-operative nepafenac 0.1% and oxybuprocaine0.4%. No effort was made to randomize the pre-operative nepafenac 0.1% group from the group that did not receive such NSAIDs.

All procedures were performed by the same consultant ophthalmic surgeon. The Infinity Phacoemulsification Machine by Alcon was used throughout the study. Patients underwent the same three stage approach; capsulorrhexis, hydrodissection and phacoemulsification, followed by IOL insertion. An effort was made to maintain the same size of main incision whilst also making use of the same phaco pressures as these may influence the discomfort experienced. Foldable posterior chamber intra-ocular lenses by Alcon were used.

Intra-operative and post-operative discomfort was assessed by the same consultant surgeon. Verbal response, restlessness and facial grimacing observed were used to identify any discomfort. An official pain score scale by patients was not utilized in order to avoid patient variability and bias.

Results

A total of 199 eyes were used for this study. Only patients who completed the surgery without intra-operative complications were deemed fit to be included in the study.

The mean age of patients used in the study was 76 years, with ages ranging from 32 years to 90 years of age. Over 95% of patients were Caucasian. 108 of the eyes belonged to female patients and 91 belonged to male patients. There was no significant difference in the degree of discomfort witnessed between male and female patients.

Discomfort was witnessed in 28% of patients who were not provided with pre-operative nepafenac 0.1% but in only 9% of patients to whom nepafenac 0.1% was given pre-operatively *(Figures 1-3)*. By using Fisher's exact test, the results prove to be statistically significant, with a P value of 0.0009.

In both groups, discomfort was most evident in the myopic sub-group, with 22.2% of myopic patients in the pre-operative nepafenac 0.1% group experiencing some form of discomfort as opposed to 37.5% of myopes who were not given nepafenac 0.1% pre-operatively. Furthermore, the greater the degree of myopia observed, the greater the degree of perceived discomfort. Least discomfort was evident in the hypermetropes, with discomfort evident in 2.6% of patients in the pre-operative NSAID subgroup and 4.3% of patients who were not given pre-operative nepafenac 0.1% *(Figure 4)*.

Irrespective of one's refractive error, discomfort was most evident on insertion of the phaco-handpiece, amounting to 72.7% of all the discomfort felt throughout the cohort. Such a pattern was evident in all refractive error groups in both those patients treated with or without pre-operative nepafenac 0.1%. Least discomfort was noted on insertion of the intra-ocular lens (IOL) *(Figure 5)*.

Figure 1: *Graph showing the percentage of discomfort witnessed in each refractive error group in patients who were not given pre-operative topical NSAIDs. Discomfort being most evident in the myopic sub-group.*

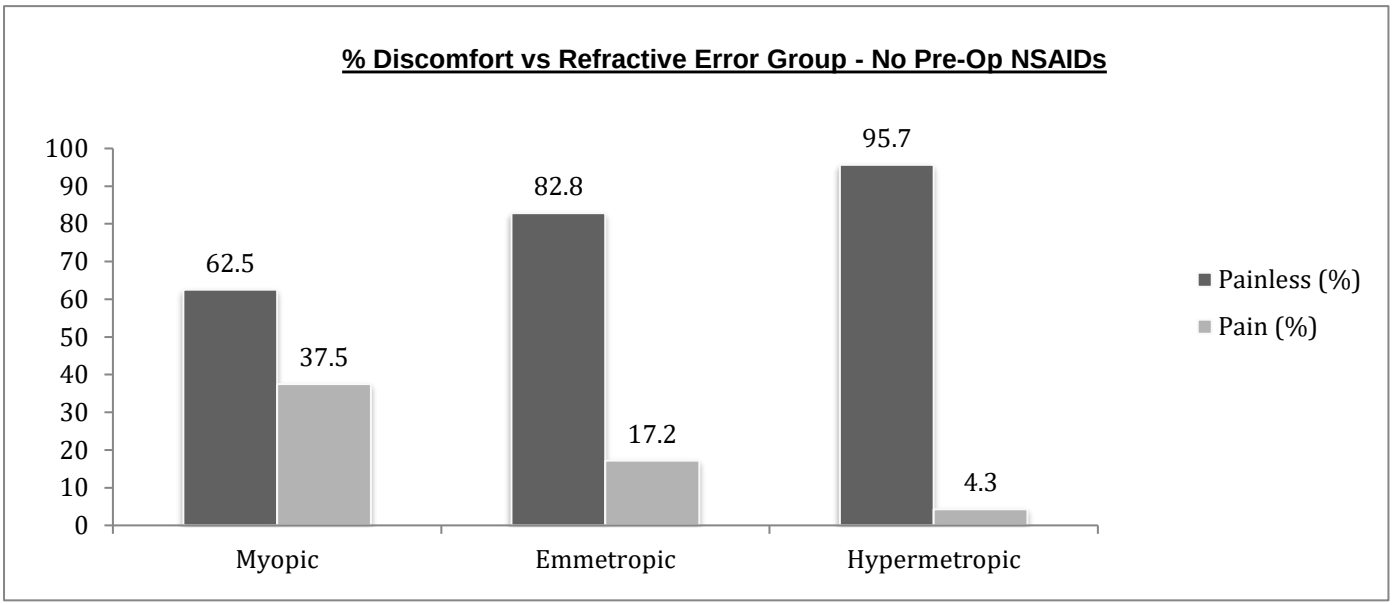


Figure 2: *Graph showing the percentage of discomfort witnessed in each refractive error group in patients who were given pre-operative topical NSAIDs. Discomfort being most evident in the myopic sub-group*

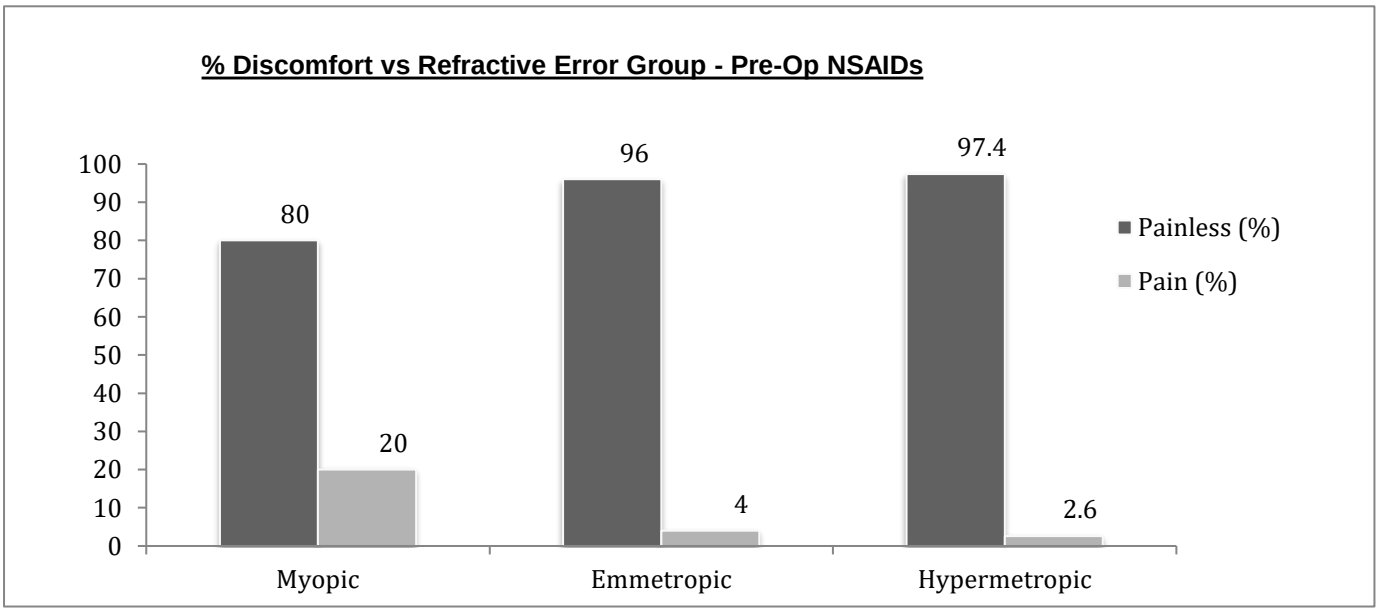


***Figure 3**: Graph showing the percentage of discomfort witnessed in each refractive error group in patients who were given pre-operative topical NSAIDs vs those who were not given pre-operative NSAIDs.*

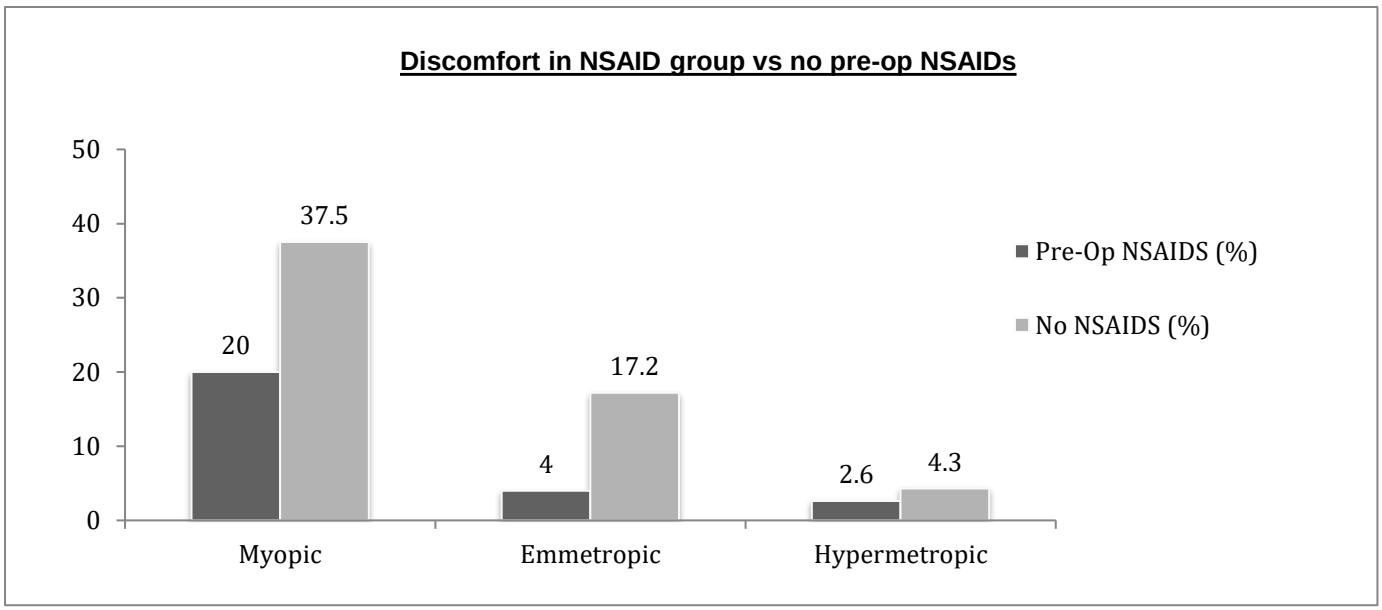


***Figure 4:** Graph showing the increase in discomfort witnessed with increasing myopic severity.*

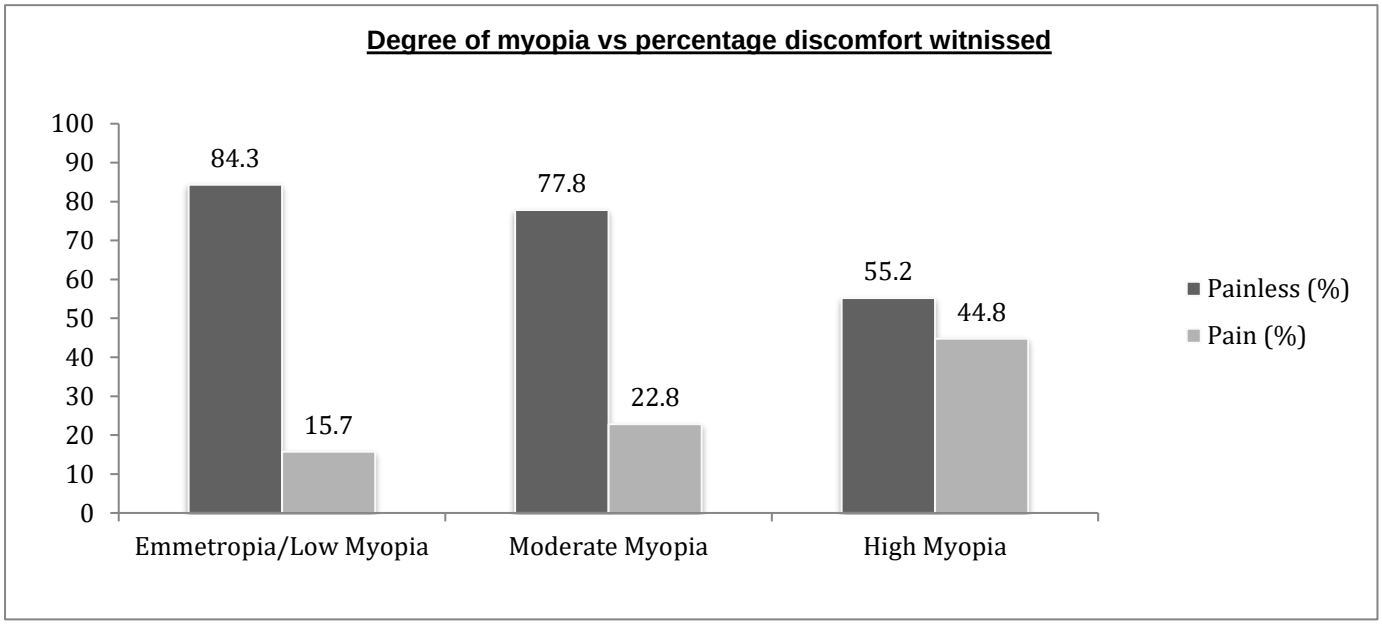
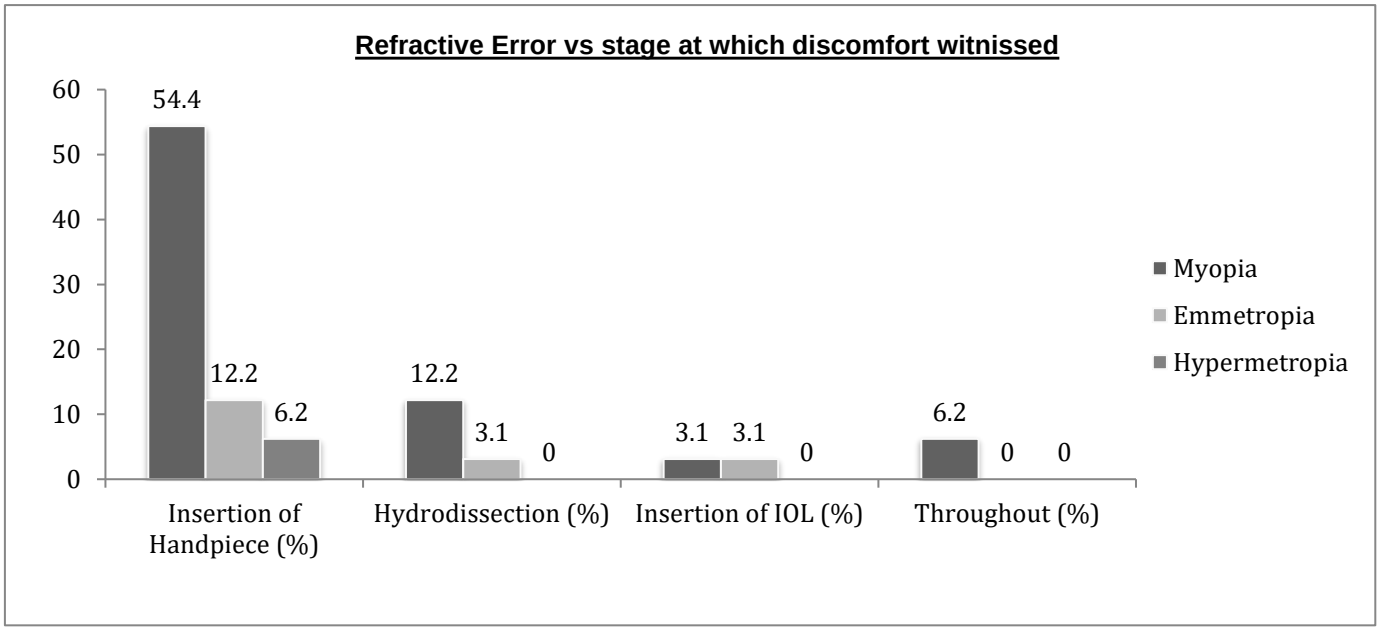


***Figure 5**: Graph showing the stage at which discomfort was witnessed within each refractive error group*



There was no statistical correlation between patient age and perceived intra-operative discomfort. The same may be said for patient sex.

Discussion

Modern day cataract surgery is a quick, relatively painless and routine procedure, performed primarily under local anaesthetic.[2] It involves extraction of the natural lens and replacing it with an artificial intra-ocular lens. The power of the artificial lens is calculated and adjusted pre-operatively.[3] Advances in cataract surgery have meant that this relatively routine procedure has come a very long way since the first recorded procedures in India in the 5th century BC.[4]

Cataract surgery is today performed with the aid of phacoemulsification and is routinely performed under topical anaesthesia. Regional or local anaesthesia is also commonly employed, but recently comparative studies have shown equivalent results in intra-operative and post-operative pain relief.[5]

Topical anaesthesia is commonly performed using ocular anaesthetics, Benoxinate (oxybuprocaine 0.4%) being the most commonly used due to its favorable side effect profile, being less toxic to the corneal epithelium when compared to amide anaesthetics such as lidocaine and bupivacaine. A study by S. Waheeb et.al showed that topical anesthesia solely using topical oxybuprocaine proved to be a safe alternative to retro- or peribulbar injections, being less time consuming and less risky.[6]

Ocular inflammation is a common phenomenon during and after cataract surgery, resulting in intra-operative and postoperative pain. Topical NSAIDs reduce inflammation by reducing prostaglandin synthesis and have been shown to control and reduce inflammation after surgery.[7]

Nepafenac 0.1% was used for the purpose of this study. Unlike other NSAIDs, nepafenac is unique in that it has a prodrug structure, making it a neutral molecule with rapid corneal permeability. The drug is rapidly hydrolyzed to amfenac, the active moiety of the drug. [7] It is understood that such conversion is targeted to the iris and ciliary body. Results from our study reveal that most discomfort is experienced on insertion of the phaco handpiece, the point at which there is a sudden surge in intra-ocular pressure and deepening of the anterior chamber, accompanied by stretching of the zonular fibers. We postulate that the targeted nature of nepafenac 0.1% helps in inhibiting or dampening the pain response felt when such events are set in motion.

Our experience with pre-operative topical NSAIDs has been very encouraging, proving to be extremely beneficial in reducing intra-operative discomfort when compared to using topical oxybuprocaine alone. We postulate that such results are due inhibition of prostaglandin pathways that are immediately activated on manipulation of the

anterior chamber.

It is interesting to note that most discomfort is witnessed in the myopic subgroup at all stages of the procedure. It is unclear as to why such a discrepancy is so evident, especially when one considers the larger nature of the anterior chamber in a myopic eye as opposed to a hypermetropic eye. We postulate that with advanced control of intra-ocular pressure through active fluidics and an IOP ramp, one is able to reduce the overall discomfort observed during cataract surgery, especially when considering that over 70% of discomfort witnessed is on insertion of the phaco handpiece. The IOP ramp will allow a gradual and progressive increase in the IOP as opposed to a sudden surge in IOP during insertion of the phaco handpiece, resulting in a less sudden stretch of the anterior chamber.

Our study is limited in that although strict exclusion and inclusion criteria were implemented, no efforts were made to introduce a control group or a means of blinding. A placebo would have proven beneficial, reducing both performance bias as well as observer bias from the surgeon involved. Whilst this ensures an adequate sample size for both groups of patients by being able to cater for drop outs, it does leave the door open to operator bias. That being said, data was collected over a relatively short period of time, not allowing for changes in operator technique over time, serving to counteract the Hawthorn effect. It is important to note that patients on any source of conflicting extraneous treatment such as any other pain relief medication were excluded for the purpose of this study. Furthermore, although the sample size used was substantial, it must be pointed out that no power calculation was performed in order to assess the true size of the sample needed.

Conclusion

Topical anesthesia is a satisfactory means of pain relief when undertaking phacoemulsification and IOL insertion. Furthermore, pre-operative topical NSAID application reduces discomfort rates in all refractive error subgroups.

There is no association between patient age or sex and discomfort witnessed.

It is evident that the greater the degree of myopia, the greater the rate of discomfort witnessed. Discomfort is also mostly witnessed on insertion of the phaco-handpiece, most prevalent in the myopic sub-group.

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