Study on immediate postoperative pain following cataract surgery: intraoperative endovenous administration of dipyrone

Estudo da dor no período pós-operatório de cirurgia de catarata: utilização de dipirona no intraoperatório

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ABSTRACT

Objectives: Evaluate the effect of intraoperative endovenous administration of dipyrone on postoperative pain in patients submitted to phacoemulsification by correlating pain scores with duration of surgery and the amount of cumulative dissipated energy (CDE) delivered to the eye. Methods: The sample consisted of 104 eyes from 52 patients submitted to phacoemulsification under topic anesthesia and sedation. In each patient, one eye was treated intraoperatively with 1g dipyrone. Information was collected on cataract grade/type, duration of surgery and CDE. Postoperative pain was scored on a visual analog scale at 15 min and 24 hours. Results: Between 15 min and 24 hours, pain decreased significantly (p=0.004) among patients not treated with dipyrone, but no change was observed in patients receiving dipyrone. Caratact severity was positively associated with postoperative pain (p=0.046). **Conclusion:** The absence of a measurable effect of dipyrone on pain scores matched the literature. The decrease in pain scores at 24 hours among patients not treated with dipyrone may be explained by the influence of subjective psychological factors on pain perception. Higher grades of cataract were associated with greater postoperative pain.

Keywords: Pain/etiology; Cataract extraction/adverse effects; Phacoemulsification; Dipyrone/administration & dosage; Anesthesia and Analgesia; Postoperative period; Perioperative period.

RESUMO

Objetivos: Quantificar a dor dos pacientes submetidos a cirurgia de facoemulsificação sob anestesia tópica e anestesia tópica mais dipirona e avaliar se há correlação da dor com o tempo operatório, a graduação da catarta e a Energia Ultrassônica Dissipada Acumulada. Métodos: Cento e quatro olhos de 52 pacientes foram submetidos a cirurgia de catarata por facoemulsificação. Um olho foi submetido a anestesia tópica associado à sedação. O outro olho foi submetido a anestesia anterior acrescida de 1g de dipirona venosa. 15 minutos e 24 horas após a cirurgia, uma Escala Visual de Dor era respondida. Registraram-se a graduação da catarata, tempo cirúrgico, energia ultrassônica. Resultados: Dor no grupo sem dipirona 15 minutos e 24 horas apresentou decréscimo com correlação estatística significativa (p=0,004). Não houve significância estatística na redução da dor no grupo submetido à infusão de dipirona. Pacientes com cataratas de maior graduação apresentaram dor maior no pós-operatório (p=0,046). Conclusão: Ausência de redução significativa da dor com a dipirona apresentou resultados semelhantes a outros estudos. Redução da dor 24 horas após a cirurgia no grupo sem o analgésico pode ser devido à subjetividade da dor. Pacientes com cataratas de grau mais avançados apresentam dor mais intensa.

Descritores: Dor/etiologia, Extração de catarata/efeitos adversos; Facoemulsificação; Dipirona/administração & dosagem; Anestesia e Analgesia; Período pós-operatório; Período perioperatório

Institution where the study was carried out: Hospital Santa Casa de Misericórdia de Vitória/ES

The authors declare no conflicts of interests.

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Introduction

n ophthalmology, pain is present in a range of morbidities. From a simple ocular foreign body, a case of glaucoma, to surgical procedures.

From this perspective, it can be noted that in ophthalmologic conditions pain is routinely present, as in cases of cataract correction surgery by means of crystalline extraction with intraocular lens implant. Cataract surgery is the most commonly performed ophthalmic procedure in the world. (1) It is estimated that 300,000 people in the United Kingdom, 500,000 in France, and 2 million in the United States are submitted to phacoemulsification annually, and the last decades showed great development in surgical and anesthetic techniques. (1,2) For many years, peribulbar anesthesia was the only method used to control pain in the procedures of crystalline extraction. (3) However, the safety of this method was questioned due to a number of documented complications such as eyeball perforations, retrobulbar hemorrhage, extraocular musculature dysfunction, and occlusion of retinal vessels. (3) Currently, several anesthetic options are used, such as retrobulbar, peribulbar, subtenonian and topical. The choice depends on the surgeon's experience, the type of surgery, and the patient's emotional characteristics. (4-6) Routinely, topical anesthesia is the most used because of providing relative comfort to the patient with lower incidence of complications when compared to other methods. (7) However, in some cases the analgesia reached is insufficient and requires additional associations. (7)

Several investigations were carried out to verify the efficacy and cost of associations of certain steroidal or non-steroidal analgesic or anti-inflammatory drugs as adjuvants in patients' analgesia in ophthalmologic procedures. (8-10) Comparisons of medications such as topical prednisolone and subtenonian triamcinolone, (9) topical nepafenac and ketorolac, (10) topical dexamethasone and subtenonian betamethasone,(8) and oral paracetamol⁽¹⁾ were tested in clinical trials to determine the analgesic potential in the intra and postoperative periods of the drugs and their real effectiveness in protecting the patient from pain. There are studies comparing common drugs in the public health system to control postoperative pain in several surgeries, such as dipyrone, opioids and non-steroidal anti-inflammatory drugs (NSAIDs).(11) However, pain control remains a major controversy due to the range of possibilities with many advantages and disadvantages intrinsic to each option available. An example of this is the fact that dipyrone is considered safer than NSAIDs in avoiding lesions in the gastrointestinal tract and in the kidneys, although it is considered a potential agranulocytosis factor even at low risk. (12) No studies were found in the literature evaluating the influence of intraoperative intravenous use of analgesics on postoperative pain.

In this context, the search for ways to determine whether analgesic medications may exert effects in the treatment of intra- and postoperative pain in ophthalmology is justified. For this, it is important to study easily accessible medications in the public health system in surgeries widely performed in Brazil. Thus, assessing the efficacy of Dipyrone in phacoemulsification may contribute to the symptomatic management of patients in order to provide them relief after the procedure and help them rest and avoid complications. The present study aims to quantify the pain of patients undergoing phacoemulsification surgery under topical anesthesia, and to evaluate whether the use of perioperative intravenous dipyrone (EV) in synergy with topical

anesthesia during phacoemulsification surgery helps reduce postoperative pain. In addition, the study analyzes whether there are correlations between perceived pain, operative time and the amount of accumulated dissipated ultrasound energy (EDA) during surgery with and without the use of dipyrone.

METHODS

We studied 104 eyes from 52 patients undergoing phacoemulsification with intraocular lens implant at Hospital Santa Casa de Misericórdia de Vitória/ES The study was divided into two stages:

At one stage, patients underwent phacoemulsification by a single experienced surgeon under topical anesthesia (Anestalcon®) and sedation given immediately prior to surgery. Fifteen minutes after the end of the surgical procedure, the patient responded to the visual pain scale to quantify pain at that time. The same procedure was repeated twenty-four hours after surgery. The standardized Visual Analog Pain Scale was used, as well as in several studies previously published (Figure 1). (1.3.4.7.11)

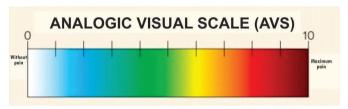


Figure 1: . Visual Analog Pain Scale.

In another stage, the same patients had their contralateral eye submitted to phacoemulsification by the same surgeon, but with 1g of dipyrone EV at the time of surgery along with topical anesthesia and sedation. Fifteen minutes after the end of it, the patient responded to a visual scale to quantify pain at that time. The same procedure was repeated twenty-four hours after surgery.

The choice of which eye to operate first and whether the patient would receive dipyrone in the surgery of the first or second eye was performed by means of a draw among those responsible for the study. Patients did not know in which surgery they received dipyrone associated with the topical anesthetic. All participants signed a free and informed consent form.

Patients with previous ophthalmologic surgeries, ophthalmologic conditions causing pain such as uveitis and glaucoma, rheumatic problems, chronic use of medications that can mask pain, such as analgesics, hormonal and non-hormonal anti-inflammatories were excluded from the study.

The preoperative cataract graduation, surgery time, and the amount of accumulated dissipated ultrasound energy (EDA) were recorded in each phacoemulsification surgery.

After data collection and typing, they were correlated with pain after the first and second surgeries, and we verified whether or not there was change with the use of dipyrone EV. Data on pain were further stratified by age and sex of the participants who signed a free and informed consent form on participation in the study prior to the development of the same.

Initially, all variables were analyzed descriptively. For the quantitative variables, this analysis was by observing the minimum and maximum values and calculating the averages, standard deviations, and median. For qualitative variables, the absolute and relative frequencies were calculated.

Wilcoxon's nonparametric test was used to compare the two groups, since the assumption of normality of data was rejected. The software SPSS 17.0 for windows was used for calculations. The level of significance used for the tests was 5%.

RESULTS

Fifty-two patients aged 56-77 years (average of 67.15 years with standard deviation of 5.20 years and median of 67.50 years) were evaluated.

Twenty-eight (53.8%) patients were male, and 24 (46.2%) were female.

The distribution of cataract classification and surgery time are presented in Tables 1 and 2. There was no significant difference between the groups (p = 0.350).

Table 1
Absolute and relative frequencies of the degree of cataract in the eyes of patients undergoing facectomy surgery with or without intraoperative use of dipyrone

| | Use of dipyrone * | | | | | |
|--------------------|-------------------|--------|--------------|------|--|--|
| | Yes | (n=52) | No (n=52) | | | |
| Degree | N | % | \mathbf{N} | % | | |
| Cortico-Nuclear 2+ | 6 | 11.5 | 2 | 3.8 | | |
| Cortico-Nuclear 3+ | 2 | 3.8 | 2 | 3.8 | | |
| Nuclear 1+ | 6 | 11.5 | 4 | 7.7 | | |
| Nuclear 2+ | 36 | 69.2 | 40 | 76.9 | | |
| Nuclear 3+ | 2 | 3.8 | 4 | 7.7 | | |

^{*} Intravenous dose of 1g

Table 2

Duration of phacoemulsification surgery (in minutes) in the groups with and without administration of intravenous intravenous dipyrone 1g

| Dipyrone | Average | SD | Median | Min | Max | Valor de p* |
|----------|---------|------|--------|------|-------|-------------|
| Yes | 7.32 | 1.25 | 7.00 | 5.00 | 10.00 | 0.350 |
| No | 7.58 | 1.68 | 8.00 | 5.00 | 11.00 |) |

^(*) descriptive level of probability of the Wilcoxon non-parametric test

There was no significant difference between the groups regarding EDA during cataract surgery (Table 3).

Table 3
Descriptive values of accumulated dissipated ultrasonic energy (EDA) in phacoemulsification surgeries in the groups with and without administration of intraoperative intravenous dipyrone 1g

| Dipyrone | Average | SD | Median | Min. | Max. | P-value* |
|----------|---------|------|--------|------|-------|----------|
| Yes | 7.40 | 4.71 | 6.68 | 1.74 | 26.61 | 0.949 |
| No | 7.52 | 5.55 | 6.04 | 1.59 | 27.71 | |

^(*)descriptive level of probability of the Wilcoxon non-parametric test

Table 4 shows the descriptive values of the degree of pain in 15 minutes and 24 hours after surgery in each group.

Table 4
Descriptive values of the degree of pain in 15 minutes and 24 hours after cataract surgery in the groups with and without administration of intraoperative intravenous dipyrone 1g

| Dipyron | e Moment | Average | SD | Median | Min. | Max. | P-value* |
|---------|----------|---------|------|--------|------|------|----------|
| Yes | 15 min. | 2.31 | 1.83 | 2.00 | 0.00 | 7.00 | 0.004 |
| | 24 hours | 1.31 | 1.32 | 1.00 | 0.00 | 5.00 | |
| No | 15 min. | 1.96 | 1.40 | 2.00 | 0.00 | 5.00 | 0.794 |
| | 24 hours | 2.23 | 2.44 | 1.00 | 0.00 | 9.00 | |

(*)descriptive level of probability of the Wilcoxon non-parametric test

For Table 4, we observed that in the group without Dipyrone there is a significant decrease in pain from time 15 minutes to 24 hours. In the group with Dipyrone we did not observe significant alteration. Wilcoxon's non-parametric test also showed that the groups did not present significant differences between the groups in the degree of pain at the time 15 minutes (p = 0.511) and 24 hours (p = 0.071), although Figure 2 shows that the group with dipyrone had a lower pain rate 15 minutes after surgery and a higher rate 24 hours compared to the group that did not use the medication.

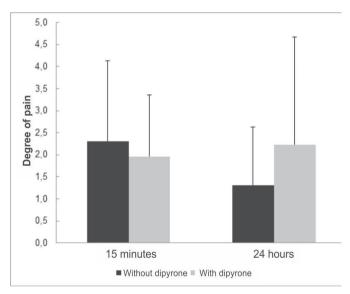


Figure 2: Comparison of pain between groups with and without administration of intraoperative intravenous dipyrone 1g at 15 minutes and 24 hours after phacoemulsification surgery.

The figures below show the pain rate at 15 and 24 hours after surgery between the groups. It can be seen that the degree of pain perceived by the patient tends to stabilize in relation to the time of surgery in the groups with and without the use of dipyrone after 15 minutes of surgery (Figures 3 and 4) and a growing tendency after 24 hours of surgery (Figures 5 and 6), but without statistical significance

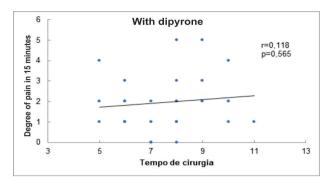


Figure 3: Degree of pain 15 minutes after phacoemulsification surgery in the group that received intraoperative intravenous dipyrone 1g.

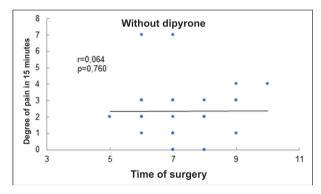


Figure 4: Degree of pain 15 minutes after phacoemulsification surgery in the group without intravenous dipyrone.

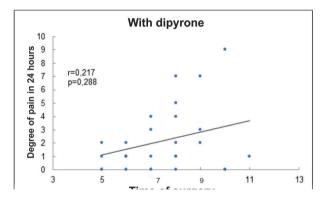


Figure 5: Degree of pain 24 hours after phacoemulsification surgery in the group with administration of 1g of intravenous dipyrone.

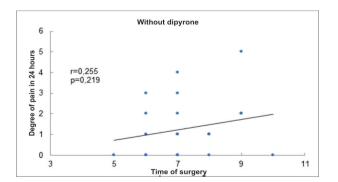


Figure 6: Degree of pain 24 hours after phacoemulsification surgery in the group without administration of intravenous dipyrone.

Table 5 shows the study of the correlation between the time of surgery and EDA with the degree of pain.

Table 5
Spearman's correlation coefficients for pain ratio between the groups with and without administration of intravenous dipyrone 1g with time of surgery and accumulated dissipated ultrasound energy (EDA)

| | | Without | Dipyrone | With Dipyrone | | | |
|------|---|------------|-----------|----------------|----------|--|--|
| | _ | Degree | e of pain | Degree of pain | | | |
| | | 15 minutes | 24 hours | 15 minutes | 24 hours | | |
| Time | R | 0.064 | 0.255 | 0.118 | 0.217 | | |
| | p | 0.760 | 0.219 | 0.565 | 0.288 | | |
| EDA | R | 0.199 | 0.271 | 0.007 | 0.008 | | |
| | p | 0.329 | 0.180 | 0.971 | 0.970 | | |

Table 5 shows that there is no significant correlation between the degree of pain at times 15 minutes and 24 hours and surgery time and the EDA for the two study groups.

Evaluating the correlation between the degree of cataract and the pain rate, it is observed that:

- 1) In the group without dipyrone, the cataract gradient presented a positive and significant correlation with the pain degree in 15 minutes (r = 0.403, p = 0.046), and did not present significant correlation with pain in 24 hours (r = 0.090; p = 0.668). Therefore, in the group without dipyrone the higher the degree of cataract, the higher the pain index in 15 minutes. For example, a cataract Nuclear 3 + would present a higher pain rate when compared to a Nuclear 1+
- 2) In the group with dipyrone, the degree of cataract did not present a significant correlation with the pain rate in 15 minutes (r = -0.074, p = 0.726) and 24 hours (r = -0.045, p = 0.830).

Discussion

The objective of the present study was to verify if the use of intravenous dipyrone would be effective in the control of postoperative pain, and analyze the correlation between pain perception and operative time and the levels of EDA. Thus, we could verify if there is any advantage in using it more widely because of having a lower cost and being easily available in hospitals and public and private clinics, or if its prescription would not be interesting. Quantifying and characterizing patients' pain becomes essential in order to suggest a way of prevent it. The fact of pain being significantly lower 15 minutes after the end of surgery in the group that did not use the medication could be an indication that its use would be a greater expenditure. However, the fact that algia is lower in the absence of medication may also be correlated with the subjective experience of pain and its rather psychologically influential character of the patients (1) to the point where a "placebo effect" is noticed.

The profile of participants of the present study shows similarities with studies of the same kind with regard to age, gender and type of cataract. (3-5)

The present study did not show significant differences between the groups, as well as similar studies carried out with other analgesic or anesthetic substances. Thus, in our review, there were no articles presenting significant statistical differences in comparing the topic Anesthesia (6), Peribulba $r^{(4)}$, Subtenonian, (11) Oral acetaminophen (3), and topical anti-inflammatory drugs (12). Furthermore, the degree of pain reported by the patients in the Pain Visual Scale is close or even equal to those reported in these same studies. (3,4,10,12)

There are no previous reports on the study of pain during cataract surgery and its relation with operative time and with EDA. However, it is important to describe the influence of such factors in determining analgesia and in the success of the surgical procedure, in order to instruct surgeons to use this parameter in a parsimonious way so as to provide greater efficiency to surgery.

(13) It is known, for example, that surgical time increases the risk of endophthalmitis, so it would not be nonsense to suppose that surgical time could also be correlated with the pain rates reported by patients. One of the reasons would be the greater manipulation of instruments in the anterior segment of the eye as a cause of greater inflammatory effect, which may explain the increasing tendency of pain 24 hours after surgery in the longer procedures, as previously shown. However, we did not observe statistical correlations in the present study.

CONCLUSION

The present study showed that intraoperative intravenous dipyrone did not present a significant reduction of pain in the sample studied. In addition, operative time and EDA were not statistically significant factors in the patients' perception of pain. Patients with cataracts with higher degree of maturation presented greater pain perception. However, to corroborate these facts, we suggest greater reproduction of the present study so that you would see how the subjectivity of pain is mitigated.

REFERENCES

- Kaluzny BJ, Kazmierczak K, Laudencka A, Eliks I, Kaluzny JJ.
 Oral acetaminophen (paracetamol) for additional analgesia in
 phacoemulsification cataract surgery performed using topical
 anesthesia Randomized double-masked placebo-controlled trial. J
 Cataract Refract Surg. 2010;36(3):402-6.
- 2. Nouvellon E, Cuvillon P, Ripart J, Viel EJ. Anaesthesia for cataract surgery. Drugs Aging. 2010;27(1):21–38.
- Coelho RP, Weissheimer J, Romão E, Velasco e Cruz AA. Pain induced by phacoemulsification without sedation using topical or peribulbar anesthesia. J Cataract Refract Surg. 2005;31(2):385-8.

- Duguid IG, Claoué CM, Thamby-Rajah Y, Allan BD, Dart JK, Steele AD. Topical anaesthesia for phacoemulsification surgery. Eye (Lond). 1995;9 (Pt 4):456-9.
- Stevens JD. A new local anesthesia technique for cataract extraction by one quadrant sub-Tenon's infiltration. Br J Ophthalmol. 1992;76(11):670-4.
- Tavares VN, Colossi CG, Saalfeld V, Vilela MA. Facoemulsificação sob anestesia tópica: série de casos. Rev Bras Oftalmol. 2013;72(3):178–80.
- Apiol A, Kartal B, Ekinci M, Cagatay HH, Keles S, Ceylan E, et al. Topical Anaesthesia for catardt surgery: the patients?persperctive. Pain Res Treat. 2014;2014:1–6.
- Dieleman M, Wubbels RJ, van Kooten-Noordzij M, de Waard PW. Single perioperative subconjunctival steroid depot versus postoperative steroid eyedrops to prevent intraocular inflammation and macular edema after cataract surgery. J Cataract Refract Surg. 2011;37(9):1589-97.
- Paganelli F, Cardillo JA, Melo LA Jr, Oliveira AG, Skaf M, Costa RA; Brazilian Ocular Pharmacology and Pharmaceutical Technology Research Group. A single intraoperative sub-Tenon's capsule triamcinolone acetonide injection for the treatment of post-cataract surgery inflammation. Ophthalmology. 2004;111(11):2102-8.
- Duong HV, Westfield KC, Chalkley TH. Ketorolac tromethamine LS 0.4% versus nepafenac 0.1% in patients having cataract surgery. Prospective randomized double-masked clinical trial. J Cataract Refract Surg. 2007;33(11):1925-9
- Konijnenbelt-Peters J, van der Heijden C, Ekhart C, Bos J, Bruhn J, Kramers C. Metamizole (Dipyrone) as an alternative agent in postoperative analgesia in patients with contraindications for nonsteroidal anti-inflammatory drugs. Pain Pract. 2017;17(3):402-8.
- 12. Hinz B, Cheremina O, Jouri B, Renner B, Zolk O, Fromm MF, et al. Dipyrone elicits substantial inhibition of peripheral cyclooxygenases in humans: new insights into thepharmacology of an old analgesic. FASEB J. 2017;21(10):2343–51.
- Chen M, Chen M. Comparison of CDE data in phacoemulsification between an open hospital-based ambulatory surgical center and a free-standing ambulatory surgical center. Clin Ophthalmol. 2010; 4:1287-9.

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