A comparative study between Ketorolac versus Metamizole in the Treatment of acute postoperative pain in children undergoing adenotonsillectomy

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ABSTRACT

Pain is the first general cause of consultation in most medical specialties, being also the most frequent cause of suffering and disability that seriously affects the quality of life of millions of people in the world. The aim is to evaluate the effectiveness of the use of ketorolac and metamizole in the treatment of postoperative acute adenotonsillectomy pain in children. An interventional clinical trial study included 80 children who were optionally subjected to adenotonsillectomy, within the age in the ranged from 5 to 12 years of age. Patients divided in two groups according to the analgesic regimen they received in the operating room, 40 children received Metamizole and 40 children received Ketorolac. In the Ketorolac group, 67.5% did not experience post-anesthetic recovery on the Ocher scale, and 32.5% had mild to moderate pain (1 to 6). In the Metamizole group, 27.5% of children reported no pain, and 72.5% rated their pain as mild to moderate. The degree of pain relief measured on the Oucher scale was higher in patients receiving Ketorolac (p <0.001). We concluded that Ketorolac is reducing postoperative pain significantly than metamizole in children undergoing Adeno-tonsillectomy.

INTRODUCTION

Pain is the first general cause of consultation in most medical specialties, being also the most frequent cause of suffering and disability that seriously affects the quality of life of millions of people in the world. (Bujedo et al., 2015). Pain is one of the most pressing human experiences and is characterized by being subjective, variable from one individual to another. The International Association for the Study of Pain (IASP) defines pain as a sensory and emotional experience associated with a current or potential tissue damage or described in terms of damage. (Chan and Parikh, 2014). Postoperative pain is a variant of acute nociceptive pain, originating from an injury, in this case the surgical wound that includes skin, tissue and viscera. According to Simon (2012) the intensity of postoperative pain is not influenced by race, sex, age or by the existence of previous operations, what influences is the type or location of the incision, psychological emotional factors, preoperative preparation, the place and nature of the operation. (Pace et al., 2006).
of the first publication in which the poor control of pain was demonstrated in the postoperative period until today, little has been done to solve the problem and approximately 75% of the operated patients receive insufficient analgesic treatment.

The most commonly used method for pain control after surgery remains the intramuscular injection of an analgesic prescribed by the surgeon and administered by the nursing staff when the patient has pain. However, the ineffectiveness of this method for pain control is recognized. (Oliveira et al., 2012)

This technique allows ineffective treatment, with inadequate doses and inappropriate intervals between doses, resulting in a recurrence of the pain cycle (gradual relief, excessive edition and return of pain).

According to Bolívar (1997), it is shown that adequate pain relief in the intra and postoperative period reduces morbidity, decreases hospitalization time and consequently the expenses for this concept. (Fieler et al., 2015)

Among the conventional procedures for treating postoperative pain, we have regional blockages, opioids and nonsteroidal anti-inflammatory drugs (NSAIDs). The most commonly used are opioids, but due to the excessive propensity for side effects and addiction, they give rise to the current insufficient treatment of pain, resulting in non-steroidal anti-inflammatories as an alternative for the management of postoperative pain. (Gan, 2017)

The prevention of postoperative pain beginning before, during or after surgery usually decreases the intensity of postoperative pain and the pharmacological requirements for its treatment. Recently the importance of the prevention of postoperative pain has been highlighted, through premedication as an effective measure to treat it. Based on this principle the importance of the present study, whose purpose is to demonstrate the efficacy of Ketorolac, which is a non-steroidal anti-inflammatory analgesic in postoperative analgesia, administered preventively in patients scheduled for abdominal hysterectomy, surgery whose anesthetic wake is accompanied by severe pain, hemodynamic instability and irritability among others. (Garimella and Cellini, 2013)

It is now accepted that pain control is predicted and controlled safely and effectively in all children, so it determines that pain management techniques should be applied before the pain stimulus. (Gobble et al., 2014) In recent years, children’s control of acute pain has undergone very positive changes. Pain assessment tools have been developed at various stages of development, and routine pain measurements are carried out at many centers. (Granadillo et al., 2001) Considering the concepts of pain management, we decided to compare the usefulness of two analgesics that are controversial in children but widely used in pain management.

PATIENTS AND METHODS

Study population
An interventional clinical trial study carried at three hospital (Ghazi Al-Hariri Teaching hospital, Al-Karkh general hospital and Al-Diwania Teaching hospital.

Study was included 80 children who optionally underwent adenoid-tonsillectomy, who were between 5 and 12 years of age attending the hospital. Two groups were formed: those receiving intraoperative ketorolac and those receiving Metamizole. Analgesia was administered 20 minutes before the end of the operation.

The variables evaluated in the immediate postoperative period were: the level of pain on the Oucher scale, the degree of change in vital signs, such as heart rate, blood pressure and oxygen saturation up to 2 hours after surgery and admission status after admission, according to analgesia.

In the immediate postoperative period, when the pain was greater than or equal to 4, rescue analgesia was administered to the patients on a scale of Oucher.

Ethical consideration
The principle of the declaration on the right of the subject was employed for this study. The respondents signed on informed consent then included in the current study.

Statistical analysis
The statistical analysis was based on the Chi-square test for the pain values obtained in the ward after anesthetic recovery and the presentation of the following data in the tables describing the pain as: 0 = no pain, 1 to 3 mild pain, 4 - 6 moderate pain, 7 - 9 severe pain, and 10 very severe pain. Data were processed in Excel 2010 and SPSS version 22 software. A p value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Study participants
The age distribution of the population in the study is not statistically different (p = 0.2). 65% of patients receiving Metamizole were male and 35% were female. Whereas 70% of those receiving Ketorolac
Table 1: Demographic characteristics according to medications used.

| Variable | Ketorolac     | Metamizole   | P value |
|----------|---------------|--------------|---------|
| Age      | 7.5±2.4       | 6.7±3.2      | Ns*     |
| Gender   | Male 28 (70%) | Male 26 (65%)| Ns      |
|          | Female 12 (30%) | Female 14 (35%) |         |

*Ns=Not significant

Table 2: Ouscher scale according to Analgesia used

|        | Ketorolac | Metamizole | Total | P value |
|--------|-----------|------------|-------|---------|
| 0      | 27 (67.5%)| 11 (27.5%) | 38    | <0.001  |
| 1 *    | 6 (15%)   | 12 (30%)   | 18    | Ns*     |
| 23     | 4 (10%)   | 5 (12.5%)  | 9     | Ns      |
| 3      | 0         | 2 (5%)     | 2     | Ns      |
| 4      | 1 (2.5 %) | 2 (5%)     | 3     | Ns      |
| 5      | 0         | 0          | 0     | -       |
| 6      | 2 (2.5%)  | 6 (15%)    | 8     | Ns      |
| 7      | 0         | 2 (5%)     | 2     | Ns      |
| Total  | 40        | 40         | 80    |         |

*Ns= not significant

Table 3: Distribution of vital sign according to the Analgesia used

|                   | Metamizole | Ketorolac | P value |
|-------------------|------------|-----------|---------|
| Systolic BP       | 94±8.3     | 94.5±7.1  | Ns*     |
| Diastolic BP      | 56.7±4.2   | 57±4.4    | Ns      |
| Heart rate        | 116±18.2   | 115.9±17.9| Ns      |
| Spo2              | 99.1±1.2   | 99.3±1.4  | Ns      |
| Post-anesthesia unit/30 min recovery | | |
| Systolic BP       | 92.3±6.8   | 92.3±6.8  | Ns      |
| Diastolic BP      | 56.4±4.5   | 56.4±3.8  | Ns      |
| Heart rate        | 112±13.2   | 111±13.3  | Ns      |
| Spo2              | 99.6±0.8   | 99.6±0.8  | Ns      |
| PAR 60 min        |            |           |         |
| Systolic BP       | 91.2±5.7   | 91.2±5.8  | Ns      |
| Diastolic BP      | 56.1±5.1   | 56.4±4.8  | Ns      |
| Heart rate        | 108.7±12.1 | 107.2±10.9| Ns      |
| Spo2              | 99.7±0.9   | 99.7±0.9  | Ns      |

Ns= not significant, BP= Blood pressure, SpO2: oxygen saturation
were male and 30% were female (Table 1). Management of postoperative pain in children should be comprehensive and, where possible, prevented before treatment. (Kim et al., 2013) The evaluation of pediatric pain should be practical and take into account the child’s ability to refer to the intensity of pain and the type of drug used and to correlate it at the time of assessment. (Lerman et al., 2010)

Choosing a tool that can measure the intensity of pain is very important. Children between the ages of 5 and 12 were able to determine the intensity of pain on the scale of the Oucher, as it is an easy-to-use and practical scale. Treatment with a pain reliever started before surgery is more effective in reducing postoperative pain than treatment in a recovery room.

Ouscher scale according to Analgesia used
The difference in analgesia produced by the two drugs, given the values reported by patients in the post-anesthetic recovery department, was statistically highly significant in favor of Ketorolac (p <0.001) (Table 2).

Vital sign according to the Analgesia used
Systolic and diastolic blood pressure after admission to the post-anesthetic ward remained within the normal range for age and slight changes were observed for two postoperative hours. In patients receiving Ketorolac, the heart rate at admission to the recovery ward was lower than in patients receiving Metamizole and equalized 2 hours postoperatively.

Oxygen saturation, measured by pulse oximetry, was maintained at 99% since the patient was admitted to the recovery ward up to 2 hours after surgery [Table 3].

In our study, patients receiving Ketorolac did not show severe pain unlike patients receiving Metamizole. In addition, patients who did not experience pain during recovery and received Ketorolac in the operating room had three times more patients than Metamizole. Various studies on the use of ketorolac and metamizole have emphasized that they are good analgesics for the management of postoperative pain, but give some benefit to the use of ketorolac.

Gobble et al. (2014) In their study, they point to ketorolac as a potent non-steroidal anti-inflammatory drug that should be considered for the treatment of postoperative pain, especially to limit the use of opioid analgesics. (Málek et al., 2017) Our findings are similar to other previous studies reported Ketorolac as a non-steroidal anti-inflammatory agent that can be safely used in children. No side effects were found in the study after analgesics. (Peñuelas-Acuña et al., 2003; Phillips et al., 2017)

Oliveira et al. (2012) Concludes that a single dose of systemic ketorolac is an effective supplement to multimodal regimens to reduce postoperative pain other than nausea and vomiting. (Bennet et al., 2009)

Contrary to the above, Peñuelas-Acuña et al. (2003) indicates no statistically significant differences in the analgesia produced by Ketorolac and Metamizol. (Simon, 2012) The fact that the child does not feel pain or that it is minimal after the end of adenotonsillectomy is the goal of preventive analgesia; what should be used frequently in practice; as pain is not only a subjective symptom, it can lead to respiratory complications, cardiovascular, endocrinological and autonomic nervous system. (Verghese, 2010; Zhao et al., 2019)

CONCLUSIONS
A prospective multi center study evaluated the use of metamizole in children under six who underwent surgery, with a particular focus on severe adverse reactions to hemodynamics, anaphylactic, respirators, agranulocytosis, and concluded that respiratory adverse effects were also directly related clinical signs of agranulocytosis have been reported with a probability of occurring below 0.3%. Ketorolac were reducing postoperative pain significantly than metamizole in children undergoing to Adenotonsillectomy.

No conflicts of interest
Self-funding source
Ethical clearance
From the Iraqi Ministry of health and Environment/scientific committee

REFERENCES
Bennet, M., Carter, B., Dooley, F. 2009. The Recognition and Assessment of Acute Pain in Children. pages 1–73, London, England: Royal College of Nursing.

Bujedo, B. M., Santos, S. G., Azpiazu, A. U., Noriega, A. R., Salazar, D. G., Andueza, M. A. 2015. Multimodal analgesia for the management of postoperative pain. Pain and treatment.

Chan, D. K., Parikh, S. R. 2014. Perioperative ketorolac increases post-tonsillectomy hemorrhage in adults but not children. The Laryngoscope, 124(8):1789–1793.
Cohen, M., Quintner, J., van Rysewyk, S. 2018. Reconsidering the International Association for the Study of Pain definition of pain. *PAIN Reports, 3*(2):e634–e634.

Fieler, M., Eich, C., Becke, K., Badelt, G., Leimkühler, K., Messroghli, L., Boethig, D., Sümpelmann, R. 2015. Metamizole for postoperative pain therapy in 1177 children: A prospective, multicentre, observational, postauthorisation safety study. *European Journal of Anaesthesiology (EJA)*. 32:839–882.

Gan, T. J. 2017. Poorly controlled postoperative pain: prevalence, consequences, and prevention. *Journal of Pain Research, Volume 10*:2287–2298.

Garimella, V., Cellini, C. 2013. Postoperative Pain Control. *Clinics in Colon and Rectal Surgery, 26*(03):191–196.

Gobble, R. M., Hoang, H. L. T., Kachniarz, B., Orgill, D. P. 2014. Ketorolac does not increase perioperative bleeding: a meta-analysis of randomized controlled trials. *Plastic and Reconstructive Surgery, 133*(3):741–755.

Granadillo, G., Claudio, E., Guerra, M., &zúñiga, M. 2001. Premedicación con Ketorolac para Analgesia Postoperatoria en Cirugía Ginecológica. *Archivos Venezolanos de Farmacología y Terapéutica*. 20:69–79.

Kim, D., Doo, A. R., Lim, H., Son, J. S., Lee, J. R., Han, Y. J., &ko, S. 2013. Effect of ketorolac on the prevention of emergence agitation in children after sevoflurane anesthesia. *Korean Journal of Anesthesiology, 64*(3):240–240.

Lerman, J., Coté, C. J., Steward, D. J. 2010. Postoperative Care and Pain Management. *Manual of Pediatric Anesthesia*, pages 214–231.

Málek, J., Ševčík, P., Bejšovec, D. 2017. Postoperative pain management. *Mlada fronta: Prague*.

Oliveira, G. S. D., Agarwal, D., Benzon, H. T. 2012. Perioperative Single Dose Ketorolac to Prevent Postoperative Pain.

Pace, M. C., Mazzariello, L., Passavanti, M. B., Sanske, P., Barbarisi, M., Aurilio, C. 2006. Neurobiology of pain. *Journal of Cellular Physiology, 209*(1):8–12.

Peñuelas-Acuña, J., Oriol-López, S. A., Hernández-Bernal, C. E., Castelazo-Arredondo, J. A. 2003. Ketorolacos metamizol analgesia preventiva en niños. *Cirugía y cirujanos, 71*(1):50–54.

Phillips, J. K., Ford, M. A., Bonnie, R. J. 2017. Pain Management and the Intersection of Pain and Opioid Use Disorder. In *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use*. US. National Academies Press.

Simon, L. S. 2012. Relieving pain in America: A blueprint for transforming prevention, care, education, and research. 26:197–198.

Verghese, S. 2010. Acute pain management in children. *Journal of Pain Research, 3*:105–105.

Zhao, S., Chen, F., Feng, A., Han, W., Zhang, Y. 2019. Risk Factors and Prevention Strategies for Postoperative Opioid Abuse. *Pain Research and Management, 2019*:1–12.