Preemptive activity of incision infiltration with 0.75% ropivacaine in patients submitted to inguinal hernia repair*

Atividade preemptiva da infiltração da incisão com ropivacaína a 0,75%, em pacientes submetidos à herniorrafia inguinal

André Laranjeira de Carvalho¹, Fábio Bonini Castellana (in memorian)², Bruno Emanuel Oliva Gatto², Silvia Katlauskas Muraro², Fabio Augusto Schiavuzzo², Hazem Adel Ashmawi³, Joaquim Edson Vieira⁴, Edivaldo Utiyama⁴, Irimar de Paula Posso⁴

* Received from Clinicas Hospital, School of Medicine, University of São Paulo. São Paulo, SP.

SUMMARY

BACKGROUND AND OBJECTIVES: The effectiveness of preemptive analgesia as compared to the conventional regimen for postoperative pain control is still controversial. This study aimed at evaluating the effectiveness of local infiltration with 0.75% ropivacaine before and after the incision of inguinal hernia repair surgeries in postoperative pain intensity, analgesics consumption and time elapsed for first analgesic dose request.

METHOD: After the Institutional Research Ethics Committee approval, 60 patients, physical status P1 or P2, aged between 15 and 65 years, submitted to inguinal hernia repair under general anesthesia with isoflurane and fentanyl were randomly distributed in three groups: A – skin, subcutaneous and muscle infiltration before incision with 2 mg/kg of 0.75% ropivacaine; D – skin, subcutaneous and muscle infiltration after incision with 2 mg/kg of 0.75% ropivacaine; and C – control group, without infiltration. All patients received dipirone (2 g), 30 minutes before the end of anesthesia. A patient-

controlled analgesia pump with morphine was used after anesthetic recovery. Pain intensity with visual analog scale, total morphine consumption and time for the first morphine dose request were evaluated during 24 hours.

RESULTS: Morphine consumption was significantly lower in the A group (1.5 mg) as compared to the D group (5.5 mg) or to the control group (17 mg). Time for first morphine dose request was significantly longer for the A group and pain intensity was lower in all moments as compared to C group and in the last 18 h as compared to the group.

CONCLUSION: Preoperative incision infiltration with ropivacaine significantly decreases postoperative pain intensity and morphine consumption and delays the time for first morphine dose request.

Keywords: Analgesia, Inguinal hernia, Local anesthetics, Surgery.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A eficiência da analgesia preemptiva em relação ao regime convencional no controle da dor pós-operatória continua a ser controversa. O objetivo deste estudo foi avaliar a eficácia da infiltração local com ropivacaína a 0,75% antes e depois da incisão em operações de herniorrafia inguinal na intensidade da dor pós-operatória, no consumo de analgésicos e no tempo para solicitação da primeira dose de analgésico.

MÉTODO: Após a aprovação pelo Comitê de Ética em Pesquisa Institucional, 60 pacientes, estado físico P1 ou P2, com idade entre 15 e 65 anos, submetidos à herniorrafia inguinal sob anestesia geral com isoflurano e fentanil foram distribuídos aleatoriamente em três gru-

Correspondence to: André Laranjeira de Carvalho Av. Enéas Carvalho Aguiar, 255. 05403-900 São Paulo, SP. E-mail: irimar@terra.com.br

^{1.} Student of the School of Medicine, University of São Paulo (FM-USP). São Paulo, SP, Brazil.

^{2.} Former Resident in Anesthesiology, Clinicas Hospital of the School of Medicine, University of São Paulo (FM-USP). São Paulo, SP, Brazil.

^{3.} Anesthesiologist of the Clinicas Hospital, School of Medicine, University of São Paulo (FM-USP). São Paulo, SP, Brazil.

^{4.} Associate Professor of the School of Medicine, University of São Paulo (FM-USP). São Paulo, SP, Brazil.

pos: A - infiltração da pele, subcutâneo e tecido muscular antes da incisão com 2 mg/kg de ropivacaína a 0,75%; D - infiltração da pele, subcutâneo e tecido muscular após incisão com 2 mg/kg de ropivacaína a 0,75%; e o C - grupo controle - sem infiltração. Todos os pacientes receberam dipirona (2 g), 30 minutos antes do final da anestesia. Uma bomba de analgesia controlada pelo paciente com morfina foi usada depois da recuperação da anestesia. Foram avaliados durante 24 horas a intensidade da dor com a escala analógica visual, o consumo total de morfina e o tempo para a solicitação da primeira dose de morfina.

RESULTADOS: O consumo de morfina foi significativamente menor no grupo A (1,5 mg) quando comparado ao grupo D de (5,5 mg) ou controle (17 mg). O tempo para a solicitação da primeira dose de morfina foi significativamente maior para o grupo A assim como a intensidade da dor em todos os momentos quando comparado ao grupo C e nas últimas 18 h comparado ao grupo.

CONCLUSÃO: A infiltração pré-operatória da incisão com ropivacaína reduz significativamente a intensidade da dor e o consumo de morfina pós-operatória e retarda o tempo para a solicitação da primeira dose de morfina. **Descritores**: Analgesia, Anestésico local, Cirurgia, Hérnia inguinal.

INTRODUCTION

Preemptive analgesia is the administration of analgesics before starting the painful stimulation to prevent the establishment of neuronal sensitization, thus decreasing postoperative pain intensity¹. However, its effectiveness as compared to conventional regimens to manage postoperative acute pain is still controversial. Some studies could not show beneficial effects with any preemptive drug, although others have shown preemptive effect only with non-steroid anti-inflammatory drugs (NSAIDS), local anesthetics and other drugs²⁻⁷.

Local wound infiltration with local anesthetics has been recommended to decrease perioperative opioid consumption and postoperative pain, however there is a study which could not show differences in postoperative pain intensity with pre or postoperative infiltration with bupivacaína or lidocaine^{2,8,9}. Decreased analgesic consumption and increased time for rescue drug request with bupivacaína infiltration before incision as compared to postoperative infiltration has been shown in meta-analysis, however there was no evidence of decreased postoperative pain intensity¹⁰.

This study aimed at evaluating the effectiveness of local ropivacaine infiltration before and after incision of inguinal hernia repair surgeries to decrease postoperative pain intensity and analgesic consumption and to increase time for first analgesic dose request.

METHOD

After the approval of the Institution's Research Ethics Committee (informar o no do processo) and signature of the informed consent term, 60 patients, physical status P1 and P2, aged between 16 and 65 years, were submitted to inguinal hernia repair under general anesthesia induced with fentanyl, (3 ug/kg), propofol (2 mg/kg) and rocuronium (0,6 mg/kg) and maintained with 60%/40% nitrous oxide and oxygen and isoflurane in 0.5% to 1.5% concentration.

After anesthetic induction, patients were randomly distributed in three groups. Group A: skin, subcutaneous and muscle infiltration at incision site, before incision, with 0.75% ropivacaine (2 mg/kg). Group D: skin, subcutaneous and muscle infiltration at beginning of aponeurosis suture for abdominal wall closure with 0.75% ropivacaine (2 mg/kg). Group C: without infiltration before or after incision.

All patients received intravenous dipirone (2 g) 30 minutes before surgery completion and every 6 hours for 3 days. Intravenous morphine was used as rescue medication, with patient-controlled analgesia pump (PCA), programmed to administer 1 mg when requested by patient, with minimum interval of 5 minutes between doses and maximum limit of 20 mg in 4 hours.

Pain intensity was evaluated by total morphine consumption, by the time for first morphine dose request and by the visual analog scale (VAS), which was applied at post-anesthetic recovery unit admission and 30 minutes, 1, 2, 3, 6, 12, 18 and 24 hours after anesthetic recovery. Patients and researchers evaluating pain intensity were blind to the group they belonged to.

Data regarding total morphine consumption, time for first morphine dose request and pain intensity had no normal distribution and ANOVA was used for statistical analysis. Dunn test to compare groups was used when there was difference among groups.

RESULTS

Age and weight were not different among groups. Mean age was 46.5 years for group A, 48 years for group D and 47.5 years for group C (p = 0.942). Mean weight was

also not different among groups. In group A it was 75.9 kg, in group D it was 75.4 kg and in group C it was 74.9 kg (p = 0.921).

Total morphine consumption was different among groups. Median morphine consumption for group A was 1.5 mg (0 mg and 6.5 mg) with distribution in percentages of 25% and 75%; for group D it was 5.5 mg (3 mg and 13.5 mg), while for group C it was 17 mg (6 mg and 22 mg) (Table 1). Groups were also different among themselves (p=0.002) (Table 2). Data have shown significant total morphine consumption decrease with ropivacaine infiltration and there has been further

Table 1 – Total morphine consumption (mg)

Groups	N	Median	25%	75%
A	20	1.5	0.0	6.5
D	20	5.5	3.0	13.5
C	20	17.0	6.0	22.5
(p < 0.001)				

Table 2 – Comparison of total morphine consumption among groups

Comparison	Diferences	q	p
AXC	385.50	4.936	< 0.05
A X D	192.00	3.672	< 0.05
DXC	193.50	3.701	< 0.05

decrease with preemptive infiltration.

Time for first morphine dose request was also different among groups, and was compared by ordered data test. Median value for first morphine dose request (Table 3) for group A was 12 hours (2 h and > 24 h), for group D it was 3 hours (3h and 6h) and for group C it was only 30 minutes (0h and 2h30). All groups were also different among themselves (p=0.002).

There has been increase in time for first rescue drug dose request when ropivacaine was infiltrated at the end of the surgery, as compared to group C. Increased time for first rescue drug dose request was also higher when infiltra-

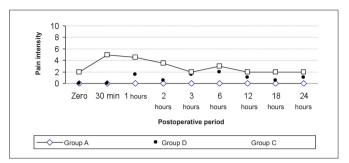
Table 3 – Time in hours for first morphine dose request

Groups	n	Median	25%	75%
A	20	12.0	2.0	24.0
D	20	3.0	1.0	6.0
C	20	0.0	0.0	2.5

tion was made before incision.

Pain intensity was different among groups (p < 0.001). Group A had values close to zero during the study period (Graph 1), being different from group C in all moments (p < 0.001). Group A was not different from Group D in the first 6 studied hours. From 6 h until the end of the

study, group A was also different from group C (p < 0.05). Group D, as compared to group C, was different during the first 18 hours of the study, and as from that moment there has been difference between both groups (Graph 1).



Graph 1 – Pain intensity

There has been pain intensity decrease in group A in the first 24 hours as compared to group C. There has been pain intensity decrease in group D in the 18 hours of study as compared to group C. When comparing groups with ropivacaine infiltration, pain intensity decrease was more significant as from the first 6 hours of study in the group receiving infiltration before incision.

DISCUSSION

Surgical inguinal hernia repair is one of most common procedures, however it induces postoperative pain, in general of moderate or severe intensity, lasting days to months, and more pronounced with movement and cough. Younger people in general refer more severe pain as compared to elderly patients. Pain is more severe in the day following surgery, when more than half the patients refer moderate to severe pain with movement. Pain may be moderate or even severe one week after in 30% of patients, and moderate in 10% of patients one month after surgery. Pain may become chronic and some patients refer severe pain 3 or more months after surgery^{11,12}.

Studies have shown that surgical wound infiltration with local anesthetics is effective to control acute postoperative pain in different procedures, because it decreases pain and opioid consumption^{2,13,14}. Wound infiltration with local anesthetics has also been recommended to decrease perioperative opioid consumption⁷.

In our study, pain intensity was evaluated by VAS, established method in the literature, since pain intensity described by patients has been referred as one of the most reliable measures to estimate analgesic treatment effectiveness⁹.

Results obtained show that ropivacaine infiltration be-

fore incision or at abdominal wall closure effectively decreases postoperative pain intensity in the first 12 hours (p < 0.01) as compared to the group not receiving infiltration with local anesthetics, and also that ropivacaine infiltration has decreased rescue analgesic consumption and that time for first rescue analgesic dose request was significantly longer.

Results obtained are in line with other studies which have also shown that pain intensity is significantly lower in patients submitted to inguinal hernia repair with 0.75% ropivacaine infiltration, using local anesthetic mass of 300 mg or 375 mg, which may be higher or lower than that used in our study, because dose was calculated by patients' weight, being established in 2 mg/kg^{15,16}. However, although 0.25% and 0.5% concentrations and lower ropivacaine doses have provided effective analgesia after 3 hours, they were less effective in terms of duration, since after 6 hours pain intensity was lower than control only for the 0.5% group. However, 0.125% solution was not more effective than placebo^{17,18}.

In our study, preemptive and postoperative ropivacaine infiltration has decreased pain intensity, however effectiveness was better with preemptive infiltration. There has been no difference in this criterion in the first six postoperative hours between infiltrating before or after, and both have equally decreased pain intensity as compared to controls.

Pain intensity was significantly lower in patients submitted inguinal hernia repair with 0.25% and 0.5% ropivacaine infiltration, however 0.125% solution was not more effective than placebo¹⁸.

In our study, from 6 to 18 postoperative hours, pain intensity was maintained lower with ropivacaine infiltration, but this was significantly better in the preemptive group. Such fact suggests a higher effectiveness of the preemptive modality. Both groups receiving ropivacaine infiltration had less pain in the first postoperative hours for having their pain conductive pathways under anesthetic block. As the blockade regresses, the difference between infiltrating before or after stars to appear. After 6 hours of study, with partial anesthetic blockade regression, group A was almost painless while the group receiving infiltration after surgery started to feel pain. This difference between groups was maintained until the end of the study, with 24 postoperative hours.

On the other hand, with anesthetic blockade regression in group D, pain intensity was similar to the control group, so that from 18 hours of study until its completion there has been no difference in pain intensity between these groups. These results might be explained

because with preemptive infiltration probably nociceptors sensitization was not present, as observed in animal studies¹⁹. Without previous nervous receptors sensitization, pain intensity was lower throughout the postoperative period and this difference was clearly observed at anesthetic blockade regression when group D, which had been sensitized and then blocked, started to present more pain, being equal to the control group at the end of the anesthetic blockade.

As to rescue analgesic consumption, which is probably the most adequate evaluation to establish the impact of preemptive analgesia, there has been clear benefit of ropivacaine infiltration and best results were also obtained with preemptive infiltration (Tables 1 and 2). Group C had consumption median of 17 mg morphine, versus 5.5 mg in Group D and 1.5 mg in Group A (p < 0.001) (Table 1), representing 67% morphine consumption decrease with postoperative infiltration, and 91% decrease with preemptive infiltration as compared to controls.

In comparing preemptive and postoperative infiltration, it was observed 72% decrease in morphine consumption (1.5 mg versus 5.5 mg) (p < 0.005). Similarly, in a different study¹⁷, the amount of requested analgesics in the first 24 hours was significantly lower in patients submitted to inguinal hernia repair with ropivacaine infiltration. Similarly, wound infiltration with ropivacaine in laparoscopic cholecystectomy and hernia repair induces satisfactory postoperative analgesia decreasing the need for opioids^{20,21}.

Time for first rescue analgesic dose request, also a criterion adopted by several studies to evaluate pain, was favorable for groups receiving ropivacaine infiltration, especially for the preemptive group (A). Control group had median time for rescue medication request of only 30 minutes, versus 3 hours for group D and 12 hours for group A (p=0.002), showing 83% increase in time for rescue medication request with postoperative infiltration and of 96% with preemptive infiltration. In comparing preemptive and postoperative infiltration it was observed 75% increase in time for rescue medication request (12 hours versus 3 hours) (p < 0.005).

Again, as for pain intensity, this difference was probably due to non sensitization of nervous receptors in the preemptive group. Group C, after residual anesthesia recovery, starts to present pain and already requests rescue medication.

Group D, for being under anesthetic block effect, has taken longer to ask for medication, however this has happened after blockade regression. The preemptive group, even after anesthetic blockade regression, remained comfortable, probably because their nervous receptors were not sensitized, which promoted better pain control, delaying the first rescue request. Time for first analgesic dose request was significantly lower in patients submitted to inguinal hernia repair with ropivacaine infiltration¹⁷.

Results have shown clear benefit for pain control with ropivacaine infiltration, especially with preemptive infiltration. In comparing pre and postoperative local anesthetics infiltration literature results are conflicting. A study testing pre and postoperative bupivacaine infiltration in tonsillectomies has not found differences in analgesic control²². Similarly, a different study has not found pain intensity differences after mastectomy with pre or postoperative incision infiltration²³. However, a study with bupivacaine infiltration before and after tonsillectomy surgeries has obtained better results with preemptive infiltration²⁴.

Pre and postoperative lidocaine infiltration in inguinal hernia repair surgeries has not presented differences in pain control²⁵. Other authors, believing that poor results of this study were due to the short-lasting action of lidocaine, have tested preemptive bupivacaine infiltration and have also not found differences⁸ However, a meta-analysis has shown significant analgesic consumption decrease and longer time for rescue medication request, although not showing pain scores reduction with preemptive infiltration of local anesthetics as compared to postoperative infiltration⁹.

CONCLUSION

Wound infiltration with ropivacaine was effective to control pain, with better results when done before incision. It has significantly decreased pain intensity and morphine consumption and has delayed rescue analgesia request promoting a more comfortable postoperative period.

REFERENCES

- 1. Kissin I. Preemptive analgesia. Anesthesiology. 2000;93(4):1138-43.
- 2. Moiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief: the role of timing of analgesia. Anesthesiology 2002;96(3):725-41.
- 3. Dahl JB, Møiniche S. Pre-emptive analgesia. Br Med Bull 2004;71:13-27.

- 4. Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia II: recent advances and current trends. Can J Anaesth 2001;48(11):1091-101.
- 5. O'Hanlon DM, Thambipillai T, Colbert ST, et al. Timing of pre-emptive tenoxicam is important for postoperative analgesia. Can J Anaesth 2001;48(2):162-6.
- 6. Trampitsch E, Pipam W, Moertl M, et al. Preemptive randomized, double-blind study with lornoxicam in gynecological surgery. Schmerz 2003;17(1):4-10.
- 7. Gramke HF, Petry JJ, Durieux ME, et al. Sublingual piroxicam for postoperative analgesia: preoperative versus postoperative administration: a randomized, doubleblind study. Anesth Analg 2006;102(3):755-8.
- 8. Kehlet H, White PF. Optimizing anesthesia for inguinal herniorrhaphy: general, regional, or local anesthesia? Anesth Analg 2001:93(6):1367-9.
- 9. Gill P, Kiani S, Victoria BA, et al. Pre-emptive analgesia with local anaesthetic for herniorrhaphy. Anaesthesia 2001:56(5):414-7.
- 10. Ong CK, Lirk P, Seymour RA, et al. The efficacy of preemptive analgesia for acute postoperative pain management: a meta-analysis. Anesth Analg 2005:100(3):757-73.
- 11. Callesen T. Inguinal hernia repair: anaesthesia, pain and convalescence. Dan Med Bull 2003;50(3):203-18.
- 12. Courtney CA, Duffy K, Serpell MG, et al. Outcome of patients with severe chronic pain following repair of groin hernia. Br J Surg 2002;89(10):1310-4.
- 13. Bianconi M, Ferraro L, Traina GC, et al. Pharmacokinetics and efficacy of ropivacaine continuous wound instillation after joint replacement surgery. Br J Anaesth 2003;91(6):830-5.
- 14. Bianconi M, Ferraro L, Ricci R, et al. The pharmacokinetics and efficacy of ropivacaine continuous wound instillation after spine fusion surgery. Anesth Analg 2004;98(1):166-72.
- 15. Pettersson N, Emanuelsson BM, Reventlid H, et al. High-dose ropivacaine wound infiltration for pain relief after inguinal hernia repair: a clinical and pharmacokinetic evaluation. Reg Anesth Pain Med 1998;23(2):189-96. 16. Pettersson N, Berggren P, Larsson M, et al. Pain relief by wound infiltration with bupivacaine or high-dose ropivacaine after inguinal hernia repair. Reg Anesth Pain Med 1999;24(6):569-75.
- 17. Johansson B, Hallerbäck B, Stubberöd A, et al. Preoperative local infiltration with ropivacaine for postoperative pain relief after inguinal hernia repair. A randomised controlled trial. Eur J Surg 1997;163(5):371-8. 18. Mulroy MF, Burgess FW, Emanuelsson BM. Ropiva-

- caine 0.25% and 0.5%, but not 0.125%, provide effective wound infiltration analgesia after outpatient hernia repair, but with sustained plasma drug levels. Reg Anesth Pain Med 1999;24(2):136-41.
- 19. Woolf CJ, Wall PD. Morphine-sensitive and morphine-insensitive actions of C-fiber input on the rat spinal cord. Neurosci Lett 1986;64(2):221-5.
- 20. Pavlidis TE, Atmatzidis KS, Papaziogas BT, et al. The effect of preincisional periportal infiltration with ropivacaine in pain relief after laparoscopic procedures: a prospective, randomized controlled trial. JSLS 2003;7(4):305-10.
- 21. Salán FO, Bartolomucci AC, Posso IP, et al. Analgesia preemptiva local complementar na colecistectomia videolaparoscópica. Rev Dor 2009;10(3):219-26.
- 22. Molliex S, Haond P, Baylot D, et al. Effect of pre-vs postoperative tonsillar infiltration with local anesthetics

- on postoperative pain after tonsillectomy. Acta Anaesth Scand 1996:40(10):1210-5.
- 23. Rica MA, Norlia A, Rohaizak M, et al. Preemptive ropivacaine local anaesthetic infiltration versus postoperative ropivacaine wound infiltration in mastectomy: postoperative pain and drain outputs. Asian J Surg 2007;30(1):34-9.
- 24. Jebeles JA, Reilly JS, Gutierrez JF, et al. The effect of pre-incisional infiltration of tonsils with bupivacaine on the pain following tonsillectomy under general anesthesia. Pain 1991:47(3):305-8.
- 25. Dierking G, Dhal JB, Kanstruup J, et al. Effect of prevs postoperative inguinal field block on postoperative pain after herniorrhaphy. Br J Anaesth 1992:68(4):344-8.

Presented in August 08, 2011. Accepted for publication in November 01, 2011.