



UNIVERSIDADE ESTADUAL DE CAMPINAS
SISTEMA DE BIBLIOTECAS DA UNICAMP
REPOSITÓRIO DA PRODUÇÃO CIENTÍFICA E INTELECTUAL DA UNICAMP



Versão do arquivo anexado / Version of attached file:

Versão do Editor / Published Version

Mais informações no site da editora / Further information on publisher's website:

http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1806-00132012000400009

DOI: 10.1590/S1806-00132012000400009

Direitos autorais / Publisher's copyright statement:

©2012 by Sociedade Brasileira para o Estudo da Dor. All rights reserved.

Comparison between lysine and paracetamol for post tooth extraction pain control*

Efeito comparativo entre clonixinato de lisina e paracetamol no controle da dor pós-exodontia

Klinger de Souza Amorim¹, Lucas Celestino Guerzet Ayres¹, Rafael Soares da Cunha¹, Liane Maciel de Almeida Souza², Mônica Silveira Paixao³, Francisco Groppo⁴

* Received from the Dentistry Department, Federal University of Sergipe (UFS). Aracaju, SE.

SUMMARY

BACKGROUND AND OBJECTIVES: Tooth extraction is practiced since the early days of mankind to surgically solve dental problems. However, as any surgical procedure, it promotes an inflammatory reaction with clinical presentation of pain. Several drugs have been used to minimize postoperative discomfort; however there is still no established protocol for its control. This study aimed at evaluating the analgesic effect of lysine and paracetamol to control post tooth extraction pain.

METHOD: Double blind randomized study with 40 patients seen by the Surgical Outpatient Setting I, Dentistry Department, Federal University of Sergipe (DOD/UFS), who needed alveolar extractions in different hemiarcs using lysine (125 mg) three times a day or paracetamol (750 mg) four times a day, both during three postoperative days. Pain was evaluated at 24 and 48 hours with the visual analog scale. Data were

submitted to Student's *t* and Friedman statistical tests.

RESULTS: There have been no statistically significant differences in age, gender and pain intensity.

CONCLUSION: Both lysine and paracetamol were effective to control post tooth extraction pain.

Keywords: Lysine, Pain, Paracetamol, Tooth extraction.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A exodontia é praticada desde os primórdios da humanidade como forma de resolver cirurgicamente os problemas dentários. Porém, como todo procedimento cirúrgico, ela promove um processo inflamatório reacional que se apresenta clinicamente com dor. Muitos fármacos têm sido usados no intuito de minimizar o desconforto pós-operatório, porém um protocolo para o seu controle ainda não está estabelecido. Este estudo teve como objetivo avaliar o efeito analgésico do clonixinato de lisina e paracetamol no controle de dor pós-exodontia.

MÉTODO: Estudo duplamente encoberto e randomizado com 40 pacientes atendidos no Ambulatório de Cirurgia I no Departamento de Odontologia da Universidade Federal de Sergipe (DOD/UFS) que necessitaram de extrações por via alveolar em hemiarcs diferentes utilizando clonixinato de lisina (125 mg) três vezes ao dia ou paracetamol (750 mg) quatro vezes ao dia, ambos por três dias no pós-operatório. A dor foi avaliada nas primeiras 24 e 48h com o uso da escala analógica visual. Os dados foram submetidos aos testes estatísticos *t* de Student e de Friedman.

RESULTADOS: Não houve diferenças estatisticamente significantes entre idade, em relação aos gêneros e em relação à intensidade da dor.

1. Student of Dentistry, Federal University of Sergipe (UFS). Aracaju, SE, Brazil.

2. Associate Professor of Anesthesiology and Surgery I, Federal University of Sergipe (UFS). Doctor in Implantodontics, São Leopoldo Mandic. Aracaju, SE, Brazil.

3. Assistant Professor of Legal Dentistry, Federal University of Sergipe. Doctor in Biotechnology, RENORBIO. Aracaju, SE, Brazil.

4. Professor of the Dentistry School, Piracicaba (FOP/UNICAMP). Doctor in Pharmacology, Anesthesiology and Drug Therapy (FOP/UNICAMP). Campinas, SP, Brazil.

Correspondence to:

Klinger de Souza Amorim

Rua Cláudio Batista s/n. Hospital Universitário - Sanatório
49060-100 Aracaju, SE.

Phone: (79) 2105-1821

E-mail: klinger28@hotmail.com

CONCLUSÃO: Tanto o clonixinato de lisina como o paracetamol foi eficaz para o controle da dor pós-exodontia.

Descritores: Dor, Exodontia, Lisina, Paracetamol.

INTRODUCTION

Tooth extraction is practiced since the early days of mankind to surgically solve dental problems. However, as any surgical procedure, it promotes an inflammatory reaction with clinical presentation of pain.

Postoperative pain control in Dentistry should be induced before the surgical procedure, since many studies suggest the prescription of steroid or non-steroid anti-inflammatory drugs or of analgesics with some anti-inflammatory property.

Many drugs have been used to minimize postoperative discomfort. Some protocols include medication after surgery. The best moment for its effective use is still not totally explained².

Paracetamol is a very important non-opioid analgesic, in general prescribed for the post tooth extraction period. The dose of 1000 mg of paracetamol induces efficient analgesia after oral surgeries. Adequate plasma concentration level is established 90 minutes after oral administration. It should be prescribed in the dose of 60 to 90 mg/kg every six hours².

Lysine is an anti-inflammatory analgesic of the carboxylic acids group, characterized by strong central and peripheral analgesic power and low anti-inflammatory action³. It acts by reversibly inhibiting cyclooxygenase, blocking prostaglandin synthesis and antagonizing prostaglandins³.

A study comparing lysine and paracetamol for oral postoperative pain has not shown significant differences between drugs⁴. In animals, lysine showed 3-hour half-life being a short-life non-steroid anti-inflammatory drug (NSAID) as compared to other drugs of its category⁵.

Orally administered, lysine has excellent biological tolerance and low incidence of side effects in the treatment of painful syndromes, such as renal pain, neurogenic pain, muscle pain, tooth pain^{6,7} and migraine⁸.

Considering the scarcity of studies with this drug in Dentistry, our study aimed at evaluating and comparing the analgesic effect of both drugs.

METHOD

This was an experimental, double-blind, crossover and randomized study including 40 patients admitted

to the Surgery I Ambulatory, Department of Dentistry, Federal University of Sergipe (DOD/UFS) from May 2011 to May 2012, submitted to alveolar extractions in different hemiarcades.

Every patient was individually approached to explain the importance of the research. Inclusion criteria were individuals of both genders, aged between 18 and 60 years, who signed the Free and Informed Consent Term. Exclusion criteria were individuals below 18 and above 60 years of age, patients with active peptic ulcer or digestive hemorrhage, infants or those allergic to paracetamol or lysine.

Patients were referred to the first investigator who delivered them a bottle with the medication A (125 mg lysine) or B (750 mg paracetamol). These drugs were manipulated in the pharmacy so that patients and remaining investigators could not identify them.

Then, patients were referred to the surgeon (second investigator) who performed the extractions according to the protocol⁹. All patients were anesthetized with 2% lidocaine with 1:100000 epinephrine, not exceeding two tubets¹⁰. After extraction, patients received all information about postoperative care and were oriented to return 24 hours later to the DOD.

After 24 hours, the third investigator has evaluated the analgesic efficacy of the drug by the 10-cm visual analog scale (VAS) were zero means no pain and 10 unbearable pain. Patients were oriented to return 48 hours later for a new pain intensity evaluation. Eight days after the first procedure, patients returned for stitch removal and for another tooth extraction with another drug to be observed (A or B), as the case might be.

After collection, data were tabulated and submitted to statistical Student's *t* and Friedman's tests with $p < 0.05$.

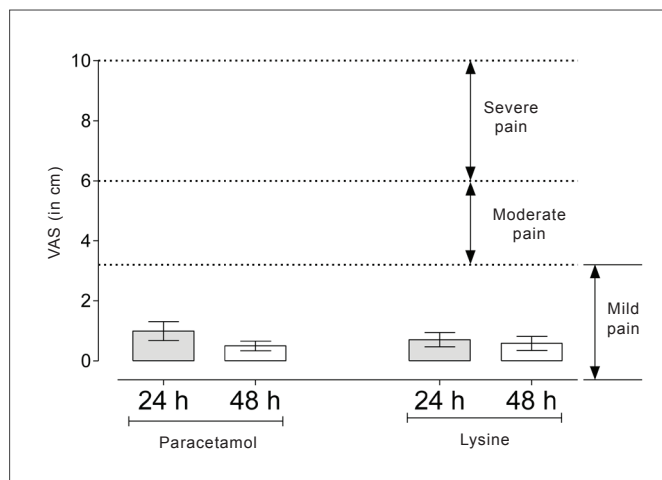
This study was approved by the Ethics and Research Committee, Federal University of Sergipe (UFS), protocol CAAE 0263.0.000.107-2011.

RESULTS

From 40 included patients, 12 were males and 28 females. There have been no statistically significant differences (*t* test, $p = 0.2176$) in age between females (3.51 ± 13.8 years) and males (41.3 ± 15 years).

Pain intensity by Friedman's test has not shown statistically significant difference ($p > 0.05$) between drugs and between periods.

Graph 1 show that patients' pain was mild when considering pain classification as mild, moderate and severe by VAS values in cm¹¹.



Graph 1 – Pain intensity by the visual analog scale (VAS).

DISCUSSION

As described in the literature¹², difference in gender was not statistically significant for post alveolar tooth extraction pain. Differently from another study¹³, this has not shown statistically significant differences in pain with regard to patients' age.

Most common VAS for postoperative pain evaluation is a 100 mm long line representing the continuum of the pain experience. Its edges have the anchor words no pain and worst possible pain. Participants are oriented to mark their pain intensity on a point of this line and scores may vary from zero to 10. Scores are obtained by measuring, in millimeters, the distance between the edge anchored by the words no pain and the point marked by the participant. This scale has the advantage of being easy to apply¹⁴. Pain evaluation by VAS is well accepted, including to evaluate postoperative patients' pain¹⁵. Our study has used VAS without pre-existing marks to prevent any type of bias when patients marked their pain intensity.

Our results have not shown statistically significant differences between paracetamol and lysine to control post alveolar tooth extraction pain³. Lysine action on the central nervous system is suggested by the presence of major analgesic effect, similar to opioids. Strong central nociceptive action does not depend on the presence of inflammatory or hyperalgesic process, which is still not totally explained. It seems that there is interaction of lysine with central opioid receptors, although the action mediated by such receptors has not been evidenced¹⁶. This study has shown good analgesic action of this drug, which is confirmed by the presence of mild pain only¹¹.

Different from other findings¹⁷ pain intensity was not

statistically significant 24 or 48 hours after surgery. Similarly to previous studies¹⁸, patients receiving lysine did not report undesirable effects, showing the good tolerability of the drug.

CONCLUSION

Both lysine and paracetamol were effective to control post tooth extraction pain. Lysine may be considered a good option for patients who cannot use other analgesic drugs.

REFERENCES

1. Gaya MVO, CapillaMV, Mateos RG. Relación de las variables del paciente y de la intervención con el dolor y la inflamación postoperatorios em la exodoncia de los terceros molares. *Med Oral*. 2002;7(5):360-9.
2. Camu F, Vanlersberghe C. Pharmacology of systemic analgesics. *Best Pract Res Clin Anaesthesiol*. 2002;16(4):475-88.
3. Bird RA, Simonetti MPB. Avaliação das atividades analgésica e antiinflamatória do clonixinato de lisina; estudo experimental em ratos. *Rev Dor*. 2000;2(1):7-12
4. Marti ML, De los Santos AR, Di Girolamo G, et al. Lysine clonixinate in minor dental surgery: double-blind randomized parallel study versus paracetamol. *Int J Tissue React*. 1993;15(5):207-13.
5. Gonzalez-Martin G, Cattan C, Zuniga S. Pharmacokinetics of lysine clonixinate in children in postoperative care. *Int J Clin Pharmacol Ther*. 1996;34(9):396-9
6. Orti E, Coirini H, Pico JC. Site-specific effects of the nonsteroidal anti-inflammatory drug lysine clonixinate on rat brain opioid receptors. *Pharmacology*. 1999;58(4):190-9.
7. Krymchantowski AV, Peixoto P, Higashi R, et al. Lysine clonixinate vs naproxen sodium for the acute treatment of migraine: a double-blind, randomized, crossover study. *Med Gen Med*. 2005;7(4):69.
8. Krymchantowski AV, Barbosa JS, Cheim C, et al. Oral lysine clonixinate in the acute treatment of migraine: a double-blind placebo-controlled study. *Arq Neuropsiquiatr*. 2001;59(1):46-9.
9. Marzola C. Técnica exodôntica. 3ª ed. Rio de Janeiro: Pancast; 2000.
10. Malamed SF. Manual de anestesia local. 5ª ed. São Paulo: Elsevier; 2005.
11. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? *Pain*. 1997;72(1-2):95-7.

12. Morin C, Lund JP, Villarroel T, et al. Differences between the sexes in post-surgical pain. *Pain*. 2000;85(1-2):79-85.
13. Wahl MJ, Overton D, Howell J, et al. Pain on injection of prilocaine plain vs. lidocaine with epinephrine. A prospective double-blind study. *J Am Dent Assoc*. 2001;132(10):1396-401.
14. Pereira LV, Sousa FAEF. Mensuração e avaliação da dor pós-operatória: uma breve revisão. *Rev Lat-Am Enfermagem*. 1998;6(1):77-84.
15. Guimarães KCN, Dorneles BAS, Mello GC. Eficácia da mensuração do quinto sinal vital no controle da dor pós-operatória: um ensaio clínico randomizado. Projeto piloto. *Rev Dor*. 2010;11(4):304-8
16. Ortí E. Evidence for NSAIDs with the central opioid receptor system. *APPTLA*. 1996;46(3):199.
17. Al-Khabbaz AK, Griffin TJ, Al-Shammari KF. Assessment of pain associated with the surgical placement of dental implants. *J Periodontol*. 2007;78(2):239-46.
18. Santos FC, Souza PMR, Toniolo Neto J, et al. Tratamento da dor associada à osteoartrose de joelho em idosos: um ensaio clínico aleatório e duplamente encoberto com o clonixinato de lisina. *Rev Dor*. 2011;12(1):6-14

Submitted in August 07, 2012.

Accepted for publication in November 14, 2012.

Comparison between lysine and paracetamol for post tooth extraction pain control*

Efeito comparativo entre clonixinato de lisina e paracetamol no controle da dor pós-exodontia

Klinger de Souza Amorim¹, Lucas Celestino Guerzet Ayres¹, Rafael Soares da Cunha¹, Liane Maciel de Almeida Souza², Mônica Silveira Paixao³, Francisco Groppo⁴

* Received from the Dentistry Department, Federal University of Sergipe (UFS). Aracaju, SE.

SUMMARY

BACKGROUND AND OBJECTIVES: Tooth extraction is practiced since the early days of mankind to surgically solve dental problems. However, as any surgical procedure, it promotes an inflammatory reaction with clinical presentation of pain. Several drugs have been used to minimize postoperative discomfort; however there is still no established protocol for its control. This study aimed at evaluating the analgesic effect of lysine and paracetamol to control post tooth extraction pain.

METHOD: Double blind randomized study with 40 patients seen by the Surgical Outpatient Setting I, Dentistry Department, Federal University of Sergipe (DOD/UFS), who needed alveolar extractions in different hemiarcs using lysine (125 mg) three times a day or paracetamol (750 mg) four times a day, both during three postoperative days. Pain was evaluated at 24 and 48 hours with the visual analog scale. Data were

submitted to Student's *t* and Friedman statistical tests.

RESULTS: There have been no statistically significant differences in age, gender and pain intensity.

CONCLUSION: Both lysine and paracetamol were effective to control post tooth extraction pain.

Keywords: Lysine, Pain, Paracetamol, Tooth extraction.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A exodontia é praticada desde os primórdios da humanidade como forma de resolver cirurgicamente os problemas dentários. Porém, como todo procedimento cirúrgico, ela promove um processo inflamatório reacional que se apresenta clinicamente com dor. Muitos fármacos têm sido usados no intuito de minimizar o desconforto pós-operatório, porém um protocolo para o seu controle ainda não está estabelecido. Este estudo teve como objetivo avaliar o efeito analgésico do clonixinato de lisina e paracetamol no controle de dor pós-exodontia.

MÉTODO: Estudo duplamente encoberto e randomizado com 40 pacientes atendidos no Ambulatório de Cirurgia I no Departamento de Odontologia da Universidade Federal de Sergipe (DOD/UFS) que necessitaram de extrações por via alveolar em hemiarcs diferentes utilizando clonixinato de lisina (125 mg) três vezes ao dia ou paracetamol (750 mg) quatro vezes ao dia, ambos por três dias no pós-operatório. A dor foi avaliada nas primeiras 24 e 48h com o uso da escala analógica visual. Os dados foram submetidos aos testes estatísticos *t* de Student e de Friedman.

RESULTADOS: Não houve diferenças estatisticamente significantes entre idade, em relação aos gêneros e em relação à intensidade da dor.

1. Student of Dentistry, Federal University of Sergipe (UFS). Aracaju, SE, Brazil.

2. Associate Professor of Anesthesiology and Surgery I, Federal University of Sergipe (UFS). Doctor in Implantodontics, São Leopoldo Mandic. Aracaju, SE, Brazil.

3. Assistant Professor of Legal Dentistry, Federal University of Sergipe. Doctor in Biotechnology, RENORBIO. Aracaju, SE, Brazil.

4. Professor of the Dentistry School, Piracicaba (FOP/UNICAMP). Doctor in Pharmacology, Anesthesiology and Drug Therapy (FOP/UNICAMP). Campinas, SP, Brazil.

Correspondence to:

Klinger de Souza Amorim

Rua Cláudio Batista s/n. Hospital Universitário - Sanatório
49060-100 Aracaju, SE.

Phone: (79) 2105-1821

E-mail: klinger28@hotmail.com

CONCLUSÃO: Tanto o clonixinato de lisina como o paracetamol foi eficaz para o controle da dor pós-exodontia.

Descritores: Dor, Exodontia, Lisina, Paracetamol.

INTRODUCTION

Tooth extraction is practiced since the early days of mankind to surgically solve dental problems. However, as any surgical procedure, it promotes an inflammatory reaction with clinical presentation of pain.

Postoperative pain control in Dentistry should be induced before the surgical procedure, since many studies suggest the prescription of steroid or non-steroid anti-inflammatory drugs or of analgesics with some anti-inflammatory property.

Many drugs have been used to minimize postoperative discomfort. Some protocols include medication after surgery. The best moment for its effective use is still not totally explained².

Paracetamol is a very important non-opioid analgesic, in general prescribed for the post tooth extraction period. The dose of 1000 mg of paracetamol induces efficient analgesia after oral surgeries. Adequate plasma concentration level is established 90 minutes after oral administration. It should be prescribed in the dose of 60 to 90 mg/kg every six hours².

Lysine is an anti-inflammatory analgesic of the carboxylic acids group, characterized by strong central and peripheral analgesic power and low anti-inflammatory action³. It acts by reversibly inhibiting cyclooxygenase, blocking prostaglandin synthesis and antagonizing prostaglandins³.

A study comparing lysine and paracetamol for oral postoperative pain has not shown significant differences between drugs⁴. In animals, lysine showed 3-hour half-life being a short-life non-steroid anti-inflammatory drug (NSAID) as compared to other drugs of its category⁵.

Orally administered, lysine has excellent biological tolerance and low incidence of side effects in the treatment of painful syndromes, such as renal pain, neurogenic pain, muscle pain, tooth pain^{6,7} and migraine⁸.

Considering the scarcity of studies with this drug in Dentistry, our study aimed at evaluating and comparing the analgesic effect of both drugs.

METHOD

This was an experimental, double-blind, crossover and randomized study including 40 patients admitted

to the Surgery I Ambulatory, Department of Dentistry, Federal University of Sergipe (DOD/UFS) from May 2011 to May 2012, submitted to alveolar extractions in different hemiarcades.

Every patient was individually approached to explain the importance of the research. Inclusion criteria were individuals of both genders, aged between 18 and 60 years, who signed the Free and Informed Consent Term. Exclusion criteria were individuals below 18 and above 60 years of age, patients with active peptic ulcer or digestive hemorrhage, infants or those allergic to paracetamol or lysine.

Patients were referred to the first investigator who delivered them a bottle with the medication A (125 mg lysine) or B (750 mg paracetamol). These drugs were manipulated in the pharmacy so that patients and remaining investigators could not identify them.

Then, patients were referred to the surgeon (second investigator) who performed the extractions according to the protocol⁹. All patients were anesthetized with 2% lidocaine with 1:100000 epinephrine, not exceeding two tubets¹⁰. After extraction, patients received all information about postoperative care and were oriented to return 24 hours later to the DOD.

After 24 hours, the third investigator has evaluated the analgesic efficacy of the drug by the 10-cm visual analog scale (VAS) were zero means no pain and 10 unbearable pain. Patients were oriented to return 48 hours later for a new pain intensity evaluation. Eight days after the first procedure, patients returned for stitch removal and for another tooth extraction with another drug to be observed (A or B), as the case might be.

After collection, data were tabulated and submitted to statistical Student's *t* and Friedman's tests with $p < 0.05$.

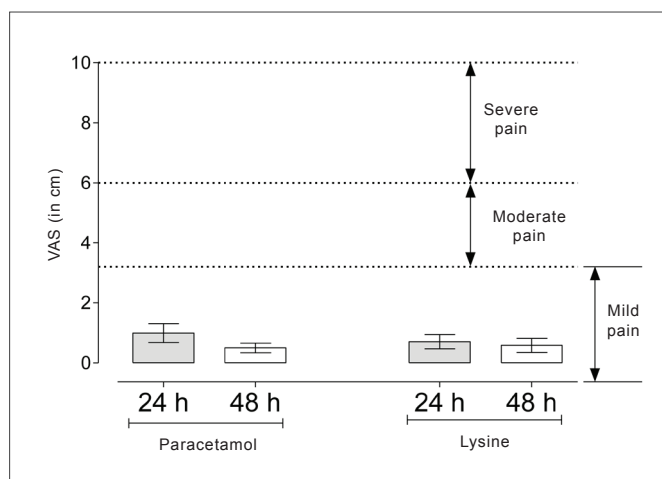
This study was approved by the Ethics and Research Committee, Federal University of Sergipe (UFS), protocol CAAE 0263.0.000.107-2011.

RESULTS

From 40 included patients, 12 were males and 28 females. There have been no statistically significant differences (*t* test, $p = 0.2176$) in age between females (3.51 ± 13.8 years) and males (41.3 ± 15 years).

Pain intensity by Friedman's test has not shown statistically significant difference ($p > 0.05$) between drugs and between periods.

Graph 1 show that patients' pain was mild when considering pain classification as mild, moderate and severe by VAS values in cm¹¹.



Graph 1 – Pain intensity by the visual analog scale (VAS).

DISCUSSION

As described in the literature¹², difference in gender was not statistically significant for post alveolar tooth extraction pain. Differently from another study¹³, this has not shown statistically significant differences in pain with regard to patients' age.

Most common VAS for postoperative pain evaluation is a 100 mm long line representing the continuum of the pain experience. Its edges have the anchor words no pain and worst possible pain. Participants are oriented to mark their pain intensity on a point of this line and scores may vary from zero to 10. Scores are obtained by measuring, in millimeters, the distance between the edge anchored by the words no pain and the point marked by the participant. This scale has the advantage of being easy to apply¹⁴. Pain evaluation by VAS is well accepted, including to evaluate postoperative patients' pain¹⁵. Our study has used VAS without pre-existing marks to prevent any type of bias when patients marked their pain intensity.

Our results have not shown statistically significant differences between paracetamol and lysine to control post alveolar tooth extraction pain³. Lysine action on the central nervous system is suggested by the presence of major analgesic effect, similar to opioids. Strong central nociceptive action does not depend on the presence of inflammatory or hyperalgesic process, which is still not totally explained. It seems that there is interaction of lysine with central opioid receptors, although the action mediated by such receptors has not been evidenced¹⁶. This study has shown good analgesic action of this drug, which is confirmed by the presence of mild pain only¹¹.

Different from other findings¹⁷ pain intensity was not

statistically significant 24 or 48 hours after surgery. Similarly to previous studies¹⁸, patients receiving lysine did not report undesirable effects, showing the good tolerability of the drug.

CONCLUSION

Both lysine and paracetamol were effective to control post tooth extraction pain. Lysine may be considered a good option for patients who cannot use other analgesic drugs.

REFERENCES

1. Gaya MVO, CapillaMV, Mateos RG. Relación de las variables del paciente y de la intervención con el dolor y la inflamación postoperatorios em la exodoncia de los terceros molares. *Med Oral*. 2002;7(5):360-9.
2. Camu F, Vanlersberghe C. Pharmacology of systemic analgesics. *Best Pract Res Clin Anaesthesiol*. 2002;16(4):475-88.
3. Bird RA, Simonetti MPB. Avaliação das atividades analgésica e antiinflamatória do clonixinato de lisina; estudo experimental em ratos. *Rev Dor*. 2000;2(1):7-12
4. Marti ML, De los Santos AR, Di Girolamo G, et al. Lysine clonixinate in minor dental surgery: double-blind randomized parallel study versus paracetamol. *Int J Tissue React*. 1993;15(5):207-13.
5. Gonzalez-Martin G, Cattan C, Zuniga S. Pharmacokinetics of lysine clonixinate in children in postoperative care. *Int J Clin Pharmacol Ther*. 1996;34(9):396-9
6. Orti E, Coirini H, Pico JC. Site-specific effects of the nonsteroidal anti-inflammatory drug lysine clonixinate on rat brain opioid receptors. *Pharmacology*. 1999;58(4):190-9.
7. Krymchantowski AV, Peixoto P, Higashi R, et al. Lysine clonixinate vs naproxen sodium for the acute treatment of migraine: a double-blind, randomized, crossover study. *Med Gen Med*. 2005;7(4):69.
8. Krymchantowski AV, Barbosa JS, Cheim C, et al. Oral lysine clonixinate in the acute treatment of migraine: a double-blind placebo-controlled study. *Arq Neuropsiquiatr*. 2001;59(1):46-9.
9. Marzola C. Técnica exodôntica. 3ª ed. Rio de Janeiro: Pancast; 2000.
10. Malamed SF. Manual de anestesia local. 5ª ed. São Paulo: Elsevier; 2005.
11. Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? *Pain*. 1997;72(1-2):95-7.

12. Morin C, Lund JP, Villarroel T, et al. Differences between the sexes in post-surgical pain. *Pain*. 2000;85(1-2):79-85.
 13. Wahl MJ, Overton D, Howell J, et al. Pain on injection of prilocaine plain vs. lidocaine with epinephrine. A prospective double-blind study. *J Am Dent Assoc*. 2001;132(10):1396-401.
 14. Pereira LV, Sousa FAEF. Mensuração e avaliação da dor pós-operatória: uma breve revisão. *Rev Lat-Am Enfermagem*. 1998;6(1):77-84.
 15. Guimarães KCN, Dorneles BAS, Mello GC. Eficácia da mensuração do quinto sinal vital no controle da dor pós-operatória: um ensaio clínico randomizado. Projeto piloto. *Rev Dor*. 2010;11(4):304-8
 16. Ortí E. Evidence for NSAIDs with the central opioid receptor system. *APPTLA*. 1996;46(3):199.
 17. Al-Khabbaz AK, Griffin TJ, Al-Shammari KF. Assessment of pain associated with the surgical placement of dental implants. *J Periodontol*. 2007;78(2):239-46.
 18. Santos FC, Souza PMR, Toniolo Neto J, et al. Tratamento da dor associada à osteoartrose de joelho em idosos: um ensaio clínico aleatório e duplamente encoberto com o clonixinato de lisina. *Rev Dor*. 2011;12(1):6-14
- Submitted in August 07, 2012.
Accepted for publication in November 14, 2012.