

# Revisão sobre o Uso de Gabapentina para Controle da Dor Pós-Operatória\*

## Review of the use of Gabapentin in the Control of Postoperative Pain\*

Jefferson Clivatti<sup>1</sup>, Rioko Kimiko Sakata, TSA<sup>2</sup>, Adriana Machado Issy<sup>3</sup>

### RESUMO

Clivatti J, Sakata RK, Issy AM — Revisão sobre o Uso de Gabapentina para Controle da Dor Pós-Operatória.

**JUSTIFICATIVA E OBJETIVOS:** A gabapentina tem sido utilizada como adjuvante no tratamento da dor pós-operatória com componente neuropático. É responsável pela inibição da sensibilização central, diminuindo a dor pós-operatória.

**CONTEÚDO:** Foram selecionados todos os estudos clínicos com distribuição aleatória que avaliaram o efeito da gabapentina na dor pós-operatória em humanos entre 2002 e 2007. Foram encontrados 26 artigos publicados. Em 17 estudos os pacientes receberam dose única pré-operatória que variou de 300 a 1.200 mg entre 30 min e duas horas antes dos procedimentos. Nos demais estudos a medicação foi iniciada entre uma e 24 horas antes dos procedimentos, foi continuada por dois a dez dias na dose de 1.200 a 1.800 mg.dia<sup>-1</sup>. Para medida de intensidade da dor foram utilizadas a Escala Analógica Visual ou Numérica. Em 75% dos que receberam somente dose pré os escores foram menores com uso de gabapentina e também em 55,6% dos que receberam dose pré e pós. O consumo de opióide foi menor em 82,4% dos que receberam dose pré e em 77,8% dos que receberam pré e pós. Em estudos que usaram pré, quatro não descreveram efeitos adversos; não houve diferença em 52,9%, mais náusea ou vômito em 11,8%, mais tontura em 5,9%, mais sedação em 5,9%, menos náusea ou vômito em um e menos retenção urinária em um. Em estudos que usaram pré e pós, quatro não descreveram efeitos adversos; não houve diferença em 22,2%, mais náusea ou vômito em 11,1%, mais tontura em 22,2% e mais sedação em 11,1%.

**CONCLUSÕES:** A gabapentina usada tanto antes como após a operação promove diminuição da intensidade da dor e da necessidade de complementação analgésica.

**Unitermos:** Dor: pós-operatória; DROGAS: gabapentina.

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### SUMMARY

Clivatti J, Sakata RK, Issy AM — Review of the Use of Gabapentin in the Control of Postoperative Pain.

**BACKGROUND AND OBJECTIVES:** Gabapentin has been used as adjuvant in the treatment of postoperative pain with a neuropathic component. It is responsible for the inhibition of central sensitization, decreasing postoperative pain.

**CONTENTS:** All clinical, randomized studies that evaluated the effects of gabapentin on postoperative pain in humans between 2002 and 2007 for a total of 26 studies were selected. In 17 studies, patients received a single preoperative dose, which ranged from 300 to 1,200 mg, 30 minutes to two hours before surgery. In the remaining studies, the administration of the drug was initiated one to 24 hours before the procedure and continued for 10 days, in doses that ranged from 1,200 to 1,800 mg.day<sup>-1</sup>. To measure pain severity, the Visual Analog or Numeric Rating Scale was used. In 75% of patients who received a single dose of gabapentin, scores were lower, and the same was seen in 55.6% of patients who received the drugs pre- and postoperatively. Opioid consumption was reduced in 82.4% of patients who received a single dose, and in 77.8% of patients who received pre- and postoperative gabapentin. Among the studies using a single dose of gabapentin, four did not describe adverse effects; 52.9% showed no differences, 11.8% detected more nausea or vomiting, 5.9% experienced more dizziness, 5.9% more sedation, less nausea or vomiting in one, and less urinary retention in one. Among the studies with pre- and postoperative administration of gabapentin, four did not describe adverse effects; 22.2% showed no differences, 11.1% had more nausea or vomiting, 22.2% more dizziness, and 11.1% more sedation.

**CONCLUSIONS:** Gabapentin, used before as well as before and after surgery, decreased pain severity and the need of analgesic supplementation.

**Key Words:** DRUGS: gabapentin; PAIN: postoperative.

### INTRODUÇÃO

A dor pós-operatória tem um componente nociceptivo e outro neuropático<sup>1,2</sup>. O componente nociceptivo resulta da ativação de receptores periféricos e condução dos impulsos pelas vias da dor e percepção na região supra-espinhal. Esse componente pode ser aliviado de forma adequada com antiinflamatórios e opióides. O componente neuropático resulta da lesão de fibras nervosas, com alteração da modulação da dor e sensibilização central, que cria mecanismos de amplificação da dor, hiperalgesia e alodinia. O tratamento da dor pós-operatória consiste basicamente no uso de três classes de fármacos: os antiinflamatórios, os

Na grande maioria dos estudos ocorreu redução significativa no consumo de analgésico ou nos escores de intensidade da dor no grupo tratado com gabapentina. O efeito anti-hiperálgico do fármaco promoveu diminuição do componente neuropático da dor pós-operatória melhorando a qualidade da analgesia pós-operatória.

Poucos desses estudos avaliaram o efeito da gabapentina na dor pós-operatória crônica. Uma vez que esse medicamento inibe a sensibilização central, que é um dos mecanismos atribuídos ao desenvolvimento das síndromes dolorosas crônicas, pode-se esperar que o mesmo tenha lugar na prevenção dessas síndromes.

Comparando os estudos que utilizaram dose única pré-operatória com os que utilizaram gabapentina pré- e pós-operatória, houve redução do consumo de analgésico em 82,4% dos estudos que usaram dose única, frente a 77,8% do outro grupo (Tabela IV). Resultado semelhante foi encontrado na avaliação das escalas de medida da intensidade da dor, com redução do escore em 70,6% nos que receberam tratamento somente no pré-operatório e 55,6% nos que receberam no pré e no pós-operatório (Tabela VI). Para se conseguir melhora na analgesia pós-operatória imediata, parece ser suficiente a utilização de dose única no pré-operatório. A utilização de gabapentina em doses maiores e por um período maior aumentou a incidência de efeitos colaterais relacionados, como sedação e tontura.

Para tentar encontrar a melhor dose e o melhor intervalo antes da operação para administrar o fármaco os dados foram organizados nas Tabelas III, V, VI e VII. A administração de dose única de 600 mg foi a menor a mostrar resultado significativo em todos os estudos em que foi utilizada; no entanto, essa dose foi utilizada em apenas dois estudos. Na maioria dos estudos a medicação foi administrada uma hora antes do procedimento cirúrgico, o que facilita o seu uso na prática clínica.

## CONCLUSÕES

A gabapentina administrada tanto antes do procedimento cirúrgico como antes e após promove diminuição da intensidade da dor e da necessidade de complementação analgésica.

Mais estudos são necessários para a incorporação definitiva do fármaco no arsenal utilizado atualmente para o tratamento da dor pós-operatória. Contudo, os resultados até então parecem muito promissores.

## *Review of the use of Gabapentin in the Control of Postoperative Pain\**

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### INTRODUCTION

Postoperative pain has nociceptive and neuropathic components<sup>1,2</sup>. The nociceptive component activates peripheral receptors and the conduction of impulses through pain and perception pathways in the supra-spinal region. Anti-inflammatories and opioids can adequately relieve this component. The neuropathic component results from nerve fiber damage that causes changes in pain modulation and central sensitization. This creates pain amplification mechanisms, hyperalgesia, and allodynia.

The treatment of postoperative pain consists basically on the use of three classes of drugs: anti-inflammatories, opioids, and local anesthetics. The majority of drugs in those classes have side effects that limit their clinical use as single agents. Analgesic techniques can affect different sites of the pain pathway in the peripheral and central nervous system. Combining drugs from different classes and with different mechanisms of action results in the desired analgesic effect with a reduction in side effects. Multimodal analgesia, using the association of different classes of analgesics, provides better results. The association of drugs with different mechanisms of action can improve analgesia and decrease side effects, since it allows the reduction in the total dose of each drug. Balanced analgesia is an effective way of treating acute pain, and it should be used whenever possible<sup>3</sup>. Studies have demonstrated the benefits of this association<sup>4,5</sup>.

Gabapentin, with its anti-hyperalgesic action and mechanism of action that differs from that of the drugs commonly used, creates a new perspective in the treatment of postoperative pain. Gabapentin (1-aminomethyl-cyclohexaneacetic acid) is an amino acid that has the structure of the neurotransmitter GABA but it does not have a significant interaction with this or any other neurotransmitter<sup>6,7</sup>. It is an anti-convulsant whose side effects are well tolerated.

Gabapentin has good absorption after oral administration, independently of the ingestion of food. Maximal plasma concentration is seen after two to three hours<sup>7,8</sup>. Protein binding is low (less than 3 to 5%) and it is widely distributed, involving almost all tissues (volume of distribution of 58 liters)<sup>7</sup>. It is not metabolized, it does not have enzymatic induction, and it easily crosses the blood-brain barrier. It is eliminated unchanged through the kidneys, but a small proportion is eliminated in the stool, and it has an elimination half-life of five to nine hours<sup>9</sup>.

The mechanism of action of anti-hyperalgesic drugs, like gabapentin, consists in the reduction of the lesion-induced hyper-

excitability of posterior horn neurons, which is responsible for central sensitization<sup>10</sup>. It is believed that the anti-hyperalgesic action is due to the postsynaptic binding of gabapentin to the  $\alpha_2$ -delta subunit of voltage-dependent calcium channels of dorsal horn neurons, decreasing calcium entry in nerve endings and the release of neurotransmitters. Other cellular mechanisms have been proposed to explain gabapentin's analgesia, including effects on NMDA receptors, sodium channels, monoaminergic pathways, and opioid system<sup>6,7,11-13</sup>. Somnolence, fatigue, ataxia, peripheral edema, and dizziness are the most common side effects<sup>6,12,14</sup>. Several studies have demonstrated that the perioperative use of gabapentin contributed for the reduction of postoperative pain. The objective of the present study was to evaluate published evidence on the subject.

## METHODS

A bibliographic research of data base on the Internet (PubMed) was undertaken using combinations of the following words as descriptors: Gabapentin, Pain, Analgesia, Anesthesia, and Postoperative. All controlled, randomized, clinical studies that assessed the effects of gabapentin on acute postoperative pain in humans were selected.

## RESULTS

Twenty-six randomized, placebo-controlled, clinical studies that were published between 2002 and 2007 evaluating the effects of gabapentin were selected. A total of 2,066 patients, including 1,020 patients who received gabapentin, participated in those studies.

In 17 studies, patients only received the drug in the preoperative period (PRE Group) and in the remaining studies (nine), patients in the treatment group received pre- and postoperative gabapentin (Pre-Post Group).

### Description of the Studies in the PRE Group

Seventeen studies, with a total of 1,437 patients from different surgical subspecialties (gynecology, orthopedics, neurosurgery, ENT, and urology) were included in this group (Table I). In 13 of those studies, general anesthesia was used; one study used local anesthesia with sedation; one used interscalene block with general anesthesia; one used neuroaxis block with general anesthesia or sedation, and one used regional intravenous block.

The doses of gabapentin ranged from 300 to 1,200 mg; in six studies they were associated with a benzodiazepine, and in one of them with a non-steroidal anti-inflammatory. All studies with gabapentin associated to another drug used the same drug in the control group.

The medication was administered 30 to 120 minutes before surgery.

All studies used the postoperative consumption of opioids to assess the effects of gabapentin. The majority of the studies

(16) used an evaluation scale to assess pain severity; the Visual Analog Scale (VAS) was used in 14 studies and the numeric scale (NS) was used in one; only one study did not use neither scale.

Postoperative opioid consumption in the gabapentin group was lower in 14 of 17 studies. In 13 of 15 studies that used the VAS, a difference favoring gabapentin was observed, but differences were not observed in studies that used the NS.

### Description of the Studies in the PRE-POST Group

Nine studies, totaling 629 patients, were included in the PRE-POST Group. The surgical subspecialties involved included gynecology, ENT, and orthopedics (Table II).

Patients underwent general anesthesia and the daily gabapentin dose ranged from 1,200 to 1,800 mg administered in divided doses. A benzodiazepine was associated to gabapentin in one study as pre-anesthetic medication, and the same drug and dose was administered to the control group. Treatment was initiated between one and 24 hours before surgery and continued for one to 10 days after the surgery.

In one of the studies, opioid consumption and an assessment scale (VAS, in six; NS, in three) were used to evaluate the effects of gabapentin. Opioid consumption was lower in patients treated with gabapentin in seven studies, and in two studies differences were not observed. As for pain severity, in five studies the results showed statistically significant differences favoring gabapentin.

Four studies conducted late pain evaluation (30 days after surgery in two, and three months afterwards in two), and only one of them demonstrated differences.

### First Dose

Gabapentin was administered (the first or the only dose) 30 minutes to 24 hours before surgery. In the PRE Group, gabapentin was administered more often 60 and 120 minutes before surgery in seven studies each, and in the PRE-POST Group, 60 minutes and 24 hours in five and four studies, respectively (Table III).

### Supplementary Analgesia

Opioid consumption reduced significantly in 14 (82.4%) of 17 studies of the PRE Group, and in seven (77.8%) of nine studies in the PRE-POST Group (Tables IV and V).

Grouping the studies according to the dose of gabapentin, the following results were observed: in the PRE Group, 1,200 mg was used in 12 studies and among them a significant reduction in opioid consumption was observed in nine studies (75.7%). On the remaining studies, the doses ranged from 300 to 900 mg, but a reduction in opioid consumption was not observed with 800 mg of gabapentin.

In the PRE-POST Group, the daily dose of gabapentin ranged from 1,200 mg to 1,800 mg but the majority of the studies used 1,200 mg or 1,600 mg. Postoperative opioid consumption was lower in 100% of the studies that used 1,200 mg and 1,800 mg, but only in 33% of the studies that used 1,600 mg.

Table I – Studies with a Single Dose of Preoperative Gabapentin<sup>15-21</sup>

References	Type of Surgery	Anesthesia	N	Dose (mg)	Beginning	Control	Other Group	Opioid Consumption	Pain scale
Dirks J, 2002 <sup>15</sup>	Mastectomy	Ge	70	1,200 mg + triazolam 0.125mg	1h	Placebo		< in treatment Group	VAS
Pandey CK, 2004 <sup>16</sup>	Discectomy	Ge	56	300 mg + lorazepam	2h	Lorazepam		< in treatment Group	VAS
Rorarius MGF, 2004 <sup>17</sup>	Hysterectomy	Ge	75	1,200 mg	2h	Oxazepam 15mg		< in treatment Group	VAS
Turan A, 2004 <sup>18</sup>	Nasal septum or sinuses	Local + Sedation	50	1200 mg + midazolam 0,1mg/kg	1h	Midazolam 0.1mg/kg		< in treatment Group	VAS
Turan A, 2004 <sup>19</sup>	Histerectomy	Ge	50	1200 mg + midazolam 0,1mg/kg	1h	Midazolam 0.1mg/kg		< in treatment Group	VAS
Turan A, 2004 <sup>20</sup>	Discectomy	Ge	50	1200 mg + midazolam 0,1mg/kg	1h	Midazolam 0.1mg/kg		< in treatment Group	VAS
Pandey CK, 2004 <sup>21</sup>	Laparoscopic cholecistectomy	Ge	459	300 mg	2h	Placebo	Tramadol 100mg	< in treatment Group	VAS
Pandey CK, 2005 <sup>22</sup>	Nephrectomy	Ge	60	600 mg	2h	Placebo		< in treatment Group	VAS
Radhakrishnan M, 2005 <sup>23</sup>	Laminectomy and discectomy	Ge	60	800 mg	NR	Placebo		No dif	NS
Menigaux C, 2005 <sup>24</sup>	Knee arthroscopy	Ge	40	1,200 mg	1h	Placebo		< in treatment Group	VAS
Pandey CK, 2005 <sup>25</sup>	Discectomy	Ge	100	300, 600, 900,1,200 mg	2h	Placebo		< in treatment Group (600 mg or more)	VAS
Bartholdy J, 2006 <sup>26</sup>	Laparoscopic tubal ligation	Ge	76	1,200 mg + lornoxicam 8 mg	30 min	Lornoxicam 8 mg		No dif	VAS
Adam F, 2006 <sup>27</sup>	Shoulder arthroscopy	IE block + Ge	60	800	2h	Placebo		No dif	VAS and NS
Al-Mujadi H, 2006 <sup>28</sup>	Thyroidectomy	Ge	72	1,200 mg	2h	Placebo		< in treatment Group	VAS
Hayashida K, 2007 <sup>29</sup>	Orthopedic or Genitourinary	Spinal and/or epidural block with sedation or Ge	44	1,200 mg	90 min	Placebo		< in treatment Group	NA
Durmus M, 2007 <sup>30</sup>	Hysterectomy	Ge	75	1200	1h	Placebo	Gabapentin + paracetamol	< in treatment Group	VAS
Turan A, 2007 <sup>31</sup>	Upper limb	Bier	40	1,200 mg + midazolam 0.4mg/kg	1h	Midazolam 0.4mg.kg <sup>-1</sup>		< in treatment Group	VAS

Dif: difference; Ge: general; IE: interscalenic; NA: not assessed; NS: numeric scale; VAS: visual analog scale.

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Table II – Studies with Pre- and Postoperative Administration of Gabapentin <sup>32-40</sup>

Reference	Type of Surgery	Anest	N	Daily dose (mg)	First dose (preop)	Dur (days)	Control	Other Groups	Opioid consumption	Scale	Pain severity	Late effect	SE
Fassoulaki A, 2002 <sup>32</sup>	Breast cancer	Ge	75	1,200 mg	24 h	10	Placebo	Mexiletine 600 mg	< in treatment Group	VAS	< in treatment Group	Pain after 3 min: SD	NA
Dierking G, 2004 <sup>33</sup>	Histerectomy	Ge	80	1,200 mg	1 h	1	Placebo		< in treatment Group	VAS	No dif		No dif
Fassoulaki A, 2005 <sup>34</sup>	Breast cancer	Ge	50	1,200 mg	24 h	8	Placebo		< in treatment Group	VAS	< in treatment Group	Pain after 3 min: < Treatment Group	NA
Gilron I, 2005 <sup>35</sup>	Hysterectomy	Ge	110	1,800 mg	1 h	4	Placebo	Rofecoxib 50 mg e and Gaba + Rofecoxib	< in treatment Group	VAS	< in treatment Group	Pain after 1 min: No dif	More sedation
Mikkelsen S, 2006 <sup>36</sup>	Tonsillectomy	Ge	54	1,200 mg	1 h	5	Placebo		No dif	NS	No dif PONV and dizziness		More
Fassoulaki A, 2006 <sup>37</sup>	Hysterectomy	Ge	60	1,200 mg	24 h	5	Placebo		No dif	VAS	No dif		No dif
Turan A, 2006 <sup>38</sup>	Hysterectomy	Ge	100	1,200 mg	1 h	2	Placebo	Rofecoxib 50 mg e Gaba + Rofecoxib	< in treatment Group	NS	< in treatment Group		Less PONV
Turan A, 2006 <sup>39</sup>	Lower limb	Ge	40	1,200 mg + MDZ 0.4 mg.Kg <sup>-1</sup>	1 h	2	midazolam 0.4 mg.kg <sup>-1</sup>		< in treatment Group	NS	< in treatment Group		More dizziness
Fassoulaki A, 2007 <sup>40</sup>	Hysterectomy	Ge	60	1,600 mg	24 h	7	Placebo		< in treatment Group	VAS	SD	Pain after 1 min: No dif	No dif

Anest: anesthesia; Dif – difference; Dur – duration; Ge – general; NA – not assessed; NS – numeric scale; PONV – postoperative nausea and vomiting; SE – side effects; VAS – visual analog scale.

Table III – Initial Dose

Group	Time before surgery					Total
	30 min	60 min	90 min	120 min	24h	
Pre	1	7	1	7	0	16
Pre + post	0	5	0	0	4	9

One of the studies did not inform the exact time of the dose.

Table IV – Decreased Need of Supplementary Analgesia

	N	%	Total
Pre	14	82.4	17
Post	7	77.8	9

**Pain Evaluation Scales**

In the PRE Group, 16 studies used scales to assess pain severity in the postoperative period, and in 12 of them (75%) the scores were significantly lower in patients who received gabapentin. The same assessment of the PRE-POST Group

Table V – Decreased Need of Supplementary Analgesia According to the Doses Used

Dose	Preoperative Gabapentin			Pre- and Post-Operative Gabapentin		
	N	%	Total	N	%	Total
300 mg	2	100.00	2			
600 mg	2	100.00	2			
800 mg	0	0.0	2			
900 mg	1	100.00	1			
1,200 mg	11	91.7	12	3	100.00	3
1,600 mg				3	100.00	3
1,800 mg				2	66.7	3

showed that pain scores decreased in five (55.6%) of nine studies (Tables VI and VII).

Grouping the studies according to the dose of gabapentin, the results were very similar to those of postoperative opioid consumption.

Table VI – Reduction in Postoperative Pain Scores

Group	N	%	Total
Pre	12	75.0	16
Pre and Post	5	55.6	9

One of the studies did not use a scale to evaluate the effects.

Table VII – Reduction in Postoperative Pain Scores According to the Doses Used

Dose	Preoperative Gabapentin			Pre- and Post-Operative Gabapentin		
	N	%	Total	N	%	Total
300 mg	1	50.0	2			
600 mg	2	100.0	2			
800 mg	0	0.0	2			
900 mg	1	100.0	1			
1,200 mg	9	75.7	12	3	100.0	3
1,600 mg				1	33.3	3
1,800 mg				1	100.0	1

### Reports of Adverse Effects

Adverse effects reported included postoperative nausea and vomiting (PONV), sedation, and dizziness (Table VIII). In the PRE Group, a reduction in the incidence of nausea and vomiting in patients treated with gabapentin was seen in two studies and an increase in this incidence was seen in one study. A higher incidence of sedation was seen in one study and of dizziness in another study.

In the PRE-POST Group, an increase in the incidence of PONV in patients treated with gabapentin was observed in one study, increased sedation was seen in one study, and an increase in the incidence of dizziness was seen in two studies.

Table VIII – Reports of the Incidence of Side Effects

Dose	Preoperative Gabapentin			Pre- and Post-Operative Gabapentin		
	N	%	Total	N	%	Total
Reduction in PONV	2	11.8	17			
Increased PONV	1	5.9	17	1	11.1	9
Increased sedation	1	5.9	17	1	11.1	9
Increased dizziness	1	5.9	17	2	22.2	9

PONV – postoperative nausea and vomiting.

### DISCUSSION

A small number of studies on the subject were published from 2002 to 2007 in which both anesthetic techniques and surgeries varied considerably. The type of surgeries varied from laparoscopic tubal ligation to laminectomies.

The dosing schedules of gabapentin also varied considerably. It ranged from a single 300 mg dose to 1,800 mg.day<sup>-1</sup> in divided doses for four days.

In some studies, gabapentin was associated with midazolam or lornoxicam, and the control group also received a combination of drugs, which should also be considered when analyzing the conclusions.

A significant reduction in analgesic consumption or in pain scores in the group treated with gabapentin was observed in most studies. The anti-hyperalgetic action of this drug reduced the neuropathic component of postoperative pain, improving the quality of postoperative analgesia.

A small number of studies evaluated the effects of gabapentin on chronic postoperative pain. Since this drug inhibits central sensitization, one of the mechanisms of chronic pain syndromes, one can expect the same effect in their prevention.

Comparing the studies that used a single preoperative dose with those that used pre- and postoperative gabapentin, analgesic consumption decreased in 82.4% of the studies that used a single dose and in 77.8% of the studies in the other group (Table IV). A similar result was seen in the evaluation of pain scores, with a reduction in the score in 70.6% of the patients in the PRE Group, and in 55.6% of those in the PRE-POST Group (Table VI). A single preoperative dose seems to be enough to improve analgesia in the immediate postoperative period.

The use of higher doses of gabapentin for a prolonged period increased the incidence of side effects such as sedation and dizziness.

Trying to find the best dose and the best interval before surgery to administer the drug, the data were organized in Tables III, IV, V, VI, and VII. A single 600 mg dose was the lowest dose associated with a significant result; however, this dose was used only in two studies. In most of the study, the drug was administered one hour before surgery, facilitating its use in clinical practice.

### CONCLUSIONS

Gabapentin, used both before the surgery and before and after, promoted a reduction in pain severity and the need for analgesic supplementation.

More studies are necessary to include gabapentin definitively in the pharmacologic arsenal currently used in the treatment of postoperative pain; however, so far the results are promising.

## REFERÊNCIAS — REFERENCES

01. Woolf CJ, Max MB — Mechanism-based pain diagnosis: issues for analgesic drug development. *Anesthesiology*, 2001;95:241-249.
02. Scholz J, Woolf CJ — Can we conquer pain? *Nat Neurosci*, 2002; 5:1062-1067.
03. Kehlet H — Controlling acute pain. Role of pre-emptive analgesia, peripheral treatment, and balanced analgesia, and effects on outcome. *Pain* 1999. *An Update Review*. IASP, 459-462.
04. Breivik H — Postoperative pain: toward optimal pharmacological and epidural analgesia. *Pain* 2002. *An Update Review*. IASP, 337-349.
05. Van Elstraete AC, Pastureau F, Lebrun T et al. — Caudal clonidine for postoperative analgesia in adults. *Br J Anaesth*, 2000; 84: 401-402.
06. Rowbotham MC — Treatment of neuropathic pain: perspectives on current options. In *Pain -An Update Review: Refresher Course Syllabus*. IASP 2005; 107-19.
07. Gidal B, Billington R — New and emerging treatment options for neuropathic pain. *Am J Manag Care*, 2006; 12:269-278.
08. Elwes RDB, Binnie CD — Clinical pharmacokinetics of newer antiepileptic drugs. Lamotrigine, vigabatrin, gabapentin and oxcarbazepine. *Clin Pharmacokinet*, 1996;30:403-415.
09. Comstock TI, Sica DA, Bockbrader HN et al. — Gabapentin pharmacokinetics in subjects with various degrees of renal function. *J Clin Pharmacol*, 1990;30:862.
10. Maneuf YP, Gonzalez MI, Sutton KS et al. — Cellular and molecular action of the putative GABAmimetic, gabapentin. *Cell Mol Life Sci*, 2003;60:742-750.
11. Taylor CP, Gee NS, Su TZ et al. — A summary of mechanistic hypotheses of gabapentin pharmacology. *Epilepsy Res*, 1998; 29:233-249.
12. Dahl JB, Mathiesen O, Moiniche S — Protective premedication: an option with gabapentin and related drugs? An review of gabapentin and pregabalin in the treatment of postoperative pain. *Acta Anaesthesiol Scand*, 2004; 48:1130-1136.
13. Sills GJ — Not another gabapentin mechanism. *Epilepsy Curr*, 2005;5:75-77.
14. Markman JD, Dworkin RH — Ion channel targets and treatment efficacy in neuropathic pain. *J Pain*, 2006; 7:538-547.
15. Dirks J, Fredensborg BB, Christensen D et al. — A randomized study of the effects of single-dose gabapentin versus placebo on postoperative pain and morphine consumption after mastectomy. *Anesthesiology*, 2002; 97:560-564.
16. Pandey CK, Sahay S, Gupta D et al. — Preemptive gabapentin decreases postoperative pain after lumbar discectomy. *Can J Anesth*, 2004;51:986-989.
17. Rorarius MGF, Mennander S, Suominen P et al. — Gabapentin for the prevention of postoperative pain after vaginal hysterectomy. *Pain*, 2004;110:175-181.
18. Turan A, Memis D, Karamanlioglu B et al — The analgesic effects of gabapentin in monitored anesthesia care for ear-nose-throat surgery. *Anesth Analg*, 2004;99:375-378.
19. Turan A, Karamanlioglu B, Memis D et al. — The analgesic effects of gabapentin after total abdominal hysterectomy. *Anesth Analg*, 2004;98:1370 -1373.
20. Turan A, Karamanlioglu B, Memis D et al. — Analgesic effects of gabapentin after spinal surgery. *Anesthesiology* 2004;100:935-938.
21. Pandey CK, Priye S, Singh S et al. — Preemptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy. *Can J Anaesth*, 2004;51:358-363.
22. Pandey CK, Singhal V, Kumar M et al. — Gabapentin provides effective postoperative analgesia whether administered pre-emptively or post-incision. *Can J Anaesth*, 2005;52:827-831.
23. Radhakrishnan M, Bithal PK, Chaturvedi A — Effect of pre-emptive gabapentin on postoperative pain relief and morphine consumption following lumbar laminectomy and discectomy: a randomized, double-blinded, placebo-controlled study. *J Neurosurg Anesthesiol*, 2005;17:125-128.
24. Menigaux C, Adam F, Guignard B et al. — Preoperative gabapentin decreases anxiety and improves early functional recovery from knee surgery. *Anesth Analg*, 2005;100:1394 -1399.
25. Pandey CK, Navkar DV, Giri PJ et al. — Evaluation of the optimal preemptive dose of gabapentin for postoperative pain relief after lumbar discectomy: a randomized, double-blind, placebo-controlled study. *J Neurosurg Anesthesiol*, 2005;17:65-68.
26. Bartholdy J, Hilsted KL, Hjortsoe NC et al. — Effect of gabapentin on morphine demand and pain after laparoscopic sterilization using Filshie clips. A double blind randomized clinical Trial. *BMC Anesthesiol*, 2006;6:12.
27. Adam F, Menigaux C, Sessler DI et al. — A single preoperative dose of gabapentin (800 milligrams) does not augment postoperative analgesia in patients given interscalene brachial plexus blocks for arthroscopic shoulder surgery. *Anesth Analg* 2006; 103:1278 -1282.
28. Al-Mujadi H, A-Refai AR, Katzarov MG et al. — Preemptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery. *Can J Anesth* 2006;53:268-273.
29. Hayashida K, DeGoes S, Curry R et al. — Gabapentin activates spinal noradrenergic activity in rats and humans and reduces hypersensitivity after surgery. *Anesthesiology*, 2007;106:557-562.
30. Durmus M, Kadir But A, Saricicek V et al — The post-operative analgesic effects of a combination of gabapentin and paracetamol in patients undergoing abdominal hysterectomy: a randomized clinical trial. *Acta Anaesthesiol Scand*, 2007;51:299-304.
31. Turan A, White PF, Karamanlioglu B et al. — Premedication with gabapentin: the effect on tourniquet pain and quality of intravenous regional anesthesia. *Anesth Analg*, 2007;104:97-101.
32. Fassoulaki A, Patris K, Sarantopoulos C et al. — The analgesic effect of gabapentin and mexiletine after breast surgery for cancer. *Anesth Analg*, 2002;95:985-991.
33. Dierking G, Duedahl TH, Rasmussen ML et al. — Effects of gabapentin on postoperative morphine consumption and pain after abdominal hysterectomy: a randomized, double-blind trial. *Acta Anaesthesiol Scand*, 2004;48:322-327.
34. Fassoulaki A, Triga A, Melemenis A et al. — Multimodal analgesia with gabapentin and local anesthetics prevents acute and chronic pain after breast surgery for cancer. *Anesth Analg*, 2005; 101:1427-1432.
35. Gilron I, Orr E, Tu D et al. — A placebo-controlled randomized clinical trial of perioperative administration of gabapentin, rofecoxib and their combination for spontaneous and movement-evoked pain after abdominal hysterectomy. *Pain*, 2005;113:191-200.
36. Mikkelsen S, Hilsted KL, Andersen PJ et al. — The effect of gabapentin on post-operative pain following tonsillectomy in adults. *Acta Anaesthesiol Scand*, 2006;50:809-815.
37. Fassoulaki A, Stamatakis E, Petropoulos G et al. — Gabapentin attenuates late but not acute pain after abdominal hysterectomy. *Eur J Anaesth* 2006; 23: 136-141.
38. Turan A, Kaya A, Karamanlioglu B et al. — Effect of oral gabapentin on postoperative epidural analgesia. *Br J Anaesth*, 2006; 96:242-246.
39. Turan A, White PF, Karamanlioglu B et al. — Gabapentin: an alternative to the cyclooxygenase-2 inhibitors for perioperative pain management. *Anesth Analg*, 2006;102:175-181.
40. Fassoulaki A, Melemenis A, Stamatakis E et al. — A combination of gabapentin and local anaesthetics attenuates acute and late pain after abdominal hysterectomy. *Eur J Anaesthesiol*, 2007; 24:521-528.

## RESUMEN

Clivatti J, Sakata RK, Issy AM — Revisión sobre el Uso de Gabapentina para el Control del Dolor Postoperatorio.

**JUSTIFICATIVA Y OBJETIVOS:** La gabapentina ha sido utilizada como adyuvante en el tratamiento del dolor postoperatorio con componente neuropático. Es responsable de la inhibición de la sensibilización central, disminuyendo el dolor postoperatorio.

**CONTENIDO:** Fueron seleccionados todos los estudios clínicos con distribución aleatoria que evaluaron el efecto de la gabapentina en el dolor postoperatorio en humanos entre 2002 y 2007. Se encontraron 26 artículos publicados. En 17 estudios, los pacientes recibieron dosis única preoperatoria que varió entre 300 y 1200mg y entre 30min y dos horas antes de los procedimientos. En los demás estudios, la medicación fue iniciada entre una y 24 horas antes de los procedimientos, y continuada por dos a 10 días en la dosis de 1.200 a 1.800 mg.día<sup>-1</sup>. Para una medida de inten-

sidad del dolor, fueron utilizadas la Escala Analógica Visual o Numérica. En un 75% entre los que recibieron solamente la dosis pre, los puntajes fueron menores con el uso de la gabapentina y también en un 55,6% entre los que recibieron dosis pre y pos. El consumo de opioide fue menor en un 82,4% de los que recibieron dosis pre y en un 77,8% en los que recibieron pre y pos. En estudios que usaron pre, cuatro no arrojaron efectos adversos; no hubo diferencia en un 52,9%, más náusea o vómito en un 11,8%, más mareos en un 5,9%, más sedación en un 5,9%, menos náusea o vómito en uno y menos retención urinaria en uno. En estudios que usaron pre y pos, cuatro no arrojaron efectos adversos; no hubo diferencia en un 22,2%, más náusea o vómito en 11,1%, más mareo en 22,2% y más sedación en un 11,1%.

**CONCLUSIONES:** La gabapentina usada tanto antes, como antes y después de la operación, promueve la reducción de la intensidad del dolor y de la necesidad de complementación analgésica.