Analgesic effect of pregabalin and magnesium sulfate after mastectomy with axillary lymphadenectomy

Efeito analgésico da pregabalina e do sulfato de magnésio no pós-operatório de mastectomia com linfadenectomia axilar

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ABSTRACT

BACKGROUND AND OBJECTIVES: Mastectomy with lymphadenectomy is a surgery associated with moderate to severe pain in the immediate postoperatory. Several safe adjuvant drugs that provide good analgesia with few adverse effects have been researched. Pregabalin and magnesium sulfate are drugs that promote analgesia with few adverse effects. The objective of the present study was to evaluate the analgesic effect of pregabalin and magnesium sulfate in the postoperatory of mastectomy with axillary lymphadenectomy.

METHODS: Double-blinded, randomized study involving 80 patients submitted to mastectomy with axillary lymphadenectomy under general anesthesia. The patients were distributed into 4 groups: Control (CG, did not receive the proposed adjuvant drug); Magnesium+Placebo (MG, received magnesium sulfate during anesthesia); Pregabalin+Magnesium (P+MG, received magnesium added to pregabalin 150 mg before and 12 h after surgery); and Pregabalin+Placebo (PG, received pregabalin). All patients completed the *Self-Report Questionnaire* 20 (SRQ-20) to screen for possible mental disorders and had their physical status monitored at 1 h, 12 h, and 24 h after surgery, through anamnesis, pain questionnaire, opioid consumption, and presence of complications and/or adverse events such as nausea, vomiting, and sleepiness. Randomization was performed using sealed opaque envelopes without the knowledge of the anesthesiologist (researcher) and the patient.

RESULTS: For each group, twenty patients were randomized, which were analyzed at the end of the study. The number of patients presenting absent/mild pain in P+MG was significantly higher than in CG, MG and PG after one hour. After 12 hours, P+MG and PG had more patients with absent/mild pain than CG and MG. At 24 hours postoperatively, all patients in all evaluated groups had no moderate/severe pain. There was no difference in the frequency of patients presenting nausea or vomiting, nor in the scores of the sleep evaluation after surgery in the four groups.

CONCLUSION: The combination of magnesium sulfate and pregabalin provided satisfactory analgesia in the first hour after mastectomy with axillary lymphadenectomy. Nevertheless, magnesium sulfate isolated presented no analgesic benefit for the patients, and pregabalin isolated was only slightly effective at the first hour after surgery.

Keywords: Postoperative pain, Pregabalin, Magnesium sulfate.

RESUMO

JUSTIFICATIVA E OBJETIVOS: Mastectomia com linfadenectomia é uma cirurgia que causa dor moderada ou intensa no pós-operatório imediato. Muitos fármacos adjuvantes, seguros, que promovem boa analgesia e com poucos efeitos adversos têm sido pesquisados. A pregabalina e o sulfato de magnésio são fármacos que promovem analgesia com poucos efeitos adversos. O objetivo deste estudo foi avaliar o efeito analgésico da pregabalina e do sulfato de magnésio no pós-operatório de mastectomia com linfadenectomia axilar.

MÉTODOS: Estudo randomizado e duplo-cego envolvendo 80 pacientes submetidas à mastectomia com linfadenectomia axilar sob anestesia geral. As pacientes foram divididas em quatro grupos: Controle (GC, não receberam o fármaco adjuvante proposto); Magnésio+Placebo (GM, receberam sulfato de magnésio durante a anestesia); Pregabalina+Magnésio (GP+M, receberam magnésio adicionado a pregabalina 150 mg antes e 12 h após a cirurgia); e Pregabalina+Placebo (GP, receberam a pregabalina). Todas as pacientes responderam o *Self-Report Questionnaire* 20 (SRQ-20) para rastrear possível transtorno mental e foram seguidas, monitorando o estado físico 1h, 12h e 24h após a cirurgia, através de anamnese, questionário de dor, consumo de opioides e presença de complicações e/ou eventos adversos como náusea, vômito e sonolência. A randomização foi realizada por meio de envelopes opacos e selados sem o conhecimento do anestesiologista (pesquisador) e do paciente.

RESULTADOS: Foram randomizadas 20 pacientes para cada grupo, as quais foram analisadas ao fim do estudo. O número de pacientes apresentando dor ausente/leve no GP+M foi significantemente maior que nos GC, GM e GP após uma hora. Após

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12 horas, GP+M e GP apresentaram maior número de pacientes com dor ausente/leve que GC e GM. Em 24 horas do pós-operatório, todos os pacientes de todos os grupos avaliados não apresentaram dor moderada/severa. Não houve diferença na frequência de pacientes apresentando náusea ou vômito, nem nos escores da avaliação do sono após a cirurgia nos quatro grupos.
CONCLUSÃO: A associação de sulfato de magnésio e pregabalina causa boa analgesia de mastectomia com linfadenectomia axilar na primeira hora do pós-operatório. No entanto, o uso isolado do sulfato de magnésio não trouxe benefício para analgesia nestas pacientes, assim como a pregabalina sozinha se mostrou pouco efetiva na primeira hora de avaliação.
Descritores: Dor pós-operatória, Pregabalina, Sulfato de magnésio.

INTRODUCTION

Breast carcinoma is the most common cancer in women and one of the two most frequent causes of death related to female malignant tumor[1].
The treatment of breast cancer is complex, and many variables must be considered. Of these, the most important is the disease staging, based on the patient's clinical condition. There are three main goals of treatment: to control the local disease, prevent metastasis, and improve the patients' quality of life. The most common therapeutic approaches are radiotherapy, chemotherapy, and surgery, such as mastectomy with axillary lymphadenectomy. Of patients undergoing mastectomy, approximately 50% present moderate pain and about 25% report severe pain during this period[2,3].
Because postoperative pain (POP) is a multifactorial process, multimodal analgesia is used, which is a type of analgesia that acts in different stages of the nociceptive stimuli conduction pathways and uses several analgesic substances and/or procedures with the objective of increasing the response with lower drug doses, synergistic or additive effect, sparing the use of opioids and thus reducing the unpleasant adverse effects of these substances. Non-steroidal anti-inflammatory drugs (NSAIDs), opioids, gabapentinoid anticonvulsants, antidepressants, glucocorticoids, acetaminophen, N-Methyl-D-Aspartate (NMDA) receptor blocker, α_2-adrenergic agonist, regional analgesic blockade, wound infiltration, and others are used. Nevertheless, the use of all these substances or procedures generates adverse effects such as nausea, vomiting, drowsiness, dizziness, hypotension, and others[4].
Pregabalin is an anticonvulsant used to treat epilepsy and anxiety and an adjuvant in the treatment of chronic pain[5]. Studies indicate that the antinociceptive action of pregabalin is related to its interaction with the descending noradrenergic and serotoninergic pathways of pain modulation in the spinal cord and that it reduces the release of excitatory neurotransmitters in the spinal cord and in some areas of the brain in a hyperactive neuronal state, such as in neuropathic pain[6]. Pregabalin would be a good option for reducing POP in orthopedic surgeries when used in the perioperative period, reducing the use of opioids and the incidence of chronic pain, despite increasing sedation in some patients[7]. However, there is still no consensus on the dose of pregabalin for the treatment of POP[8,9].
Magnesium is a natural physiological calcium antagonist and a natural antagonist of NMDA receptors[10]. A meta-analysis on the effect of magnesium as an analgesic adjuvant for abdominal, hysterectomy, and orthopedic surgeries, concluded that magnesium causes decreased opioid use, decreased pain intensity when given intravenously in *bolus* or *bolus* and continuous infusion or continuous infusion only, without causing major changes in the cardiovascular system. The *bolus* dose of magnesium ranges from 30 to 50 $mg.kg^{-1}$ and the total dose, when associated with continuous infusion, ranges from 1.03 to 23.5 g[11].
No studies have been found on the analgesic effect of magnesium and pregabalin sparing the use of opioids in mastectomy with axillary lymphadenectomy.
Pain is an unpleasant and personal sensation, thus it is difficulty to quantify in each patient. There are some pain scales that serve as tools to measure it. Of these scales, the most commonly used are the Visual Analog Scale (VAS), the Numerical Rating Scale, and the Verbal Scale. The Numerical Rating Scale consists of 11 points from 0 to 10, where zero indicates the patient reports no pain and 10 referrers to the worst pain imaginable. It has an advantage over the others because it provides easier data for statistical analysis[12].
Therefore, the present study's objective was to evaluate the isolated or combined analgesic effect of pregabalin and magnesium sulfate in the postoperative period of mastectomy with axillary lymphadenectomy. Secondarily, the aim was to evaluate the frequency of nausea and/or vomiting in the association of pregabalin and magnesium sulfate; to evaluate the frequency of sleepiness in the association of pregabalin and magnesium sulfate; and to verify the relation of possible mood disorders with pain intensity in the patients.

METHODS

A randomized, placebo-controlled, parallel, double-blind, four-arm clinical trial. The work was carried out at the Haroldo Juaçaba Hospital - Ceará Cancer Institute. The study sample was screened for patients who would undergo mastectomy with axillary lymphadenectomy. The study was conducted in the operating room, continuing in the recovery room and hospital wards, from March 2015 to November 2017. This clinical trial is registered in the Brazilian Registry of Clinical Trials (ReBEC) under number RBR-59m3sj. All patients signed the Free and Informed Consent Term (FICT). The CONSORT Statement was used for the reporting of this clinical trial.
Eighty women were included, aged 18 years or older; with an indication for mastectomy with axillary lymphadenectomy; in a physical status compatible with the American Society of Anesthesiologist (ASA) I and II classification (healthy patient without organic alterations or with mild or moderate systemic alterations caused by surgical or systemic disease); who had not previously experienced intolerance to pregabalin and/or magnesium; had no history of allergy to ketoprofen and/or dipyrone; had no previous history of liver or kidney disease, or any other disease with contraindications for the use of pregabalin or magnesium; had not consumed opioids 48 h before surgery, and were not on calcium channel blockers. Patients were excluded from the study if they reported an allergic reaction to dipyrone and/or ketoprofen

and/or pregabalin and/or magnesium sulfate; had any clinical event indicating that the procedure should be interrupted, such as hypotension or severe bradycardia that was difficult to control, except due to withdrawal of the magnesium sulfate infusion.

In the preanesthetic room, the Self-Report Questionnaire 20 (SRQ-20) was applied. Developed by the World Health Organization and validated in Brazil in 1986, the SRQ-20 helps to detect psycho-emotional disorders, such as anxiety or depression, which could cause confounding bias.

After simple randomization with sequentially numbered sealed opaque envelopes one hour before surgery, patients were distributed into four study groups, with 20 participants in each, as follows: PG group (Pregabalin + Placebo) received pregabalin 150 mg orally 90 min before the anesthetic procedure and 12 h after surgery and, during surgery, received saline without magnesium sulfate; MG group (Magnesium + Placebo) received pregabalin placebo 90 min before and 12 h after surgery and, during the induction of anesthesia, received 50 mg/kg of magnesium sulfate intravenously, with maintenance of 10 mg/kg/h; P+MG group (Pregabalin + Magnesium) received pregabalin 150 mg orally 90 minutes before the anesthetic procedure and 12 h after surgery and, during the induction of anesthesia, received 50 mg/kg of magnesium sulfate intravenously, with maintenance of 10 mg/kg/h; and CG group (Control) received pregabalin placebo 90 minutes before and 12 h after surgery and, during surgery, received saline without magnesium sulfate.

All patients underwent the same anesthetic schedule, consisting of midazolam at a dose of 0.03 mg/kg intravenously 30 min before general anesthesia, followed by propofol, fentanyl, remifentanil, cisatracurium, and sevoflurane. A balanced general anesthesia was applied to the patients. The total dose and the time of the last fentanyl administration were recorded at the end of surgery. All patients received dipyrone 20 - 30 mg/kg and ketoprofen 100 mg intravenously after the start of surgery. Any changes in blood pressure (BP), pulse oximetry, heart rate (HR), and capnography were recorded.

In the post-anesthetic recovery room, all patients received analgesic drugs (dipyrone and tramadol) at a pre-established time. The researcher carried out follow-ups during the 24 h period after surgery, monitoring the patient's status at 1, 12, and 24 hours through anamnesis, pain intensity measurement (Numerical Rating Scale), which was the main objective of this study, development of pain symptoms, need for opioid use, and presence of complications and/or adverse events such as nausea, vomiting, and drowsiness by the Ramsay Scale.

In the Ramsay Scale, grade 1 is given to the patient who is agitated; grade 2 to the quiet patient; grade 3 to the drowsy patient who is already responding to commands; grade 4 to the patient who is sleeping but responds quickly to vigorous sound stimulus; grade 5 to the sleeping patient who responds slowly to vigorous sound stimulus; and grade 6 to the patient who is sleeping and does not respond to any stimulus. Furthermore, the absence or presence of nausea or vomiting was correlated with points from zero to 2, where zero is the absence of these symptoms, 1 when the patient feels nausea, and 2 if vomiting is present.

All patients received 1 g of dipyrone intravenously every 6 h in the postoperative period until hospital discharge and received 100 mg of tramadol intravenously, if requested, due to pain, and the time of this drug was recorded for further assessment.

The study was approved by the Research Ethics Committee (CEP – CAAE: 30802414.0.0000.5528).

Statistical analysis

Numerical data were expressed as mean and standard deviation, analyzed by the Kolmogorov-Smirnov test, and compared using ANOVA/Bonferroni (parametric data) or Kruskal-Wallis/Dunn (non-parametric data) tests. Categorical data were expressed as absolute and percentage frequency and compared using the Chi-square test. The software used was the Statistical Package for the Social Sciences (SPSS) version 20.0 for Windows, adopting a 95% confidence level.

RESULTS

Demographic characteristics of the study's patients, such as age, weight, height and body mass index, are presented in table 1.

The mean anesthesia time (at the time of extubation) and the consumption of fentanyl and sevoflurane are presented in Table 2, with no statistically significant difference between groups.

In the CG and PG, there was no magnesium sulfate administration. In the other groups there was no significant difference regarding the amount of magnesium administered. In all patients, only the initial dose of muscle relaxant, cisatracurium, was used, with no additional dose during the anesthetic procedure, and all reached TOF>0.9 before the time of extubation (Table 2).

The mean SRQ-20 score also showed no statistically significant difference between the studied groups (p=0.233), namely: CG (5.45±3.73), MG (4.25±2.27), P+MG (3.90±2.65) and PG (3.85±2.11).

Regarding the time to request the first analgesic, tramadol, most patients used the opioid within the first 60 minutes after surgery. However, the groups treated with pregabalin had a higher frequency of patients using tramadol after more than 60 minutes (n=6, 30.0%) than the MG (n=3, 15.0%) and CG (n=0, 0.0%) (p=0.044) (Table 3).

Table 1. Demographic characteristics of patients

Variables	Control	Magnesium + Placebo	Pregabalin + Magnesium	Pregabalin + Placebo	p-value*
Age (years)	55.50±11.61	55.20±14.30	58.40±11.23	56.90±12.67	0.843
Weight (kg)	66.20±10.73	62.80±8.42	60.75±9.68	61.05±8.18	0.236
High (cm)	153.40±7.35	151.90±5.08	150.30±5.48	152.55±6.34	0.437
BMI (kg/m^2)	28.06±3.71	27.19±3.11	26.81±3.50	26.30±3.67	0.444

BMI = body mass index; *ANOVA/Bonferroni test (mean±SD).

Table 2. Characteristic of the anesthesia applied in the groups

Characteristics of anesthesia	Control	Magnesium + Placebo	Pregabalin + Magnesium	Pregabalin + Placebo	p-value
Sulfate (mg)	0.00±0.00	4393.55±726.52	4223.60±815.32	0.00±0.00	<0.001
Fentanyl (µg)	206.25±53.73	222.50±34.32	222.50±49.93	215.00±32.85	0.600
Sevoflurane (mL)	30.75±8.32	31.25±8.72	28.25±8.63	33.50±7.80	0.273
Anesthesia time (min)	124.50±26.70	117.75±24.95	115.50±28.42	114.00±26.39	0.613

*ANOVA/Bonferroni test (mean±SD).

Table 3. Time to first request for analgesic

		Groups				
First analgesic (tramadol)	Total	Control	Magnesium + Placebo	Pregabalin + Magnesium	Pregabalin + Placebo	p-value
Up to 60 minutes	65* (81.3%)	20* (100%)	17* (85%)	14 (70%)	14 (70%)	0.044
More than 60 minutes	15 (18.8%)	0 (0%)	3 (15%)	6* (30%)	6* (30%)	

*Chi-square test (absolute and percentage frequency).

The number of patients presenting mild pain, that is, pain intensity from zero to three, in the P+MG was significantly higher than in the other groups after 1 h. After 12 h, the groups P+MG and PG showed more patients with absent/mild pain than the CG and MG groups. At 24 h postoperatively, all patients in all evaluated groups had no moderate/severe pain (Table 4).

There was no difference in the frequency of patients experiencing nausea or vomiting after 1, 12, or 24 h between the groups. There was also no difference in sleep scores between the four groups at 1, 12, and 24 h (Tables 5 and 6).

Taking into account that patients who scored above 7 in the SRQ-20 questionnaire were suspected of having a psycho-emo-

Table 4. Frequency of pain in the groups according to intensity classification

Pain intensity	Control	Magnesium + Placebo	Pregabalin + Magnesium	Pregabalin + Placebo	p-value
1 hour					
Mild	0 (0%)	2 (10%)	11* (55%)	4 (20%)	<0.001
Moderate/severe	20* (100%)	18* (90%)	9 (45%)	16* (80%)	
12 hours					
Mild	11 (55%)	10 (50%)	19* (95%)	19* (95%)	<0.001
Moderate/severe	9* (45%)	10* (50%)	1 (5%)	1 (5%)	
24 hours					
Mild	20 (100%)	20 (100%)	20 (100%)	20 (100%)	1.000
Moderate/severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

*Chi-square test (absolute and percentage frequency).

Table 5. Frequency of nausea/vomiting in the groups studied

	Groups				
	Control	Magnesium + Placebo	Pregabalin + Magnesium	Pregabalin + Placebo	p-value
1 hour					
0 (none)	8 (40%)	13 (65%)	17 (85%)	14 (70%)	0.061
1 (nausea)	6 (30%)	5 (25%)	2 (10%)	5 (25%)	
2 (vomiting)	6 (30%)	2 (10%)	1 (5%)	1 (5%)	
12 hours					
0 (none)	20 (100%)	18 (90%)	20 (100%)	19 (95%)	0.283
1 (nausea)	0 (0%)	2 (10%)	0 (0%)	1 (5%)	
2 (vomiting)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
24 hours					
0 (none)	20 (100%)	20 (100%)	18 (90%)	20 (100%)	0.104
1 (nausea)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
2 (vomiting)	0 (0%)	0 (0%)	2 (10%)	0 (0%)	

Chi-square test (absolute and percentage frequency).

Table 6. Frequency of sleepiness in the groups studied

	Groups				
Ramsay	Control	Magnesium + Placebo	Pregabalin + Magnesium	Pregabalin + Placebo	p-value
1 hour					
1	1 (5%)	0 (0%)	1 (5%)	0 (0%)	0.251
2	17 (85%)	17 (85%)	19 (95%)	20 (100%)	
3	1 (5%)	3 (15%)	0 (0%)	0 (0%)	
4	1 (5%)	0 (0%)	0 (0%)	0 (0%)	
5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
12 hours					
1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1.000
2	20 (100%)	20 (100%)	20 (100%)	20 (100%)	
3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
4	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
24 hours					
1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1.000
2	20 (100%)	20 (100%)	20 (100%)	20 (100%)	
3	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
4	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
5	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	

Chi-square test (absolute and percentage frequency).

tional disorder and could have higher pain intensity assessed by the Visual Analog Scale, a comparison was made between these suspected and unsuspected patients and the level of pain reported at each moment assessed.

The presence or absence of suspicion of psycho-emotional disorder did not interfere in the frequency and level of POP in the four experimental groups at any of the moments assessed (Table 7).

DISCUSSION

The association of magnesium sulfate and pregabalin promoted more effective analgesia in the first hour and up to 12 hours after mastectomy surgery with axillary lymphadenectomy. However, the isolated use of pregabalin or magnesium sulfate did not improve the analgesia of these patients in the first postoperative

Table 7. Suspicion of psycho-emotional disorder in the different groups according to pain intensity

	SRQ-20 1 h			SRQ-20 12 h			SRQ-20 24 h		
Visual analog scale	Unsuspected	Suspected	p- value	Unsuspected	Suspected	p- value	Unsuspected	Suspected	p-value
Control									
Mild	0 (0%)	5 (100%)	1.000	8 (53.3%)	3 (60%)	0.604	20 (100%)	3 (60%)	1.000
Moderate/severe	15 (100%)	5 (100%)		7 (46.7%)	2 (40%)		7 (46.7%)	2 (40%)	
Magnesium + Placebo									
Mild	2 (11.1%)	0 (0%)	0.805	15 (100%)	5 (100%)	0.237	15 (100%)	5 (100%)	0.474
Moderate/severe	16 (88.9%)	2 (100%)		8 (44.4%)	2 (100%)		8 (44.4%)	2 (100%)	
Pregabalin + Magnesium									
Mild	11 (61.1%)	0 (0%)	0.189	18 (100%)	2 (100%)	0.900	18 (100%)	2 (100%)	1.000
Moderate/severe	7 (38.9%)	2 (100%)		17 (94.4%)	2 (100%)		17 (94.4)	2 (100%)	
Pregabalin + Placebo									
Mild	18 (100%)	2 (100%)	1.000	18 (100%)	2 (100%)	1.000	18 (100%)	2 (100%)	1.000
Moderate/severe	0 (0%)	0 (0%)		0 (0%)	0 (0%)		0 (0%)	0 (0%)	

*p<0.05, Fisher's Exact test or Pearson's Chi-square test.

hour. At 12 h into the postoperatory, pregabalin isolated provided satisfactory analgesia, but magnesium sulfate isolated did not provide adequate analgesia. At 24 h into the postoperative, the isolated use of pregabalin and magnesium sulfate was similarly effective for analgesia. No increased frequency of nausea, vomiting, or drowsiness was observed with the use of this association. The suspicion of psycho-emotional disorder also showed no interference with pain intensity.

A number of studies indicate that mastectomy POP is moderate or severe, and various forms of analgesia have been used. A 2013 cohort study analyzing the POP intensity of various surgeries found that mastectomy with or without axillary lymphadenectomy causes moderate intensity pain on the first day after surgery[13,14].

In this trial, the CG, which did not receive pregabalin or magnesium sulfate, had moderate to severe pain in the first hour after mastectomy with lymphadenectomy, becoming mild after 24h, despite the use of dipyrone, ketoprofen and tramadol when requested.

In the present study, the evaluation of analgesia was done considering the Numerical Rating Scale and the time when the first dose of analgesic was requested. An adequate analgesia promoted by pregabalin with pain intensity below 4 was observed only at the 12 h postoperative assessment, because in the first hour of assessment only 4 patients reached scores below 4 on the Numerical Rating Scale. However, when pregabalin was associated with magnesium sulfate, analgesia in the first hour was adequate, not reaching scores above 3 on the pain scale.

The postoperative opioid consumption was similar between the groups, as most patients requested tramadol within 1 h after surgery. Only one patient from the CG requested this drug only once in the late postoperative period before 24 h. It should be considered that comparing postoperative opioid consumption between groups is of great value to studies, but patient-controlled analgesia (PCA) would be required, however, the material used for this purpose is not always available in all hospitals.

A meta-analysis[15] concluded that magnesium sulfate analgesia occurs after orthopedic, cardiovascular, and urogenital surgeries, decreasing pain, especially at 6 h after the end of surgery. The anatomical area of surgery in the present study, the breast, is different from the surgical site evaluated, and this factor may be a reason why the same result of the meta-analysis was not found.

Adverse effects, such as nausea and vomiting and drowsiness, did not differ between groups at any time during the evaluation, unlike what was found in the meta-analysis, in which pregabalin decreases the incidence of nausea and vomiting and in single or multiple doses of 300 mg can cause sedation[16]. This fact may be related to the dosage used in the present study.

CONCLUSION

This trial showed efficacy of the multimodal therapy based on the association of magnesium sulfate and pregabalin for POP control in mastectomy with lymphadenectomy.

AUTHORS' CONTRIBUTIONS

José Nilson Fortaleza de Araújo
Funding Acquisition, Data Collection, Resource Management, Methodology, Writing - Preparation of the original, Writing - Review and Editing
Marcos Venicio Alves Lima
Writing - Review and Editing, Supervision, Visualization
Giane Nakamura
Project Management, Writing - Review and Editing, Supervision

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