

Preoperative use of gabapentin for pain reduction in open surgeries under local anesthesia for idiopathic bilateral carpal tunnel syndrome

Uso pré-operatório de gabapentina na redução da dor em cirurgias abertas com anestesia local para síndrome do túnel do carpo bilateral idiopática

Uso preoperatorio de gabapentina en la reducción del dolor en cirugías abiertas con anestesia local para el síndrome del túnel carpiano bilateral idiopático

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Abstract

This article aims to evaluate the preoperative use of gabapentin in the control of intra- and postoperative pain in patients with idiopathic bilateral carpal tunnel syndrome (CTS). A prospective, randomised, double-blind study involving 45 subjects with severe CTS, 23 receiving treatment (gabapentin 600 mg) and 22 receiving placebo (control), who underwent an open surgical approach in one hand under local anaesthesia. Information related to the patients' profile, safety of the surgical procedure, history of pain, adverse effects, numbness, and medications used were collected during the 14 days of the procedure and evaluated by Generalised Estimated Equations and Generalised Linear Mixed Models. The treatment and control groups were homogeneous regarding the patients' profile and surgical procedure data. The patients who used gabapentin 600 mg had a better evaluation during surgery ($d = 0.655$), anaesthesia ($d = 0.854$), and on the first night of sleep ($d = 1.323$), and they reported a higher degree of satisfaction with the surgery after 14 days ($d = 1.091$). The treatment group reported decreased pain in the operated hand in a 24-hour period ($r = 0.34$, 95% CI: 0.223–0.457) and in the 14-day follow-up period ($r = 0.412$, 95% CI: 0.217–0.608). These results were not impacted by the medications used and remained consistent over time. The use of a single dose of gabapentin 600 mg in the preoperative period proved to be safe and effective in reducing postoperative pain, and the improvement was noticed by the patient.

Keywords: Carpal Tunnel Syndrome; Preoperative period; Adjuvants, Anesthesia; Gabapentin.

Resumo

Esse artigo tem por objetivo avaliar o uso pré-operatório da gabapentina no controle da dor intra e pós-operatória em indivíduos com síndrome do túnel do carpo (STC) bilateral idiopática. Foi realizado um estudo prospectivo, randomizado e duplo cego com 45 indivíduos, 23 que receberam tratamento (gabapentina 600 mg) e 22 que receberam placebo (controle), os quais se submeteram a uma abordagem cirúrgica aberta em uma das mãos, sob anestesia local, com grau severo de STC. Informações relacionadas ao perfil dos indivíduos, segurança do procedimento cirúrgico, histórico de dor, efeitos adversos, dormência e medicamentos utilizados foram coletadas ao longo do procedimento, durante 14 dias, para serem avaliadas por modelos Generalized Estimated Equations (GEE) e Generalized Linear Mixed Models (GLMM). Os grupos de tratamento e de controle mostraram-se homogêneos em termos de perfil e no que concerne aos dados do procedimento cirúrgico. Os pacientes que utilizaram gabapentina 600

mg atribuíram uma melhor avaliação intraoperatória ($d = 0,655$) durante a anestesia ($d = 0,854$) e na primeira noite de sono ($d = 1,323$) e maior grau de satisfação com a cirurgia após 14 dias ($d = 1,091$). O grupo de tratamento percebeu uma melhora na dor da mão operada no período de 24 horas ($r = 0,34$; IC95%: 0,223-0,457) e no período do seguimento de 14 dias ($r = 0,412$; IC95%: 0,217-0,608). Esses resultados não foram impactados pelos medicamentos utilizados e se mantiveram consistentes ao longo do tempo. O uso de gabapentina 600 mg em dose única no pré-operatório mostrou-se seguro e eficaz na redução da dor no pós-operatório, com melhora percebida pelo paciente.

Palavras-chave: Síndrome do Túnel do Carpo; Período pré-operatório; Adjuvantes anestésicos; Gabapentina.

Resumen

Este artículo tiene como objetivo evaluar el uso preoperatorio de gabapentina para controlar el dolor intra y postoperatorio en individuos con síndrome de túnel carpiano (STC) bilateral idiopático. Se llevó a cabo un estudio prospectivo, aleatorizado y doble ciego con 45 individuos, 23 que recibieron tratamiento (gabapentina 600 mg) y 22 que recibieron placebo (control), que se sometieron a un abordaje quirúrgico en una mano, con anestesia local, con grado grave de STC. A lo largo del procedimiento se recopiló información relacionada con el perfil de las personas, la seguridad del procedimiento quirúrgico, la historia del dolor, los efectos adversos, el entumecimiento y los medicamentos utilizados durante todo el procedimiento, durante 14 días, para ser evaluados mediante modelos Generalized Estimated Equations (GEE) y Generalized Linear Mixed Models (GLMM). Los grupos de tratamiento y control eran homogéneos en términos de perfil y en términos de datos de procedimientos quirúrgicos. Los pacientes que utilizaron gabapentina 600 mg atribuyeron una mejor evaluación intraoperatoria ($d = 0,655$) durante la anestesia ($d = 0,854$) y en la primera noche de sueño ($d = 1,323$) y mayor grado de satisfacción con la cirugía después de 14 días ($d = 1,091$). El grupo de tratamiento notó una mejora en el dolor de la mano operada en 24 horas ($r = 0,34$; CI95%: 0,223-0,457) y en el período de seguimiento de 14 días ($r = 0,412$; IC95%: 0,217-0,608). Estos resultados no se vieron afectados por los medicamentos utilizados y se mantuvieron consistentes con el tiempo. El uso de gabapentina 600 mg en dosis única en el período preoperatorio demostró ser seguro y eficaz en la reducción del dolor postoperatorio, con una mejoría percibida por el paciente.

Palabras clave: Síndrome del Túnel Carpiano; Período preoperatorio; Adjuvantes anestésicos; Gabapentina.

1. Introduction

Carpal tunnel syndrome (CTS) is the most common compressive neuropathy of the upper limbs. It has a higher incidence in women aged 45-65 years, tending to be bilateral in 65% of cases (Dec & Zyluk, 2018). In the USA, due to its high prevalence, the surgical treatment of CTS has an annual cost of more than USD 2 billion (Milone et al., 2019). Brazil spent approximately BRL 30 million between 2008 and 2016 on CTS surgeries under the Unified Health System (Sistema Único de Saúde - SUS) (Magalhães et al., 2017).

The surgical treatment of this neuropathy is indicated when severe involvement of the median nerve is observed during clinical evaluation or electroneuromyography (ENMG) (Cha et al., 2016). Open surgery (OS) or endoscopic surgery (ES) can be used (Atroshi et al., 2009); several studies have indicated no statistical difference between the outcomes of OS and ES (Larsen et al., 2013; Vasiliadis et al., 2014).

OS with the palmar approach was idealised by Tubina (1990) and introduced in Brazil by Galbiatti et al. (1991) (Galbiatti et al., 1991; Tubiana, 1990). It can be performed using several anesthetic techniques, but local anesthesia with lidocaine allows the patient to keep fully awake during the procedure, which is known as WALANT (Wide Awake Local Anesthesia No Tourniquet) (Lalonde, 2019).

The combination of lidocaine and epinephrine is aimed at decreasing intraoperative bleeding and avoiding the use of a tourniquet. Sodium bicarbonate 8% can be added to decrease discomfort resulting from the anaesthetic injection (Farhangkhoei et al., 2012), and an anesthetic block can be performed through a single orifice, a technique called hole-in-one (Lalonde, 2010).

As local anaesthesia cannot maintain postoperative analgesia, postoperative surgical pain management becomes an important (Bot et al., 2014). Pain intensity can be measured subjectively using the visual analogue scale (VAS), a numerical scale from zero to ten where zero represents the absence of pain and ten represents the worst pain estimated by the patient (Delgado et al., 2018). Opioids are mainly chosen as the option to control postoperative pain. However, their excessive use has

a negative potential for patients and the community, as they can cause addiction and other side-effects (Adams et al., 2006).

In this sense, acute postoperative pain prevention can be optimised with the use of preventive analgesia, which attenuates the process by blocking pain stimulus before tissue manipulation (Katz et al., 2011). Gabapentin is promising for this purpose, as it has a multimodal effect and acts on both central and peripheral nervous systems. It can be administered for up to twenty-four hours before surgery (Crisologo et al., 2018).

A systematic review with meta-analysis showed that the preoperative use of gabapentin was effective in reducing opioid use after abdominal, spinal, and thyroid surgeries (Arumugam et al., 2016). However, there are no reports in the literature on the use of gabapentin as a preoperative analgesic strategy for OS under local anesthesia for CTS (Phillips et al., 2016).

Therefore, the aim of this study was to evaluate the effectiveness and safety of preventive gabapentin for controlling the intra- and postoperative pain in patients with idiopathic bilateral CTS.

2. Methodology

The study was approved by the ethics committee of the Irmandade da Santa Casa de Londrina (# 3,276,439). It was registered at ClinicalTrials.gov (NCT04347746), and all participants signed an Informed Consent Form (ICF). It is a study of the type prospective, randomized, and double-blind.

All participants were treated by the neurosurgery team of the Irmandade da Santa Casa de Londrina at the carpal tunnel outpatient clinic from 2018 to 2019. The inclusion criteria were an age of 18 or more years, idiopathic bilateral CTS, American Society of Anesthesiology (ASA) physical status I or II (Doyle & Garmon, 2019), and severe impairment in at least one hand using the ENMG criteria according to Stevens (1997).

All ENMG tests were performed in the same laboratory with the same machine (Dantec Ketpoint, Natus®, Pleasanton, USA) by the same specialist electrophysiologist, following the relevant reference values and the technical standards recommended by the American Association of Electrodiagnostic Medicine (Jablecki, 2002).

The exclusion criteria were history of allergy to the drugs used in this study, drug usage, psychiatric disorders or mental retardation, pregnancy, CTS treatment within the previous three months, or duration of symptoms of less than six months.

The sample size was calculated according to the recommendations of Hjerstad et al. (2011), who determined that a 30% reduction in the initial VAS score was clinically relevant (Hjerstad et al., 2011). Considering the expected effect size, a beta of > 95%, an alpha level of 5%, and an estimated standard deviation in the population of 2.44 (Harden et al., 2010), the calculated sample size was 18 patients per group.

The participants were randomized into two groups using the random function of the Excel® software. The first participant used gabapentin 600 mg, and the second (control) received a placebo. Subsequently, opaque envelopes, described as “control” or “use of gabapentin” according to the random sequence, were numbered and sealed. All the participants involved in the research were blinded to the randomization, as well as the recruitment, hospital care, outpatient follow-up, and data collection and analysis.

The participants chose an envelope on admission and, depending on the result, received either a 600 mg gabapentin tablet or a placebo tablet similar to the drug used. The patients' vital signs were assessed. The level of pain was also assessed in both hands using VAS during the preoperative period, the surgical procedure, and within the subsequent 24 hours.

The hand with severe involvement on ENMG, according to the criteria by Stevens (1997), was operated on. However, when the patient presented bilateral severe involvement, the most symptomatic hand was selected for surgery.

OS with a palmar incision and local anesthesia with 1% lidocaine solution, adrenaline 1:100,000, and sodium

bicarbonate 8% at a 1:10 ratio was used, following the guidelines described in WALANT (Lalonde, 2019). The hole-in-one technique was used for anesthetic infiltration (Lalonde, 2010). All participants were operated on with the same technique by the same neurosurgeon.

At the end of the surgery, a simple dressing was made, and the patient was instructed to keep the operated hand elevated to avoid postoperative oedema. Prophylactic antibiotic therapy and wrist-hand splints were not used during the postoperative period.

Vital signs and VAS were reevaluated on admission and repeated six, 12, and 24 hours after surgery. Paracetamol 500 mg or codeine 30 mg were used for postoperative analgesia. Paracetamol was used if the VAS score for pain was 4-7, and it was readministered if necessary at doses of up to 4 grams/day. If the VAS score for pain was equal to or greater than eight, codeine was administered at doses of up to 120 mg/day.

On discharge, the participants were encouraged to use the operated hand, and the analgesics were prescribed to be used in case of pain, according to the criteria established on admission.

The patients were asked to complete a pain diary for fourteen days, noting the level of pain in each hand based on the VAS and, when necessary, the medication used and its quantity. On the fourteenth day, data on the pain diary, side effects of the medications used, the degree of satisfaction with the surgery, and reports of night numbness in the hands compared with the preoperative period were collected.

The profile of the sample was descriptively analysed using frequencies, means, and standard deviation with the Fisher's exact test (χ^2) and the t-test for potential differences between groups (control/used gabapentin).

The same tests were used to analyse the differences in the safety of the surgical procedure in the groups after the use of gabapentin. For the t-test, the normality and homogeneity of the data were evaluated before using the Shapiro Wilk (W) and Levene's (F) tests, respectively. In general, the lack of normality and homogeneity caused no major problems; however, as a precaution, the t-test was used with a bootstrap ($n = 1,000$), corrected, and accelerated for bias. Nonparametric tests (Mann-Whitney U) were used only for ordinal variables, such as Likert-type scales.

Regarding the clinical data, the mean arterial pressure, heart rate, and O₂ saturation were used to assess the safety of the surgical procedure. The VAS scores (main outcome) were collected more than once during hospitalization.

Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) was used for the statistical analysis.

The Generalized Estimating Equations (GEE) and the estimations of the Generalized Linear Mixed Models (GLMM) [Wald (χ^2)] used the patient as the subject and time as a repeated measure. These models were based on maximum likelihood with a robust covariance matrix. The advantages of these models, compared with classic repeated sample models such as ANOVA and MANOVA, are that the probability distribution of the outcome variable can be chosen, random effects can be included, and different patterns of correlations within subjects can be evaluated.

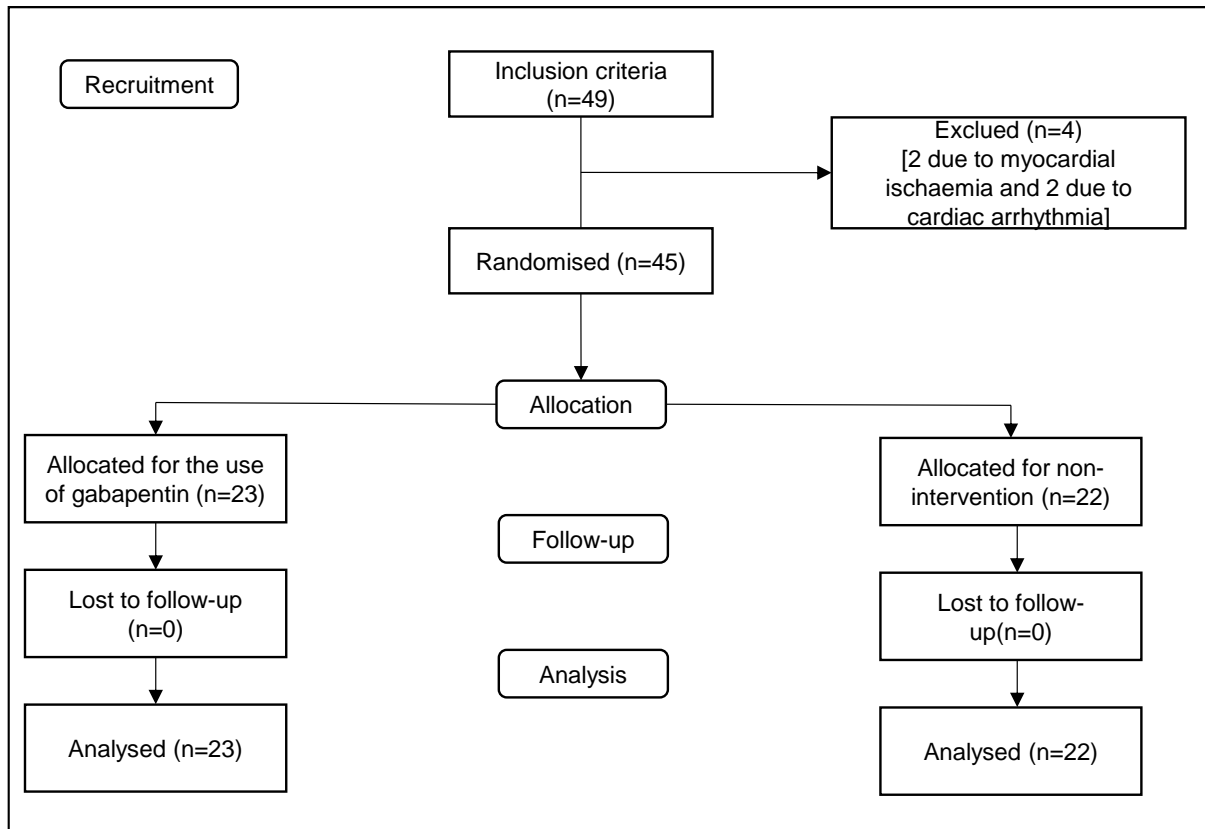
After assessing the statistical significance of the outcome variables, the size of the treatment effect was also calculated using Cohen's d statistics and odds ratios based on the post hoc procedure in the G*Power 3.1.9.7 software (Heinrich Heine, Universität Düsseldorf). Standardized coefficients were used for the parameters provided by the GEE/GLMM models. Effect size classifications were based on the recommendations of Cohen (2013) and Hattie (2012), and a p-value of < 0.05 was considered significant for all purposes (Cohen, 2013; Hattie, 2012).

3. Results and Discussion

3.1 Sample recruitment

The study followed the CONSORT recommendations. A total of 49 participants met the eligibility criteria, and four were excluded for various reasons. A total of 45 patients were randomised; 23 were included in the “gabapentin group” and 22 were included in the “control group”. There was no loss during the 14-day follow-up, as shown in Figure 1.

Figure 1. Recruitment and allocation flowchart.



Source: Authors.

3.2 Sample profile

In general, the sociodemographic and clinical profiles of the sample were homogeneous, as shown in Table 1. The operated hands of all the patients had severe CTS according to Steven’s classification. Statistically ($\chi^2 = 1.10$; $p = 0.38$), the hypothesis that the non-operated hands were different in the treatment group could not be rejected.

Table 1. Sample profile by treatment group.

Variable	Category	Use of gabapentin 600 mg						Test	
		No (n=22)		Yes (n=23)		Total (n=45)		χ^2 (t)	p
		n	%	n	%	n	%		
Sex	Female	20	90.9%	22	95.7%	42	93.3%	0.407*	0.608
Ethnicity	White	14	77.8%	14	73.7%	28	75.7%	0.084*	1.000
Marital status	Married	16	76.2%	16	72.7%	32	74.4%	0.068	1.000
Occupation	Housewife	7	33.3%	9	39.1%	16	36.4%	0.159	0.761
Education	High school	12	57.1%	12	57.1%	24	57.1%	0.000	1.000
Family income	Between BRL 1,000 and 3,000	12	60.0%	9	45.0%	21	52.5%	0.921	0.523
BMI Classification	Overweight/ Obesity	18	81.8%	20	87.0%	38	84.4%	0.226*	0.699
Dominant hand	Right	20	90.9%	21	91.3%	41	91.1%	0.002*	1.000
Operated hand	Right	13	59.1%	17	73.9%	30	66.7%	1.112	0.353
CTS Stevens classification (Non-operated hand)	Light	3	13.6%	6	26.1%	9	20.0%	1.097	0.376
	Moderate	10	45.5%	4	17.4%	14	31.1%		
	Severe	9	40.9%	13	56.5%	22	48.9%		
Age (years)	Mean (\pm SD)	52.41	(12.01)	51.09	(8.67)	51.73	(10.34)	0.425	0.673

χ^2 (t) = refers to the *Chi* Square or Fisher's exact test or the t- test in the case of age. The observations were reclassified between the most frequent (and adjacent) and less frequent (other) categories for the Fisher's exact test. The categories indicated in the table are the most frequent. For the CTS classification variable, the frequency of all categories is presented. * indicates that even with the reclassifications, an expected count of less than five was obtained in two cells. Therefore, the Fisher Exact Test was performed instead of *Chi* Square.

3.3 Safety of the surgical procedure

The mean duration of the surgical procedure was 54.33 minutes (\pm 10.58), and there was no difference between the groups ($t = -1.50$; $p = 0.15$). The same applied to the duration of anaesthesia and the amount of anaesthetic injected. The mean duration of anaesthesia was 5.53 hours (\pm 0.63), with no evidence of a difference between the groups ($t = -1.83$; $p = 0.09$). For the quantity of anaesthetic injected, there was also no difference between the groups ($t = 0.08$; $p = 0.94$), and the general mean was 18.69 ml (\pm 3.10).

Figures 2 to 4 show the mean arterial pressure, heart rate, O₂ saturation, and adverse reactions after the use of 5% lidocaine throughout the preoperative period to up to 24 hours after surgery. The illustrations show similar patterns of the groups.

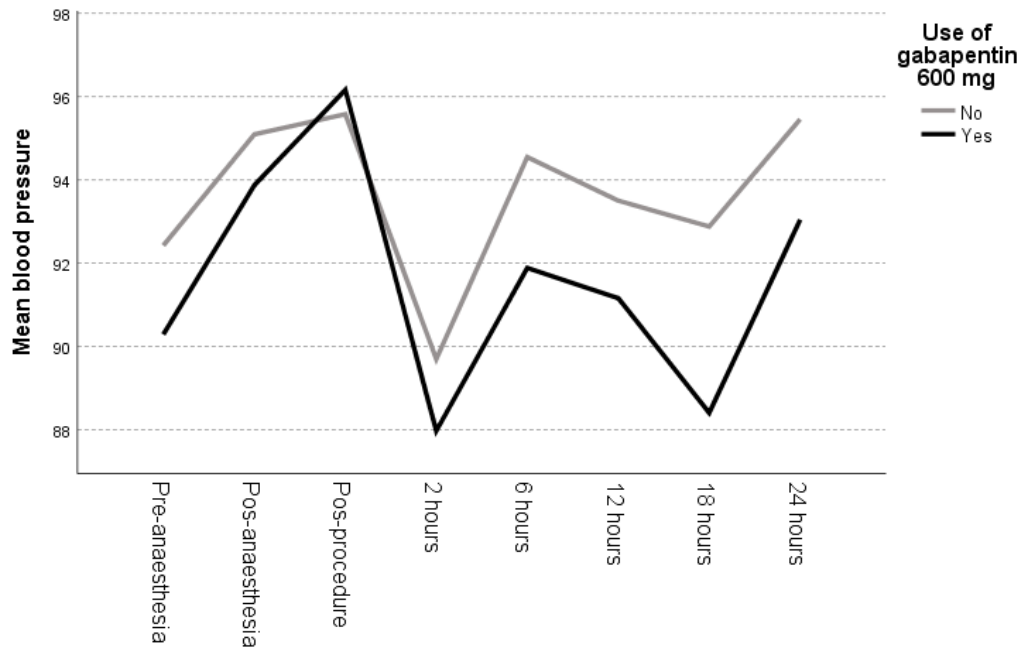
The mean arterial pressure was higher after two hours (Figure 2) in the control group; this can be attributed to the relatively higher number of hypertensive patients [$n = 14$ (63.60%)] than patients who used gabapentin [$n = 7$ (30.40%)] ($\chi^2 = 4.98$; $p = 0.03$). The GEE model of repeated measures for the mean arterial pressure, using the groups as a fixed effect, showed no evidence that the mean arterial pressure was different in the treatment group (Wald (χ^2) = 0.11; $p = 0.75$).

This result were the same if hypertensive patients were used as controls [Wald (χ^2) = 0.14; $p = 0.70$]. The gamma distribution, with a link log function and unstructured covariance matrix, was used to adjust these models, considering that the correlations showed no apparent pattern. These decisions were guided by the Quasi Information Criterion (QIC) and Quasi Information Criterion Corrected (QICC).

The similar patterns shown in Figures 3 and 4 for heart rate and O₂ saturation were confirmed by the estimated GEE model, with the use of gabapentin as a fixed effect and time as a repeated measure. For heart rate, the Wald Test (χ^2) result for

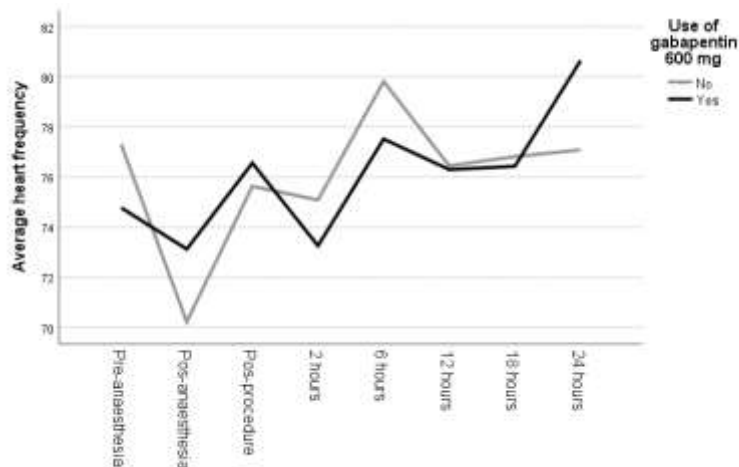
treatment effect was 0.65 ($p = 0.80$), and that of O₂ saturation was 0.05 ($p = 0.83$). The same GHG model used for the mean arterial pressure was used for heart rate and O₂ saturation (gamma distribution with link log function and unstructured covariance matrix).

Figure 2. Mean arterial pressure during the procedure and after up to 24 hours.



Source: Authors.

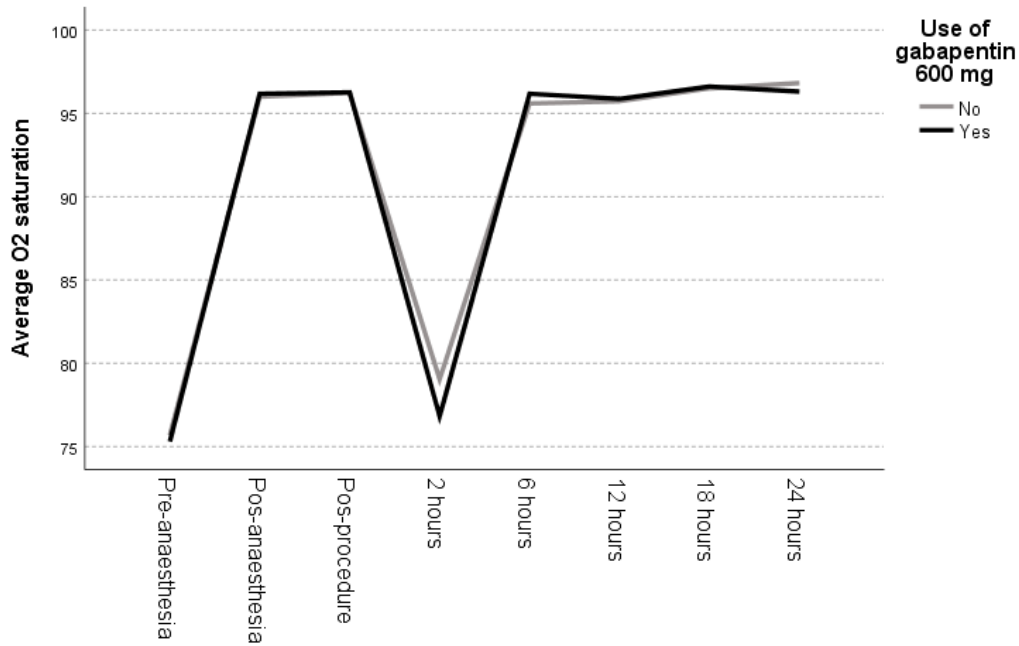
Figure 3. Mean heart rate during the procedure and after up to 24 hours.



Source: Authors.

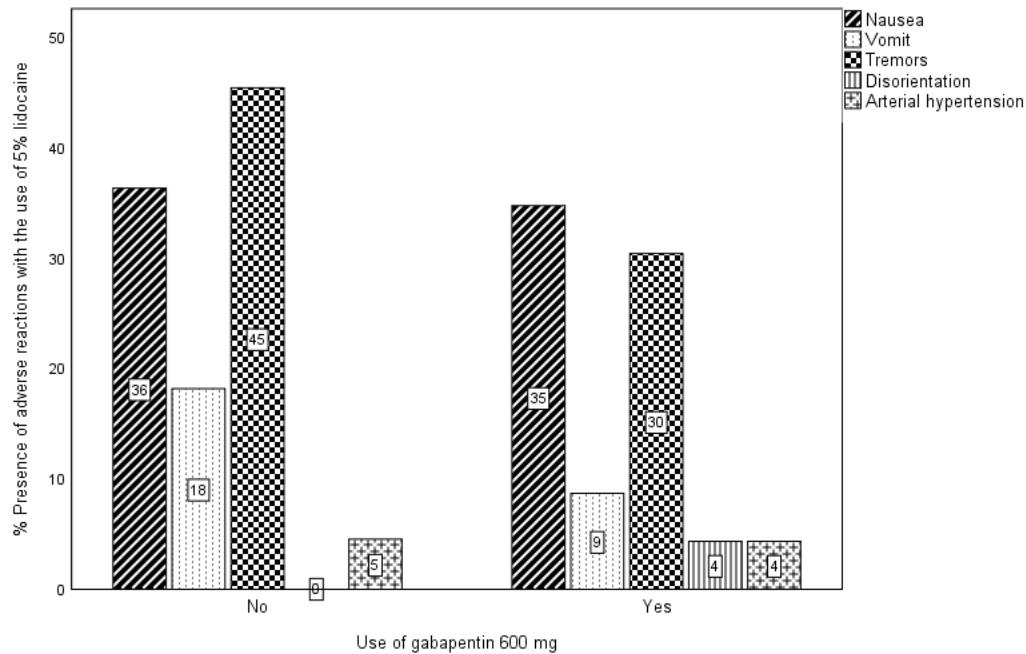
There were no cases of unconsciousness, seizure, or arrhythmia as adverse reactions from the use of 5% lidocaine in any of the groups. The adverse reactions with the use of 5% lidocaine (Figure 5) were statistically equal in the treatment groups. Fisher's exact test was performed for all confrontations, and it showed no differences in the presence/absence of adverse reactions between groups.

Figure 4. Mean O₂ saturation during the procedure and after up to 24 hours.



Source: Authors.

Figure 5. Adverse reactions with the use of 5% lidocaine.



Source: Authors.

3.4 Gabapentin effects

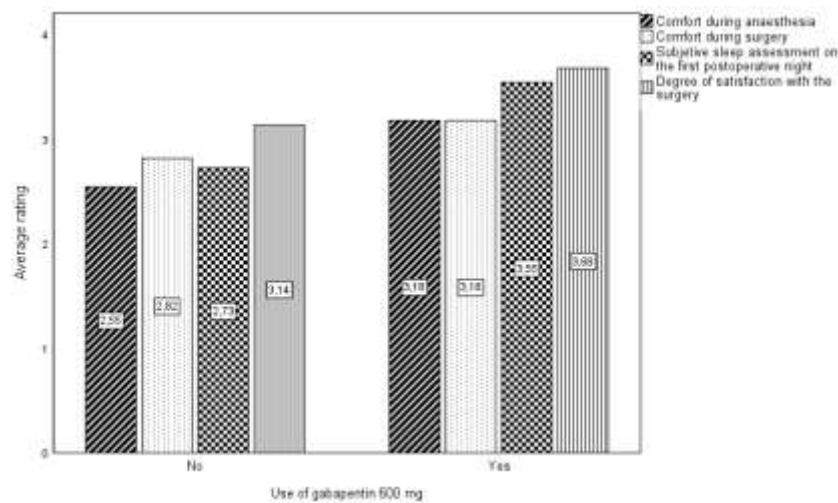
The adverse effects observed in the 23 participants using gabapentin were drowsiness and dizziness in four patients (17.39%), tinnitus in two patients (8.69%), and a metallic taste in one patient (4.34%). The Likert-type scale from 0 to 4 was

used at the end of the 24 hours in the gabapentin and control groups to evaluate comfort during anaesthesia and the surgical procedure, the first night of sleep, and the degree of satisfaction with the surgical procedure after 24 hours and 14 days (Figure 6).

The ratings by the patients in the gabapentin group were higher for all the evaluations than those of the control group. These results were statistically significant ($p < 0.05$), and the Mann-Whitney U test was used for the comparison. The smallest effect was observed for comfort during surgery ($d = 0.66$), even so, it can be considered an intermediate effect (Cohen, 2013). The other evaluations showed desired (Hattie, 2012) and large effects ($d > 0.80$) (Cohen, 2013) (Hattie, 2012).

The effects of the subjective evaluation of the first night of sleep and satisfaction with the surgery were significant ($d = 1.32$ and $d = 1.09$, respectively), respectively, and the effect of comfort during anaesthesia was also significant ($d = 0.85$).

Figure 6. Evaluation of anaesthesia, surgery, and the first night of sleep.



Source: Authors.

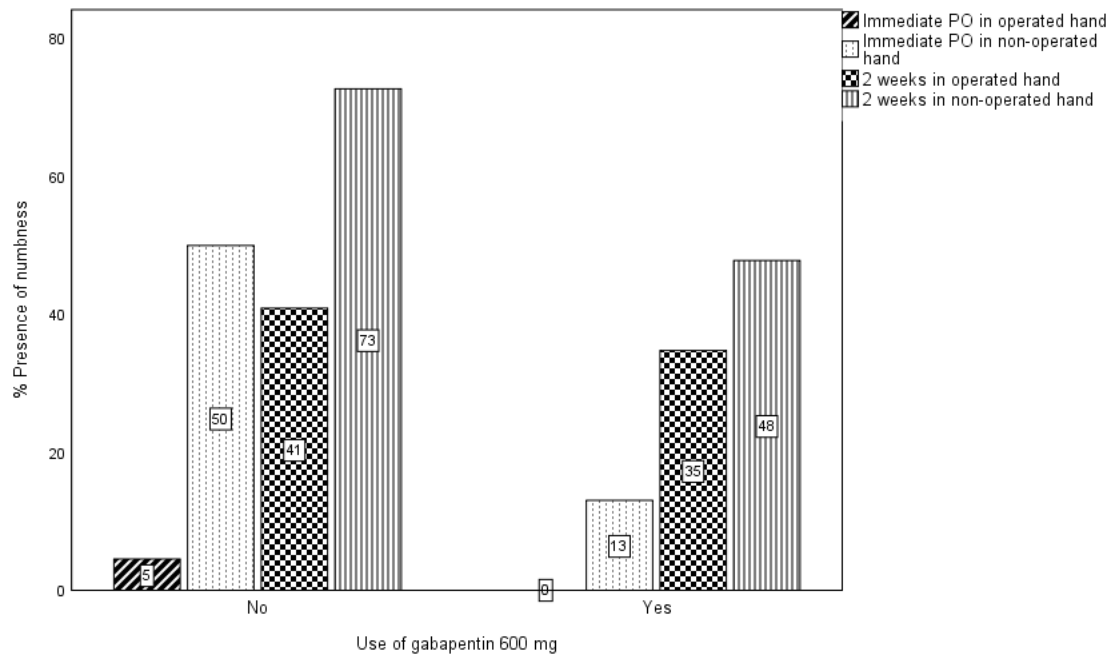
Regarding the hand numbness, the comparison of the gabapentin and control groups using the Fisher's exact test (χ^2) showed no statistically significant differences ($p > 0.05$, figure 7). However, a decreased sensation of numbness in the non-operated hand was observed immediately after the surgery ($\chi^2 = 7.17$; $p = 0.01$), confirmed by the relevant power (0.81) and odds ratio (6.69).

The pain assessment using the VAS was divided into two stages. The first stage included a comparison of the pre- and postoperative pain immediately after surgery and after six, 12, and 24 hours in both hands (Figure 8). The second stage included the analysis of pain during 14 days, using information from the pain diary (Figure 9). The participants were instructed to register their pain sensation for both hands to obtain results for the operated and non-operated hands.

During the first period, the mean VAS score for the non-operated hand was slightly lower in the gabapentin group than in the control group (Figure 8), but the estimated GEE model showed no statistically significant difference [Wald (χ^2) = 1.61; $p = 0.21$].

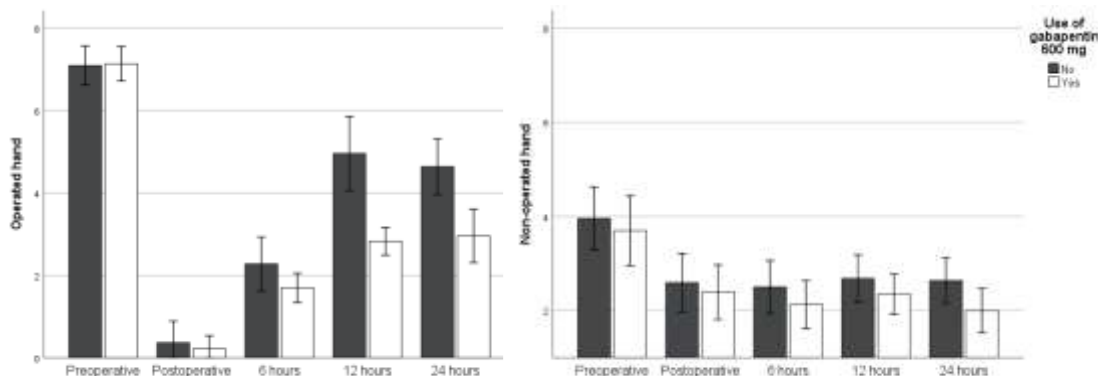
A normal function with an identity link was used to adjust the GEE model, using the follow-up/time (preoperative up to 24 hours of hospitalisation) as a repeated measure. The QIC and QICC indicated the normal function adjustment models and an AR-type covariance matrix as the most appropriate (1). The indication of a covariance matrix was expected due to the anticipated decrease in the VAS score over time, as shown in Figure 8.

Figure 7. Numbness in the operated and non-operated hands immediately and two weeks after the surgery.



Source: Authors.

Figure 8. VAS during the procedure and after up to 24 hours.



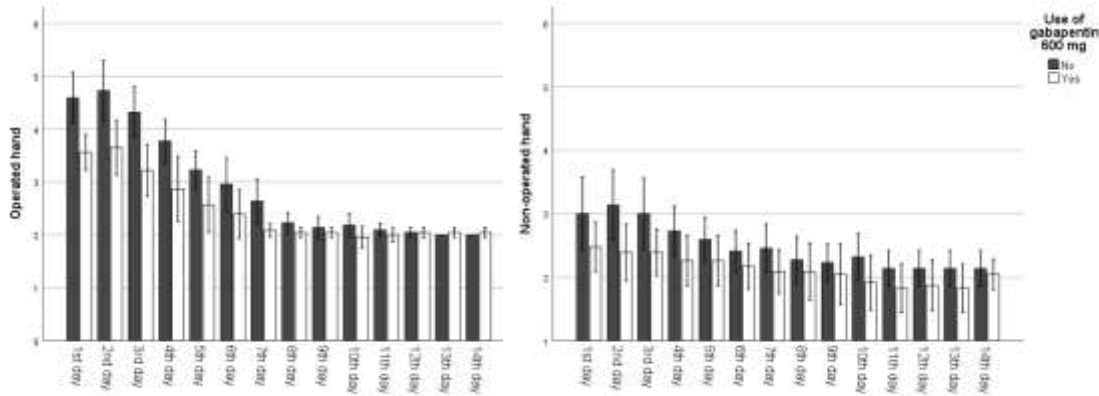
Source: Authors.

The GEE model structure estimated for the non-operated hand was also the most consistent for explaining the VAS score of the operated hand during the first stage (Figure 8). However, the operated hand showed statistically significant results [Wald (χ^2) = 32.54; $p < 0.001$]. The mean VAS score was approximately 0.91 lower (CI 95%: 0.59-1.22) in the gabapentin group than in the control group. This result was mainly influenced by the significantly decreased pain 12 and 24 hours after surgery, as shown in Figure 8.

The information criteria also showed the same structure as the normal GEE model, with the identity function and the AR covariance matrix (1) for the second stage; the 14-day follow-up period for the operated and non-operated hands. The information shown in Figure 9 was statistically proven in the operated hand, with a mean VAS score higher in the control group than in the gabapentin group [Wald (χ^2) = 17.08; $p < 0.00$]. The mean score in the gabapentin group was 0.45 lower (CI95%: 0.25-0.69) than that in the control group.

The results did not favour the hypothesis of different pain perceptions in the groups over the 14-day follow-up for the non-operated hand [Wald (χ^2) = 2.58; p = 0.11]. The results presented above for the operated and non-operated hands are similar, considering the entire VAS collection period: five collections during the first stage and 14 collections during the second stage, totalling 19 periods.

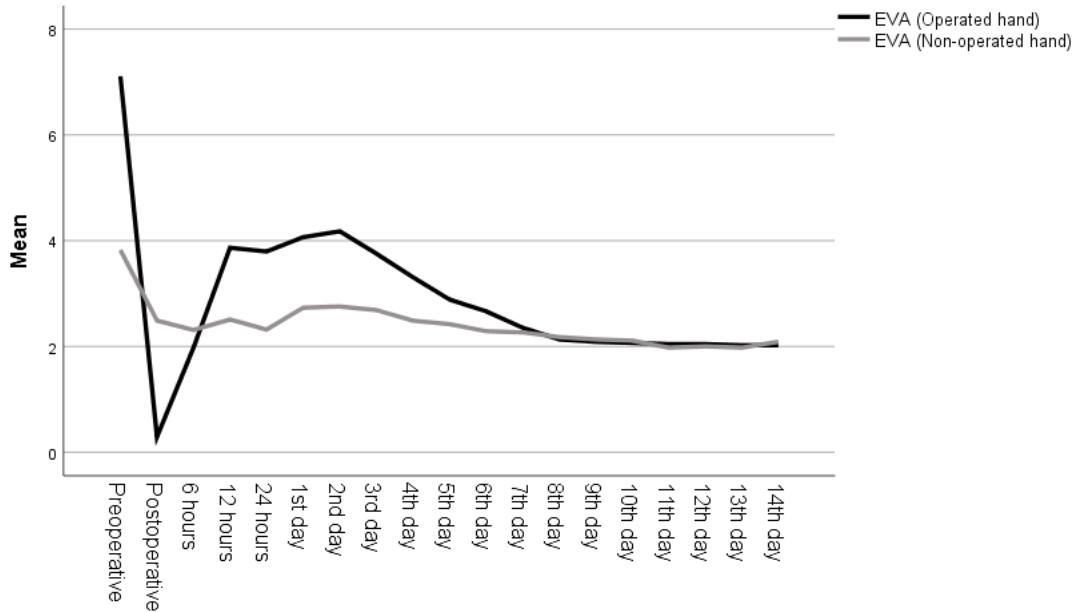
Figure 9. VAS over the 14-day follow-up period for the operated and non-operated hands in the treatment and control groups. There was no use of medication on day 14 by any of the groups.



Source: Authors.

Additionally, the GEE models for the operated hands were re-designed for stages 1 and 2, considering the VAS score. This showed the magnitude of the effect size, as the parameters of the estimated equation are the standardised coefficients. The size of the treatment effect for the operated hand model was 0.34 (CI 95%: 0.22-0.46) during the 24 hours and 0.41 (CI 95%: 0.22-0.61) during the 14-day follow-up. In both models, the effect sizes were within the desirable limits (Hattie, 2012), and they can be considered as intermediate and large, respectively, according to the criterion previously described (Cohen, 2013). Although there was no difference in the perceived pain in the non-operated hand in the groups, there was a decrease in perceived pain over the 14-day follow-up (Figure 10).

Figure 10. Effect of time on pain reduction in the operated and non-operated hands, regardless of gabapentin use.



Source: Authors.

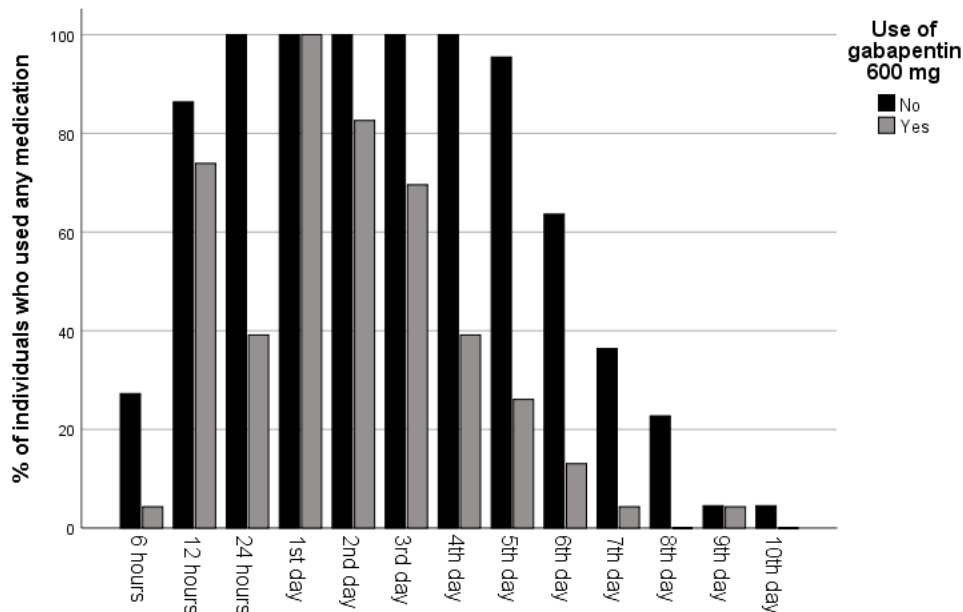
An estimated GLMM model, with treatment, time, and VAS of the operated hand as fixed effects, showed a significant F-value (39.72, $p < 0.001$) for the effect time taken to reduce pain in the non-operated hand. There was a mean reduction of 0.05 in the VAS score (CI 95%: 0.07-0.04) over the 14 days or a 1.6% reduction over the period (CI95%: 2.30% - 0.90%). This effect size is desirable (Hattie, 2012) and can be considered intermediate (Cohen, 2013); the effect size of the estimated time using the same model but standardised variables was -0.27 (CI95%: -0.35 - -0.18).

The gabapentin group presented decreased perceived pain, which was demonstrated by the lower use of medications (codeine 30 mg and paracetamol 500 mg) over the 14-day follow-up, especially during the first week (Figure 11). The patients who reported using the medication used only one pill.

The patients who used gabapentin reported a lower use of extra medication, mainly codeine 30 mg [Wald (χ^2) = 42.62; $p < 0.001$]. To assess this hypothesis, a GEE model was used for analysis; the use of medication (paracetamol, codeine, and not used) was the dependent variable and treatment was the fixed effect. A multinomial function with an accumulated logistic link and an AR-type covariance matrix was considered (1) to adjust the GEE model, using follow-up/time (six hours to 14 days) as a repeated measure.

Patients using gabapentin are approximately 249% more likely to avoid using any medication (OR = 3.49; CI95%: 2.38-5.08). This value is substantially higher when considering only 30 mg codeine; patients not using gabapentin were 430% more likely to use 30 mg codeine (OR = 5.29; CI95%: 3.50-8.00).

Figure 11. Patients who used at least one medication in the postoperative period and during ten days in the treatment and control groups.



Source: Authors.

3.5 Discussion

Gabapentin has been used at a dose of 600 mg as a pre-emptive medication for medium-sized surgery (Srivastava et al., 2010). However, the ideal dose for minor orthopaedic procedures is controversial, with indications ranging from 300 mg to 1,200 mg (Crisologo et al., 2018).

The preoperative gabapentin dose of 600 mg was effective in reducing pain in the first 24 hours in the operated hand with severe CTS. These findings could not be explained by the use of local anaesthesia, as demonstrated by Chapman et al. (2017), who assessed postoperative pain in CTS OS. The authors compared local anaesthesia using the WALANT technique *versus* intravenous sedation with midazolam, reporting no significant difference between the two groups (Chapman, 2017).

In the 14-day period, the operated hands in the gabapentin group maintained significant pain improvement compared to the control group, with a positive effect and an intermediate and significant magnitude according to the criteria by Page (2014) (Page, 2014). However, these findings differ from the study by Sadatsune et al. (2016), who compared the effect of preventive gabapentin at a dosage of 600 mg to control postoperative pain in CTS OS and found no significant difference in the two-week period compared with the placebo group (Sadatsune et al., 2016).

There are differences between this present study and the reports by Sadatsune et al. (2016), making it difficult to compare the results. Initially, the sample used in the present study was composed exclusively of bilateral idiopathic CTS, which is different from what was described by the other authors, who included patients with CTS secondary to diabetes mellitus in their evaluation and presented a different surgical result from that of idiopathic CTS (Bland, 2000).

Another difference between the studies was related to the operated hands. In the present study, all hands undergoing surgical treatment presented severe CTS, unlike the sample described by Sadatsune et al. (2016), in which the operated hands presented mild and moderate CTS. These comprised 40% of the patients who used gabapentin and 50% of the placebo group, according to the criteria to compare EMNG scales proposed by Sonoo et al. (2018) (Sonoo et al., 2018). In addition, surgical

results are different depending on the stage of this pathology (Bowman et al., 2018). Therefore, the results of this study and the ones presented by Sadatsune et al. (2016) should be carefully compared.

The non-operated hand showed decrease pain both in the first 24-hour period and in the 14-day follow-up, regardless of the use of gabapentin. Unno et al. (2015) described an improvement in the non-operated hand with bilateral CTS, both in the immediate postoperative period and maintained for six months after surgery. Therefore, the described findings may be due to surgical therapy (Padua et al., 2005).

Codeine consumption was significantly lower in the gabapentin group both in the first 24-hour period and in the 14-day follow-up. This decrease is a positive factor, as it avoids abusive prescription (Unno et al., 2015), reducing the possibility of triggering drug addiction (Miller et al., 2017). In addition, better postoperative pain control is associated with a decrease in the onset of chronic pain (Alam et al., 2012).

The use of preoperative gabapentin proved to be safe, presenting no significant side effects during the surgical procedure. The patients' assessment of the surgical treatment was better in the gabapentin group, presenting a large or intermediate effect size for all analysed items (Chapman, 2017). Therefore, the analysis of the results of a procedure should not only include the doctor's opinion but should also evaluate the procedure expectations from the patient's point of view (Chaparro et al., 2013).

The present study has limited applicability because it was conducted in a single medical centre, which restricts its external validity. However, the relevant findings in the group that used preoperative gabapentin, such as decreased post-surgical pain, decreased use of opioids, absence of significant side effects, and better assessment of the procedure by the patient, suggest that the use of pre-emptive analgesia with gabapentin is a strategy that can be recommended in daily practice.

4. Conclusion

The results showed that preemptive gabapentin has the advantage of significantly reducing opioid use in the postoperative period. The use of a single dose of 600 g of this drug in the preoperative period proved to be safe and effective in reducing postoperative pain, in addition to increasing the quality of the surgical procedure according to the participants' assessment.

CTS is the most common compressive neuropathy in the adult population, being in most cases bilateral. The use of local anesthesia for the surgical treatment of CTS is a frequent analgesic strategy. Despite the prevention of postoperative pain by optimizing analgesia with the use of gabapentin has not been demonstrated in the literature, further multicenter studies are necessary to consolidate these finding.

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