

Effect of a Single Preoperative Dose of Gabapentin on Postoperative and Chronic Pain after Breast Cancer Surgery: A Randomized Double-Blind Trial

Asma Korbi^{1*}, Mouna Gara², Ali Jlali², Arige Sellemi¹, Montacer Hafsi¹, Marwen ben Khelifa¹, Dorra Garrouch¹, Ataa Misbahi¹, Sana Bouakaz¹, Ichrak Belgaieb¹, Soukeina Ben Jaballah², Balsam Braiek¹, Ibtissem Korbi², Lotfi Grati¹

¹Department of Gynecology-Obstetrics, Centre of Maternity and Neonatology, Fattouma Bourguiba University Teaching Hospital, Monastir, Tunisia

²Department of Anaesthesia and Intensive Care 'B', Centre of Maternity and Neonatology, Fattouma Bourguiba University Teaching Hospital, Monastir, Tunisia

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*Corresponding author: Asma Korbi

Department of Gynecology-Obstetrics, Centre of Maternity and Neonatology, Fattouma Bourguiba University Teaching Hospital, Monastir, Tunisia

Abstract

Original Research Article

Postoperative pain after breast cancer surgery is common and can evolve into chronic pain. Gabapentin, an anticonvulsant with analgesic properties, could reduce these pains. Methods: Prospective, randomized, double-blind, single-center trial including 60 patients undergoing breast cancer surgery. Two groups: gabapentin 600 mg orally 2 hours before surgery (G) or placebo (P). Primary endpoint: VAS at rest and during coughing. Secondary endpoints: analgesic consumption, time to first request, adverse effects, chronic pain at 3 and 6 months. Results: Postoperative VAS scores did not differ significantly between G and P. Morphine use was lower in G (33.3% vs 56.7%, $p=0.069$) with a lower average dose (3.29 ± 1.7 mg vs 6.71 ± 3.73 mg, $p=0.144$). Chronic pain was significantly reduced at 3 months (20% vs 63.3%, $p=0.001$) and at 6 months (10% vs 43.3%, $p=0.004$) in G. Early nausea was more frequent in G at H1 ($p=0.015$). Conclusion: A single preoperative dose of gabapentin does not significantly improve acute pain but reduces the incidence of chronic pain after breast cancer surgery.

Keywords: Gabapentin, Breast surgery, Postoperative pain, Chronic pain, Randomized trial.

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INTRODUCTION

Breast cancer surgery is associated with postoperative pain that can become chronic, impacting quality of life. Multimodal analgesia is recommended but remains imperfect. Gabapentin, initially developed as an antiepileptic, has analgesic and anti-hyperalgesic properties. The objective of this study is to evaluate the effect of a single preoperative dose of gabapentin on acute pain and the prevention of chronic pain after breast cancer surgery.[1]

PATIENTS AND METHODS

Prospective, randomized, double-blind, single-center trial conducted at the Maternity and Neonatology Center of Monastir between January and December 2019. Included patients: 18-70 years old, ASA ≤ 3 , candidates for mastectomy or conservative surgery.

Randomization into two groups : gabapentin 600 mg (G) or placebo (P), 2 hours before surgery. Standardized anesthetic protocol. Primary endpoint : VAS at rest and during coughing over 24 postoperative hours. Secondary endpoints : time to first analgesic request, analgesic consumption, adverse effects, chronic pain at 3 and 6 months. Statistical analysis with $p \leq 0.05$ considered significant.

RESULTS

Sixty patients analyzed (30 per group). Initial characteristics were comparable. No significant difference in postoperative VAS scores between G and P. The time to first analgesic request was similar (8.02 ± 5 h vs 9.03 ± 4.45 h, $p=0.253$). Morphine use was lower in G (33.3% vs 56.7%, $p=0.069$), with a lower average dose (3.29 ± 1.7 mg vs 6.71 ± 3.73 mg, $p=0.144$). Early nausea at H1 was more frequent in G ($p=0.015$). Chronic

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pain was significantly reduced in G at 3 months (20% vs 63.3%, $p=0.001$) and at 6 months (10% vs 43.3%, $p=0.004$).

DISCUSSION

Following surgery performed as part of cancer treatment, patients may experience pain in the chest wall, armpit, or arm of moderate to severe intensity in 10 to 24% of operated women. While most of these pains resolve spontaneously, they can persist in some women, even long after breast surgery. This is known as post-mastectomy pain syndrome (PMPS)[1,2]. The severity of these chronic pains ranges from simple discomfort to much more debilitating suffering. PMPS can be extremely disabling for these patients who are already fighting breast cancer on a daily basis. Several studies have concluded on the effectiveness of gabapentinoids in the treatment of epilepsy[3,4], anxiety disorders, and neuropathic pain[5]. Their mechanism of action is not fully elucidated, but recent studies suggest that their primary target is the central component, particularly the first neuron-to-neuron synapse where the release of neurotransmitters by the central terminals of primary afferent fibers occurs, with calcium being the main effector of nociceptive message transmission[3]. This study demonstrated that pre-incision administration of 600 mg of gabapentin has no advantage over post-incision administration in terms of pain scores and fentanyl consumption in living donors undergoing nephrectomy. The efficacy and tolerability of pre- and postoperative gabapentin administration for controlling acute postoperative pain was evaluated in a meta-analysis [6] of 1151 patients in 16 randomized controlled trials, of which 614 received gabapentin. This review demonstrated the role of preoperative administration of gabapentin in a single dose, which reduced the time to first analgesia request by 7 minutes compared to the group receiving this molecule perioperatively in multiple doses; however, the result was reported in only four of the 16 controlled trials. In this study, the number of patients requiring morphine postoperatively was lower in the gabapentin group than in the placebo group (10 patients vs 17), and the dose was also lower in the gabapentin group with an average of 3.29 ± 1.7 mg versus 6.71 ± 3.73 mg for group P ($p=0.069$), showing morphine-sparing at low doses. These results align with a study by L. Djaziri *et al.* [7] for laparoscopic cholecystectomy, where postoperative morphine consumption in titration (in the PACU during the first postoperative hour) was significantly higher in the control group ($p < 0.0001$). In the same vein, a meta-analysis by Rachael *et al.* [8] found significantly lower opioid consumption for individuals receiving preoperative gabapentin (-14.7 mg of morphine in 24 h). Similarly, another meta-analysis published in 2017 [9] reported morphine consumption over 24 h in 51 trials involving 4193 patients; in cholecystectomy, one trial reported a 12.2 mg reduction in 24-hour morphine consumption for the gabapentin treatment group compared to controls; two hysterectomy trials showed a

1.6 mg reduction; and three orthopedic arthroplasty trials demonstrated a 4.0 mg reduction. Finally, one thoracic surgery trial reported a 6.7 mg reduction. Consistent with these results, a meta-analysis published in 2020 [10] found that the amount of opioids administered at 24 h was slightly lower with the use of gabapentinoids (25.3 mg vs 38.7 mg in the control group). With advances in breast cancer management, which prolong survival, there will be a need to control late postoperative complications, such as chronic pain and their severe impact on quality of life. The expectations of patients and prescribers are high, advocating for maximum pain relief. Our patients were recontacted at 3 and 6 months postoperatively to assess chronic postoperative pain, and it was found that at 3 months, 20% of patients receiving gabapentin complained of pain compared to 63.3% in the placebo group ($p=0.001$); at 6 months, 10% of patients who received gabapentin had pain compared to 43.3% in the placebo group ($p=0.004$). Husted *et al.* [11] documented that, among 163 women who underwent mastectomy with axillary node dissection, 45% reported scar pain (symptoms including pain, paresthesia, lymphedema, and impaired shoulder function), 45% reported pain in the ipsilateral arm, neck, or shoulder, and only 21% were asymptomatic 1 to 5 years after surgery. According to EE Morrison *et al.* [12] in 2017: Chronic pain affects one-third to one-half of the British population, motivating them to seek a better approach to combat this daily life handicap. However, they found no evidence suggesting that gabapentinoids reduce the risk of postoperative chronic pain. Similarly, in a medical review, Irwin and Kong [13] stated that: Chronic post-surgical pain (CPSP) is a bio-psycho-social complex with enormous impacts. It is defined as persistent pain that developed after a surgical procedure, lasting at least 2 months. CPSP is particularly common after amputation, inguinal hernia repair, breast surgery, and thoracotomy. In Canada, an estimated 72,000 new cases of CPSP occurred between 1999 and 2000. CPSP has inflammatory and neuropathic components, involving peripheral and central sensitization that occurs in response to tissue and nerve damage. Upregulation of the alpha-2 gamma subunit of voltage-gated calcium channels, which is a binding site for gabapentin, is involved in central sensitization induced by nerve injury. In conclusion, the administration of gabapentin at a dose of 600 mg in a single preoperative dose remains a subject of controversy. In 2018, according to the SFAR, the systematic use of gabapentinoids perioperatively is not recommended. However, in 2019, the European Society of Regional Anesthesia and Pain Therapy admitted that preoperative gabapentin is recommended (Grade A) for minor and major breast surgeries, as it has been shown to reduce postoperative pain scores and opioid consumption. However, it is recommended with caution because high doses could induce particularly concerning side effects in ambulatory patients.[10]

Study Limitations This study has several limitations beyond its single-center nature; the

calculation of intraoperative anesthetic drug sparing was not performed. Additionally, the time to first ambulation in both groups was not taken into account. Furthermore, other factors that may influence chronic postoperative pain after breast surgery, such as adjuvant radiotherapy and/or chemotherapy, were not considered. Nevertheless, gabapentin appears to be minimally effective in managing preoperative anxiety based solely on the APAIS score analysis. It would also be interesting to study its anxiolytic effect through a more in-depth analysis using other scores in future work.

CONCLUSION

Breast cancer surgery, whether radical or conservative, strongly alters body perception and requires comprehensive management including psychological preparation, pain management, anxiety, and postoperative side effects. Gabapentin, initially developed as an antiepileptic and then used against neuropathic pain, has generated growing interest for its multimodal effects in anesthesia. In this prospective, randomized, double-blind study conducted on 60 patients operated for breast cancer, the preoperative administration of a single 600 mg dose of gabapentin showed no significant benefit on postoperative pain assessed by VAS scores, nor on preoperative anxiolysis. However, a trend toward reduced postoperative morphine consumption was observed. Thus, gabapentin appears as an interesting molecule for multimodal rehabilitation after breast surgery, particularly due to its morphine-sparing effect. Nevertheless, its efficacy on anxiety remains limited, and additional studies are needed to clarify the dose-response relationship and the benefit of prolonged postoperative treatment.

REFERENCES

1. Becker C, Pham DNM, Assouad J, Badia A, Foucault C, Riquet M. Postmastectomy neuropathic pain: results of microsurgical lymph nodes transplantation. *Breast*. Oct 2008;17(5):472-6.
2. Balter RE, Cooper ZD, Haney M. Novel Pharmacologic Approaches to Treating Cannabis Use Disorder. *Curr Addict Rep*. 1 Jun 2014;1(2):137-43.
3. McLean MJ. Gabapentin in the Management of Convulsive Disorders. *Epilepsia*. Jun 1999;40(s6):s39-50.
4. Rosner H, Rubin L, Kestenbaum A. Gabapentin Adjunctive Therapy in Neuropathic Pain States: The Clinical Journal of Pain. Mar 1996;12(1):56-8.
5. Beydoun A, Uthman BM, Sackellares JC. Gabapentin: pharmacokinetics, efficacy, and safety. *Clin Neuropharmacol*. Dec 1995;18(6):469-81.
6. Goodwin SA. A review of preemptive analgesia. *J Perianesth Nurs*. Apr 1998;13(2):109-14.
7. Djaziri L, Bousselmi J, Jaoua H, Ben Fadhel K. Effet multimodal de la gabapentine au cours de la cholécystectomie laparoscopique : essai randomisé et contrôlé. *Annales Françaises d'Anesthésie et de Réanimation*. 1 Sep 2014;33:A147.
8. Fabritius ML, Geisler A, Petersen PL, Wetterslev J, Mathiesen O, Dahl JB. Gabapentin in procedure-specific postoperative pain management – preplanned subgroup analyses from a systematic review with meta-analyses and trial sequential analyses. *BMC Anesthesiol*. Dec 2017;17(1):85.
9. Zhai L, Song Z, Liu K. The Effect of Gabapentin on Acute Postoperative Pain in Patients Undergoing Total Knee Arthroplasty: A Meta-Analysis. *Medicine (Baltimore)*. May 2016;95(20):e3673.
10. Doha NM, Rady A, El Azab SR. Preoperative use of gabapentin decreases the anesthetic and analgesic requirements in patients undergoing radical mastectomy. *Egyptian Journal of Anaesthesia*. 1 Oct 2010;26(4):287-91.
11. Morrison EE, Sandilands EA, Webb DJ. Gabapentin and pregabalin: do the benefits outweigh the harms? *J R Coll Physicians Edinb*. Dec 2017;47(4):310-3.
12. Kong VKF, Irwin MG. Gabapentin: a multimodal perioperative drug? *British Journal of Anaesthesia*. Dec 2007;99(6):775-86.
13. Masson E. EM-Consulte. [cited 13 Aug 2025]. Preoperative administration of gabapentin and residual pain after thyroid surgery: a randomized double-blind placebo-controlled study. Available at: <https://www.em-consulte.com/article/920214/administration-preoperatoire-de-gabapentine-et-dou>