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The impact of intrathecal morphine blended with general anesthesia on postoperative pain in patients undergoing hysterectomy: Scoping Review of the literature

El impacto de la morfina intratecal combinada con la general anestesia sobre el dolor posoperatorio en pacientes sometidos histerectomía: revisión de la literatura

Guillermo Adolfo Madrid Díaz[1,*], Sergio Andrés Carretero Pardo[2], Julián Arturo Barrios Pinzón[1], Andrés F. Zuluaga Z.[1], Juan Fernando Parada Márquez[1]

[1] Department of Anesthesiology Hospital Fundación Santa Fe de Bogotá. Bogotá, Colombia.
[2] Faculty of Medicine, University of Los Andes. Bogotá, Colombia.

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ABSTRACT

Recent studies suggest chronic pain is a concern following hysterectomy. New techniques, like intrathecal morphine with general anesthesia, aim to improve pain control. This scoping review explored the impact of intrathecal morphine on post-surgical pain in hysterectomy patients. A literature search (Oct 2023-Dec 2023) identified 5 relevant studies from PubMed, Cochrane Library, and LILACS. These studies showed intrathecal morphine reduced pain scores for up to 72 hours after surgery, decreased opioid use, and improved patient satisfaction. These findings suggest this technique has benefits and warrant a review of current global recommendations for standard anesthetic care in hysterectomy surgery.

Keywords: Regional anesthesia, postoperative pain, hysterectomy, intrathecal morphine.

RESUMEN

Estudios recientes indican que el dolor crónico es una preocupación tras la histerectomía. Las técnicas nuevas, como la morfina intratecal con anestesia general, buscan mejorar el control del dolor. Esta revisión exploró el impacto de la morfina intratecal en el dolor posoperatorio en pacientes con histerectomía. Una búsqueda bibliográfica (octubre de 2023-diciembre de 2023) identificó 5 estudios relevantes en PubMed, Cochrane Library y LILACS. Estos estudios mostraron que la morfina intratecal redujo las puntuaciones de dolor hasta 72 h después de la cirugía, disminuyó el uso de opioides y mejoró la satisfacción del paciente. Estos hallazgos sugieren que esta técnica tiene beneficios y justifican una revisión de las recomendaciones globales actuales para la atención anestésica estándar en la cirugía de histerectomía.

Palabras clave: Anestesia regional, dolor posoperatorio, histerectomía, morfina intratecal.

Introduction

Hysterectomy is the second most common surgery among women of reproductive age[1], with an estimated rate of 350 procedures performed per 100,000 individuals annually[2]. Additionally, it is associated with a high morbidity and mortality burden owing to its inherently painful nature. Approximately 30% of patients undergoing hysterectomy experience severe postoperative pain, while 10% develop chronic pain within the first postoperative year[3].

Inadequately managed postoperative pain is linked to a higher risk of insomnia and depression, which impede proper

Guillermo Adolfo Madrid Díaz
investigacion.anestesia@fsfb.org.co
*ORCID: https://orcid.org/0000-0002-1956-8865
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recovery. Moreover, it increases opioid consumption and the risk of adverse events associated with its chronic use[4]. Furthermore, the physiological implications of pain, characterized by increased cortisol and catecholamine secretion coupled with heightened sympathetic responses, can trigger hypertensive crises and other perioperative complications[5].

Recommendations from the latest update of the Enhanced Recovery After Surgery (ERAS) guidelines for gynecological/oncological surgery in 2019 present the use of general anesthesia alongside intravenous multimodal analgesia as standard perioperative care. It has been reported that over half of the major gynecological surgeries are performed using this approach[6]. However, postoperative analgesia with this technique is inadequate. Recent studies indicate that up to 22% of patients undergoing hysterectomy continue to experience pelvic pain for up to one year after surgery[7]. Consequently, in response to this challenge, recent scientific evidence has highlighted intrathecal morphine (ITM) as a safe technique when used as an adjunct to general anesthesia, requiring a single injection and offering numerous benefits. These include reduced postoperative pain and opioid consumption, enhanced patient satisfaction with pain control, shorter hospital stays, and improved quality of recovery compared to general anesthesia with intravenous multimodal analgesia[8],[9],[10],[11],[12].

Despite the development of multiple regional anesthesia and analgesia techniques, there is a lack of consensus regarding their use in hysterectomies. The selection of strategies for effective postoperative pain control should be based on the patient's profile, surgical procedure, and available evidence, presenting a challenge for multidisciplinary collaboration[13]. This scoping review aimed to focus on the evidence concerning the use of intrathecal morphine as an adjunct to general anesthesia in hysterectomies, primarily analyzing its impact on postoperative pain.

Methods

Research Question: This scoping review aimed to explore the impact of intrathecal morphine as an adjunct to general anesthesia on postoperative pain in patients undergoing hysterectomy.

Search Strategy: This scoping review followed the PRISMA extended guidelines for Scoping Reviews and employed the SANRA scale for the quality assessment of narrative review articles. Three team members, one medical intern, and two anesthesiologists independently conducted literature searches between October 2023 and December 2023. The databases searched included PubMed, Cochrane Library, and Latin American and Caribbean Health Sciences Literature (LILACS). Search terms included: (intrathecal morphine, hysterectomy) and (morfina intratecal E hysterectomy). English terms were used for searches in PubMed and Cochrane, whereas Spanish terms were used for LILACS.

Inclusion and Exclusion Criteria: Primary studies from all geographical areas, written in English and Spanish, were included. In addition, articles were required to be published in peer-reviewed journals. Studies not written in English or Spanish, those conducted on procedures other than hysterectomy, and those involving intrathecal morphine + the use of spinal local anesthetic were excluded.

Data selection and charting process: Three researchers independently screened the most relevant articles. Initially, duplicates were removed from the search. Subsequently, a secondary analysis based on the inclusion and exclusion criteria led to exclusion of certain articles. Information regarding authors, year of publication, number of patients included, methodology, method of pain measurement, and key outcomes was collected and managed using Excel, as shown in Figure 1.

Results

The initial literature search by three researchers independently yielded a total of 31 articles. Following the analysis of duplicate articles and the application of inclusion and exclusion criteria, 5 relevant articles were obtained, as shown in Table 1, focusing on assessing the impact of intrathecal morphine in a blended technique with general anesthesia on postoperative pain in patients undergoing hysterectomy. The data were sourced globally, predominantly from studies conducted in Europe, most of which were published within the last two years.

How does the use of intrathecal morphine as an adjunct to general anesthesia impact postoperative pain?

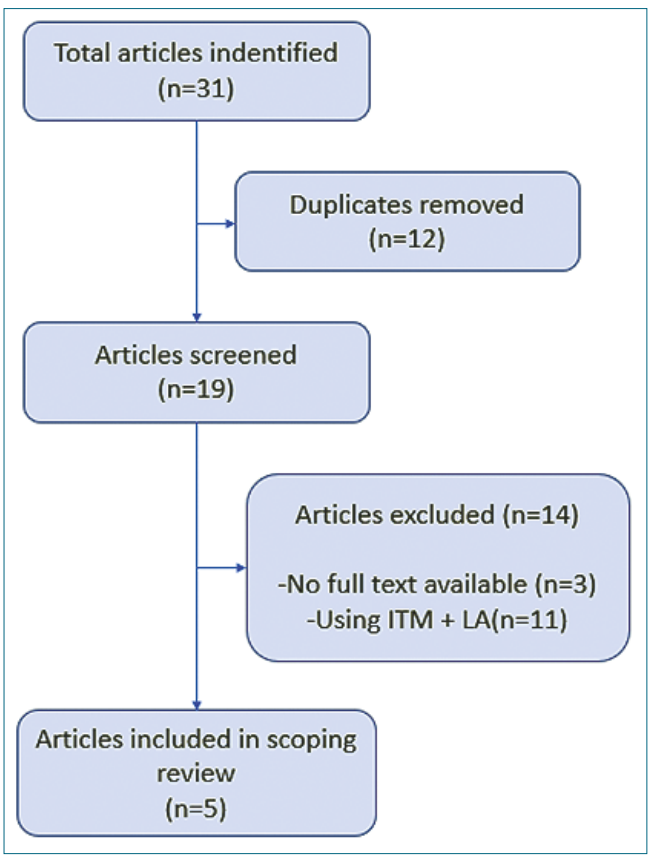

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for this scoping review on Intrathecal Morphine for hysterectomy.
-LA (Local anesthetic).

Table 1. Overview of articles relevant about the use of blended technique (GA + ITM without LA) and its impact on postoperative pain in patients undergoing hysterectomy

Authors (Publication year)	Type study	Type surgery	(n) (#) patients	Pain scale measure	ITM Dose	Results
Catarci et al. (2023)	Retrospective cohort	Laparoscopic and mini-laparotomy	644	NRS	50, 75 or 100 mcg	Cohort of patients was retrospectively divided into three groups according to the anesthetic management: GA + ITM + LA (Group 1), GA + ITM (Group 2) and GA (Group 3). NRS measured at each visit was lower Groups 1 and 2 in the first 48 hours.
Di Filippo et al. (2022)	Case-control	Laparoscopic and laparotomy	80	VAS	125 mcg	ITM patients reported a lower mean VAS in postoperative day 1 (ITM 1.85 ± 1.22 vs PCA 3.16 ± 1.3 $p < 0.002$) and day 3 (ITM 0.42 ± 0.67 vs PCA 2.56 ± 1.31 $p < 0.0001$)
Jeong Bang et al. (2022)	Clinical trial	Laparotomy	68	NRS	200 mcg	ITM group reported a lower NRS in the first 24 hours postoperative vs sham group $p < 0.0001$ with a difference in medians of 6 points (95% CI)
Rebel et al. (2011)	Retrospective cohort	Vaginal	121	VAS	1,000 mcg	ITM group reported a lower VAS up to 48 hours postoperative (1.2 ± 1.7) vs IVM (4.6 ± 2.8) $p < 0.01$
Sarma and Boström (1993)	Clinical trial	Laparotomy	80	VAS	0, 100, 300, 500 mcg	ITM patients reported a lower mean VAS up to 20 hours postoperative vs placebo group

NRS: (Numerical Rating Scale); VAS: (Visual Analogue Scale); mcg: (micrograms); ITM: (intrathecal morphine); GA: (General Anesthesia); IVM: (Intravenous Morphine); CI: (Confidence Interval).

Several articles were excluded from those identified as they involved local anesthetic within the intrathecal morphine mixture. This decision was made as our goal was to assess intrathecal morphine solely for its analgesic properties, not as an anesthetic technique, due to the advantages it presents. The oldest article dates back to 1993[10], while the most recent is from 2023[8]. A total of 993 patients across 5 studies were analyzed, comprising two clinical trials, two retrospective cohorts, and one case-control study.

The Visual Analogue Scale (VAS) and the Numerical Rating Scale (NRS) were the scales used to assess postoperative pain. A wide variety of intrathecal morphine doses were observed in the studies, ranging from low doses of 50 and 100 mcg to high doses of 500 and 1,000 mcg.

All five studies demonstrated that the use of intrathecal morphine in a blended technique with general anesthesia significantly reduced postoperative pain in patients undergoing hysterectomy, irrespective of whether the procedure was performed via laparotomy, laparoscopy, or vaginal approaches. It was noted that pain reduction occurred even within the first 72 postoperative hours[8],[9],[10],[11],12]. Additionally, intrathecal morphine was found to decrease opioid consumption during hospital stay. In the study by Retel et al., it was observed that the group receiving intrathecal morphine received significantly fewer postoperative opioids in the first 24 hours (44.9 ± 35.5 morphine equivalents) compared to the patients in the non-intrathecal morphine group (5.7 ± 8.7 morphine equivalents). Among other outcomes, Jeong's study revealed that patients receiving intrathecal morphine exhibited significantly higher satisfaction levels with pain control during the initial 48 hours.

Discussion

The administration of intrathecal morphine (ITM) was documented in 1900 by Dr. Nicolae Racoviceanu in Romania. However, neuroaxial anesthesia techniques gained popularity in the 1980s, with numerous publications reporting their use in various conditions, particularly chronic oncological pain and obstetrics[14]. ITM has already been proven to be effective in managing severe pain. It is a safe and cost-effective procedure that requires a single injection, providing effective analgesia for the initial 24-72 postoperative hours. Its benefits are so significant that its use has become a standard of care in procedures such as hip arthroplasty, using low doses of 100 µg or less[15].

The objective of applying ITM without a local anesthetic (LA) stem from evidence demonstrating no difference in postoperative pain when using intrathecal local anesthetic versus intrathecal morphine alone. Moreover, by employing this tech-

nique solely for analgesic purposes using ITM alone, we first avoided sympathetic blockade of the spinal cord, allowing for less hemodynamic instability in patients. Second, early ambulation is facilitated by avoiding motor block. Evidence also reflects better control of postoperative pain when using ITM without LA than when using a combination of ITM and LA[16].

However, the main concern in using ITM is the occurrence of late respiratory depression, a potentially fatal adverse event associated with this intervention. Carvalho et al., published a literature review in 2011 covering the period from 1945 to 2010 with the aim of evaluating this association. Following a review of 195 articles, the incidence of respiratory depression of 0.26% to 3% was estimated using the ITM. Nevertheless, multiple clinical trials analyzed within this literature review using ITM doses in the range of 200-400 mcg reported a 0% incidence of respiratory depression[17]. Similarly, scientific evidence supports the use of low ITM doses of 100 µg or even less, with references reporting a minimum effective dose of 40 µg, demonstrating no analgesic difference with doses of 100 µg[18].

Among the most frequently reported adverse effects of ITM, shivering, itching, and postoperative nausea, and vomiting (PONV) occur in at least 50% of patients receiving ITM. However, these are anticipated adverse effects that are considered minor and easily treatable[19].

The latest update of the Guidelines for Perioperative Care in Gynecologic/Oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations was published in 2019. This update mentions the standard of care for the anesthetic protocol as the use of general anesthesia, either balanced with inhalation anesthesia or total intravenous anesthesia, combined with intravenous multimodal analgesia. It does not extensively address regional anesthesia techniques or their benefits in controlling postoperative pain; thus, it does not recommend their use[6]. This might be due to recent studies demonstrating the benefits of ITM in a blended technique with general anesthesia in the years 2022 and 2023.

Conclusions

Hysterectomy is a major surgery frequently performed worldwide and is associated with significant postoperative pain and a high risk of chronic pain when not adequately controlled. ITM is a rapid, safe, and cost-effective procedure, with evidence demonstrating its benefits in terms of pain control, functionality, and patient satisfaction. However, further studies are needed to expand the current literature and evidence because of the scarcity of references. Nonetheless, based on this scoping review, the benefits of this technique are evident, suggesting a review of the existing worldwide recommendations regarding the standard anesthetic care provided to patients undergoing hysterectomy through any surgical approach.

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