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Minerva Obstetrics and Gynecology 2022 mese;74(0):000–000
DOI: 10.23736/S2724-606X.21.04961-7

ORIGINAL ARTICLE

Enhanced recovery after gynecological surgery: comparison between intrathecal and intravenous morphine multimodal analgesia

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ABSTRACT

BACKGROUND: The purpose of the present study was to compare the effectiveness of intrathecal injection of morphine, inserted in the protocols of multimodal analgesia, *versus* intravenous morphine in the control of postoperative pain and course in women undergoing gynecological surgery.
METHODS: An observational, single-center, retrospective and case-controlled study was performed. Data were collected in a group of women (N.=80) who underwent to gynecological surgery. Women were divided into two groups: group A (40 patients) laparoscopic hysterectomy and group B (N.=40) performing laparotomic myomectomy. In both groups 20 patients underwent administration of intrathecal morphine (125 mcg in 5 mL) and 20 patients underwent to intravenous morphine (1 mg maximum every 10 minutes). The primary endpoint collected was the mean VAS Score during the first 3 days after surgery, while secondary endpoints were opioid consumed during the same period, nausea, vomitus and pruritus. Among the exploratory objectives, length of hospital stay, canalization and feeding time were collected.
RESULTS: In group A, patients performing intrathecal morphine presented a significantly lowest VAS on postoperative day 1 and 3 compared to patients performing intravenous morphine while in group B mean VAS was statistically significant lower only on the first day. The emergence of pruritus was significantly higher in patients performing intrathecal morphine. The day of complete canalization was different in Group A patients in favor of intrathecal morphine as well as the length of stay.
CONCLUSIONS: Our present study showed that intrathecal morphine allows to achieve important management goals with minimal side effects and complications, in particular in case of laparoscopic hysterectomy.

(*Cite this article as*: Di Filippo A, Capezzuoli T, Fambrini M, Cariti G, Orlandi G, Vannucci G, *et al.* Enhanced recovery after gynecological surgery: comparison between intrathecal and intravenous morphine multimodal analgesia. Minerva Obstet Gynecol 2022;74:000-000. DOI: 10.23736/S2724-606X.21.04961-7)

KEY WORDS: Minimally invasive surgery; laparotomy; recovery after Surgery; Morphine; Spinal analgesia.

Women undergoing gynecological surgery develop chronic postoperative pain with a range between 4.7 and 26.2%.[1, 2] Surgical acute pain is a modifiable risk factor for the development of chronic postoperative pain and is a key component of enhanced recovery after surgery (ERAS) protocols.[3, 4]

Multimodal analgesia, *i.e.,* the administration

of two or more analgesic agents or procedures (*e.g.,* regional nerve blocks) exerting their effects along different pain pathways, contributes to the optimization of acute postoperative pain control and opioid sparing. According to gynecological surgery guidelines, multimodal analgesia combined with ERAS protocols resulted in reduced opioid consumption, less postoperative nausea and vomiting (PONV) and earlier discharge times, reducing healthcare costs.[4-9]

The aim of the present study was to compare the efficacy of intrathecal morphine (IM) injection as part of multimodal intravenous analgesia protocols with prophylaxis of postoperative nausea and vomiting *versus* intravenous patient-controlled analgesia (PCA) in women undergoing to two different gynecological surgical approaches: laparoscopic hysterectomy or laparotomic myomectomy. The dose-sparing effect of intravenous rescue analgesics, the intensity of postoperative pain, side effects and length of hospitalization were evaluated.

Materials and methods

An observational, single case-control study was performed, after the approval of the Ethical Committee (n. 17614_oss.). All patients have given their informed consent for participation in the study.

Data were collected in a group of women (N.=80) (age range between 30 and 47 years old) who were divided in 2 groups according to the gynecological surgery: group A, total laparoscopic hysterectomy (TLH) (N.=40) for benign uterine disorders (uterine fibroids, adenomyosis) and group B, laparotomic myomectomy (N.=40) (for uterine fibroids) during a 2-years period of observation by collecting data by Archimed® and Redcap®. The Archimed® system collects data related to the patient's course, the Redcap® system was originally built to collect data regarding the anesthesiologic conduct and the drugs and procedures used for each patient.

In both group A and group B, a subgroup of 20 patients underwent PONV prophylaxis with intraoperative ondansetron, administration of intraoperative non-opioid and opioid analgesics, administration of intrathecal morphine (IM) (125 mcg in 5 mL of saline), administration at set times of paracetamol (1 g x 4/day), ketorolac (30 mg x 3/day) and tramadol 50 mg as needed (if VAS>3) and another subgroup of 20 patients underwent to PONV prophylaxis with intraoperative ondansetron, administration of intraoperative non-opioid and opioid analgesics, administration at set times of paracetamol (1 g x 4/day), ketorolac (30 mg x 3/day) and morphine in patient controlled analgesia (PCA) (1 mg maximum every 10 minutes) were identified.

For each case enrolled in the study groups, *i.e.,* patients undergoing TLH or laparotomic myomectomy who received an intrathecal morphine dose, one control case was enrolled in the control groups, who had received intravenous postoperative opioid analgesia in PCA according to the following matching criteria: BMI (±2), age (±10), similar menopausal condition.

The primary endpoint collected was the mean VAS Score during the first 3 days after surgery, while secondary endpoints were opioid consumed during the same period, nausea, vomiting (PONV) and pruritus. Among the exploratory objectives, length of hospital stay, canalization and feeding time or distant complications were collected. Data were also collected regarding the type and duration of the operation.

General anesthesia was performed in all women by sevoflurane at MAC 1 and remifentanil (continuous infusion 0.15-0.25 mcg/kg/min), hypnosis by propofol 1.5-2.5 mg/kg after administration of lidocaine 1 mg/kg, curarization by rocuronium 0.6 mg/kg followed by boluses of ¼ of the initial dose every 20 minutes and decurarization with sugammadex 2 mg/kg upon recovery of the 1 response of the neuromuscular monitoring train of four.

Statistical analysis

Data were collected in an Excel file for statistical processing. The observed period (2 years) relates to the entry into use of electronic record systems in the ward and the change in pain and complication management procedures in the perioperative period. The types of procedures performed and outcome data were compared in each subgroup using Student's *t*-test for quantitative variables (mean±SD) and χ^2 for qualitative variables (fre-

quency). Significance was assigned for P<0.05. Statistical analyses were conducted using SPSS Statistics for Windows, Version 19 (IBM Corp., Armonk, NY, USA).

Results

No significant difference with regard to the main anthropometric parameters was observed among the groups.

Regarding the major endpoint of the study, in group A, patients performing IM presented a significantly lower mean VAS on postoperative day 1 than patients performing PCA (1.85±1.22 *vs.* 3.16±1.3; P<0.05) and also on day 3 (0.42±0.67 *vs.* 2.56±1.31; P<0.05) (Table I). In patients performing IM only 4 opioid administrations were required during the three days of observation (tramadol 50 mg). In group B patients performing IM mean VAS value was significantly low only on the first day after surgery (2.75±1.2 *vs.* 3.55±1.2; P<0.05) (Table II). In patients performing IM only 4 opioid administrations were required during the three days of observation (tramadol 50 mg).

In group A the emergence of PONV in the three days of observation was not significantly different between IM (4/20) and PCA (8/20) patients, while the emergence of pruritus was significantly higher in patients performing IM (IM=5/20 *vs.* PCA=0/20; P<0.05) (Table I).The day of initiation of feeding was the same for all groups (the first), while the day of complete canalization was different in group A patients in favor of IM (day 2.3±0.87 *vs.* 3.05±1.35; P<0.05) as well as the length of stay (3.35±0.74 *vs.* 4.42±1.92; P<0.05) (Table I). In group B, emergence of PONV and pruritus, initiation of feeding, canalization and length of stay were similar in patients treated with IM and PCA.

TABLE I.—*Outcome of patients undergoing total laparoscopic hysterectomy.*

	IM (N.=20)	PCA (N.=20)	P value
VAS day 1 (mean)	1.85±1.22	3.16±1.3	0.002
VAS day 2 (mean)	1.7±1.49	2.63±1.67	0.07
VAS day 3 (mean)	0.42±0.67	2.56±1.31	0.00002
PONV	4/20	8/20	NS
Pruritus	5/20	0/20	0.017
Inpatient days	3.35±0.74	4.42±1.92	0.04

IM: intrathecal morphine; PCA: patient-controlled analgesia; PONV: postoperative nausea and vomiting.

TABLE II.—*Outcome of patients undergoing laparotomic myomectomy.*

	IM (N.=20)	PCA (N.=20)	P value
VAS day 1 (mean)	2.75±1.2	3.55±1.2	0.04
VAS day 2 (mean)	2.25±1.3	2.6±1.6	NS
VAS day 3 (mean)	1.64±1.7	2.08±1.7	NS
PONV	6/20	5/20	NS
Pruritus	2/20	1/20	NS
Inpatient days	3.8±0.6	4.15±1.3	NS

IM: Intrathecal morphine; PCA: patient-controlled analgesia; PONV: postoperative nausea and vomiting.

Discussion

Our present study showed that antalgic subarachnoid injection with morphine better achieves the goals of postsurgical analgesia and recovery in TLH than in laparotomic myomectomy. It represents a part of protocols of postoperative pain control in gynecologic surgery[10-14] like in other types of surgery.[15-18]

With some differences relating the type of intervention, a reduction of pain and of need for opioids in the postoperative period were shown in gynecological surgery.[6, 7] The side effects are limited (minimum increased incidence of pruritus) and easily treatable. The results are less evident in women undergoing laparotomic myomectomy: a reduction of pain was only shown on the first day but the other parameters suggest that also laparotomic myomectomy interventions should be performed with IM. Indeed, in both groups the use of IM was associated with a more rapid restoration of vital functions (such as canalization) and a rapid discharge were observed.

It is well established that the enhanced recovery after surgery (ERAS) protocol for gynecology provides steps to achieve the best management of the perioperative period in order to minimize the psychological and physical trauma suffered by patients. The actions to be taken are multiple and occur at different times.[4, 6-9]

With regard to anesthesia it is advisable that whenever it is possible to perform the operation under regional anesthesia this should be preferred to general anesthesia; anesthesiologic techniques involving a combination of the two for both analgesic and anesthesiologic purposes

are also strongly recommended (*e.g.,* "blended anesthesia"); the aim of conducting anesthesia should be to minimize the use of opioids and inhalation anesthetics throughout the perioperative period and to initiate and then continue analgesia in a multidrug modality.[6, 7] Other recommended techniques may be various types of anesthetic blocks in adjunction to general or spinal anesthesia (transversus abdominis plane block, quadratus lumborum block, erector spinae block).[19-22]

The use of IM should, in principle, allow a postoperative free of pain, nausea, vomiting, constipation and also an early mobilization, an early restoration of physiological functions and the usual lifestyle and, ultimately, a shortening of the hospital stay and a lower incidence of complications. This effect is particularly evident in case of TLH for benign diseases, were postoperative pain and length of stay are clearly in favor of laparoscopy compared to laparotomy, even if in case of large uteri.[23-25]

Conclusions

In conclusion, our present study showed that antalgic spinal with intrathecal morphine allows to achieve important management goals with minimal side effects and complications both in TLH and laparotomic myomectomy, even though more effective in TLH.

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Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions.—Alessandro Di Filippo, Tommaso Capezzuoli, Tommaso Borracci and Felice Petraglia have given substantial contributions to the conception or the design of the manuscript; Massimiliano Fambrini, Giuseppe Cariti, Luciana Di Nardo and Marta Mezzella to acquisition, analysis and interpretation of the data. All authors have participated to drafting the manuscript; Felice Petraglia revised it critically. All authors read and approved the final version of the manuscript.

History.—Article first published online: December 1, 2021. - Manuscript accepted: November 11, 2021. - Manuscript received: September 2, 2021.