

Efficiency of postoperative pain management after gynecologic oncological surgeries with the use of morphine + acetaminophen + ketoprofen versus morphine + metamizol + ketoprofen

**D. Samulak^{1,2,3}, M. Michalska¹, M. Gaca⁴, M. Wilczak⁵,
E. Mojs⁶, M. Chuchracki^{2,7}**

¹Department of Obstetrics and Gynecology, Regional Hospital in Kalisz, ²Cathedral of Mother's and Child's Health, Poznan University of Medical Sciences, ³Clinic of Gynecological Surgery, Poznan University of Medical Sciences,

⁴Clinic of Anaesthesiology in Obstetrics and Gynecology, Poznan University of Medical Sciences,

⁵Department of Medical Education, Poznan University of Medical Sciences,

⁶Department of Clinical Psychology, Poznan University of Medical Sciences,

⁷Institute of Practical Learning of Midwifery, Poznan University of Medical Sciences (Poland)

Summary

Surgical treatment used in gynecological oncology involves acute postoperative pain which requires efficient treatment. This study covered a group of 128 patients who were randomly divided into two groups. In the postoperative period patients in group I were administered morphine subcutaneously, acetaminophen intravenously and naproxen per rectum. The pain intensity level was checked by means of the pain intensity numeric rating scale (NRS). In the instances of pain rated at 5 or more, patients were additionally administered ketoprofen intravenously. Patients in group II were administered morphine, naproxen, and metamizole instead of acetaminophen and ketoprofen additionally. In group I after the administration of morphine and acetaminophen 22 patients (34.37%) needed additional doses of ketoprofen. In group II 33 women (51.56%) required ketoprofen after the administration of morphine and metamizole (N1 = 22 vs N2 = 33, $p < 0.05$). The use of metamizol with morphine (without ketoprofen) gave worse analgesic results than acetaminophen with morphine, but the combination of morphine, acetaminophen and ketoprofen or morphine, metamizol and ketoprofen gave satisfactory analgesic results.

Key words: Postoperative analgesia; Morphine; Acetaminophen; Metamizol; Ketoprofen; Genital carcinomas.

Introduction

The foundation of the treatment process for carcinomas of the female genitals is the surgery where the main objective is maximum cytoreduction. It is very often connected with extensive surgery during which not only appendages and the uterus are removed, but also lymph nodes, the greater omentum, the appendix and sometimes sections of the intestines. These operations belong to category III and IV of surgeries and involve significant or extensive tissue injuries, which in turn involves acute postoperative pain which requires an efficient treatment process and appears when intraoperative analgesia stops working [1]. Acute or uncontrolled postoperative pain may cause persistent postoperative pain and complications. Efficient analgesia, apart from patient satisfaction, reduces the time of hospitalization and enables earlier rehabilitation [2, 3].

Basic pharmaceuticals used to overcome pain after gynecological surgeries of the third and fourth category include: weak or strong opioids (tramadol, pethidine, morphine), metamizol, ketoprofen and acetaminophen [4].

The aim of the research was to evaluate the efficiency of the management schemes of postoperative pain in women after gynecologic oncological surgeries.

Materials and Methods

The study covered a group of 128 patients aged from 42 to 82 years who underwent surgeries between 2007-2009 at the Department of Gynecology of the Regional Hospital in Kalisz due to malignant carcinomas of the genitals: cervix carcinoma, endometrial carcinoma, ovarian carcinoma. Each patient underwent laparotomy, accompanied by an intraoperative examination in the instances of ovarian carcinomas.

The scope of each surgery depended on the type of carcinoma. For cervix carcinoma Wertheim's procedure was performed, for endometrial carcinoma – extended removal of the uterus together with lymphadenectomy, for ovarian carcinoma – maximum cytoreduction together with the removal of the greater omentum and in one instance also removal of sections of the small intestine.

The patients were randomly divided into two groups (64 patients in each group).

In the postoperative period and on the day of operation patients in group I were administered morphine subcutaneously (SC) in the dose of 1 mg per 10 kg of body mass every four hours, 1 g of acetaminophen intravenously (IV) every six hours and from the first day after the operation 500 mg of naproxen in suppository form, per rectum every 12 hours. During the whole hospitalization period, the pain intensity level was checked by means of the pain intensity numeric rating scale (NRS; 0-10), where 0 indicates no pain, 5 – moderate pain and 10 – the worst pain that can be imagined. In the instances of pain rated 5 or more, patients were additionally administered 100 mg of ketoprofen IV.

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On the day of operation patients in group II were administered morphine SC in the following dose: 1 mg per 10 kg of body mass every four hours, 1 g of metamizol IV every six hours and from the first day after the operation 500 mg of naproxen per rectum every 12 hours. In the instances of pain rated 5 or more, patients were additionally administered 100 mg of ketoprofen IV.

Results

The average age of patients was 68 years. The hospitalization period lasted between five and seven days (mean 5.7 days). On the day of surgery and prior to administration of the first analgesics 48 patients in group I rated their pain at 8 on the scale, 12 patients rated the pain at 7, and four at 6. After administration of morphine and acetaminophen the pain eased off in all patients but 22 still rated it at 6 on the scale. Thus it was necessary to provide these patients with additional doses of ketoprofen IV. Other patients from group I rated the pain at 4 after being administered morphine and acetaminophen. On the first day after the surgery ten patients from group I who rated the pain at 6 and were administered ketoprofen IV. The other 54 patients rated the ailments at 4 and were routinely administered naproxen per rectum. On the second day after the surgery four patients required administration of ketoprofen, and on the third day two patients. On the fourth day no patient required any additional analgesics.

On the day of the surgery 50 patients in group II rated the pain at a score of 8 and 14 rated it at 7. After administering morphine and metamizol, the pain eased off in all patients but still 21 patients rated it at 7, and 12 rated it at 6 (altogether 33 patients) and they required additional doses of ketoprofen. Comparing group I and II at this stage, a statistically significant difference was found ($N_1 = 22$ vs $N_2 = 33$, $p < 0.05$). On the first day after the operation 14 patients rated the pain at 6 on the scale, which required administering not only naproxen but also ketoprofen. On the second day six patients rated the pain more than 4, and on the third day - three patients. On the fourth day no patient from group II required administration of any additional analgesics (Table 1).

During the entire postoperative period no side-effects connected with the application of any group of medications were observed.

Discussion

Efficient analgesic postoperative treatment is still a challenge. Oncological operations belonging to category III and IV or surgeries involve an acute postoperative pain rated > 4 (category III) and > 6 (category IV) according to the NRS and lasting > 3 days [4].

In the literature various postoperative pain treatment schemes are described for both oncological surgeries as well as extensive non-oncological abdominal surgeries. Werawatganon *et al.* [5] compared the use of patient-controlled analgesia by means of opioids (PCA) with continuous epidural analgesia (CEA) after abdominal surgeries.

Table 1. — Percentage of patients, in each group and day, suffering from pain rated > 4 points in NRS, requiring the administration of additional doses of ketoprofen. [%].

Group	Day of operation	Days after operation			
		First day	Second day	Third day	Fourth and following days
I	34.37 (N 22)	15.62 (N10)	6.25 (N 4)	3.12 (N 2)	0
II	51.56 (N 33)	21.87 (N 14)	9.37 (N 6)	4.69 (N 3)	0

Not only the efficiency of analgesics was observed but also side-effects, patients' satisfaction and the influence on surgical effects. The superiority of CEA over PCA was proved as far as relieving pain was concerned. However, patients who were administered CEA suffered from intense pruritus.

Comparison of the use of patient-controlled analgesia by means of PCA with patient-controlled epidural analgesia (PCEA) after gynecologic oncological surgeries was made by Chen *et al.* [6]. They did not report any superiority of PCEA over PCA in oncological patients but better pain relieving effects after the application of PCEA.

Hudcova *et al.* [7], Bell *et al.* [8] as well as Pearl *et al.* [9] studied the efficiency of analgesics by means of opioids administered in various ways. Hudcova *et al.* [7] reported better control of pain in patients being administered PCA than in patients being administered conventional analgesics ("on request"). However, higher consumption of morphine was reported as well as intense pruritus with the use of PCA. In their random study, Bell *et al.* [8] did not report any difference as far as analgesic effects and patients' satisfaction were concerned in any group in which opioids were administered, either in the PCA system or intravenously or subcutaneously. Similarly to Hudcova *et al.* [7], Bell *et al.* [8] reported higher consumption of pharmaceuticals and the occurrence of pruritus in the group with PCA. Pearl *et al.* [9] studied the efficiency of early (since the first 24 hours) oral application of morphine and proved no difference as far as pain relieving effects and side-effects were concerned between the oral and intravenous PCA system with the application of morphine.

Numerous side-effects of opioids make researchers look for new analgesic treatment schemes and application of non-opioid pharmaceuticals in multimodal analgesia which makes use of the possibility of multidirectional inhibition of nociception as well as modulation of pain-related information flow [10, 11]. Mugabure Bujedo *et al.* [12] as well as Buvanendran *et al.* [13] proved that multimodal analgesia enables convalescence and first of all reduces demand for opioids, limiting side-effects typical for them. Many researchers reported the efficiency of the application of non-steroid anti-inflammatory drugs in multimodal analgesia, as well as metamizol and acetaminophen administered intravenously, both in combination with opioids and without [14-16]. McNicol *et al.* [17] studied the usefulness of the application of non-steroid anti-inflammatory drugs and acetaminophen together with opioids or without them in pain resulting from

malignant carcinomas. However, the results obtained were ambiguous and did not allow any final conclusions to be formulated.

Analgesic treatment after gynecologic oncological surgeries applied by us and presented in this paper was compliant with the rules of multimodal analgesia, gave satisfactory results in the form of inhibition of very acute pain and at the same time allowed many side-effects connected with the application of only one group of medications to be avoided.

Conclusions

The combination of morphine, acetaminophen and ketoprofen or morphine, metamizol and ketoprofen gives satisfactory analgesic results even when it comes to operations belonging to category III and IV of surgeries.

The use of metamizol with morphine in the treatment scheme on the day of operation (without ketoprofen) gave worse analgesic results than acetaminophen with morphine, and the difference proved to be statistically significant ($p < 0.05$).

Application of multimodal analgesia prevents side-effects from appearing when only one group of medication is administered.

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Address reprint requests to:
M. MICHALSKA, M.D.
Department of Obstetric and Gynecology
Regional Hospital in Kalisz
ul. Torunska 7
62-800 Kalisz (Poland)
e-mail: magdalena-m-michalska@wp.pl