

Effect of Levobupivacaine Wound Infiltration on Postoperative Pain and Tramadol Consumption After Wertheim-Meigs Procedure

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Abstract

Introduction: Wound infiltration with local anesthetic before wound suture could be a possible way to provide postoperative analgesia and reduce the need for opioid analgesics as well as their side effects. The aim of this study was to evaluate whether wound infiltration with local anesthetic can reduce postoperative pain and opioid requirements after Wertheim-Meigs procedure.

Methods: Randomised double-blind clinical study was conducted at the National cancer research center of Serbia and included 28 women who were scheduled for Wertheim-Meigs procedure. They were randomised into two groups: study group received wound infiltration with 20 ml of 0.25% levobupivacaine before the closure of the abdomen, in the control group wound was infiltrated with 20 ml of sterile saline. Patients in both groups received paracetamol 1g 30 minutes before the end of the operation. After the end of surgery postoperative pain was assessed using numeric scale for the first 24 hours at rest and during the mobilisation of the patient. If the patients assessed the intensity of pain as 4 or less they received non-opioid analgesic. If they assessed the intensity of pain as 5 or more they received tramadol.

Results: Mean pain scores were significantly lower in the study group compared to control group ($p < 0.05$) for the whole 24-hour period of follow-up. Opioid requirements were also significantly lower in the study group compared to control group ($p < 0.05$) as well as mean total daily dose of opioid analgesic.

Conclusion: This study showed that wound infiltration with 0.25% levobupivacaine before surgical closure of the abdomen after Wertheim-Meigs procedure significantly reduced pain scores and the need for opioid analgesic in the first 24 hours after the operation.

Keywords: Analgesia; Wound Infiltration; Wertheim-Meigs; Levobupivacaine; Tramadol

Abbreviations

ASA: American Society of Anesthesiologists; PACU: Post-Anesthesia Care Unit

Introduction

Although there are various different techniques available for dealing with postoperative pain, adequate postoperative analgesia is still achieved only in a small number of patients [1]. Inadequate dealing with postoperative pain significantly influences the quality of life of patients and can be the cause of development of chronic pain. There are various factors which influence the intensity of postoperative pain including age, individual sensitivity to pain, type and duration of surgical procedure, type of analgesia and all these factors can make

more difficult postoperative pain control [2]. The ideal analgesia technique for postoperative pain therapy should provide high level of analgesia with minimal side effects.

Abdominal surgery causes significant postoperative pain due to the trauma of the anterior abdominal wall and visceral organs [3]. Opioid analgesics are still one of the primary treatments for moderate to severe postoperative pain but their use is limited by their significant side effects [4]. These side effects include the possibility of development of respiratory depression, excessive sedation, nausea, vomiting, obstipation, delay in hospital discharge [5,6].

Local wound infiltration lowers the need for the postoperative pain therapy and side effects of these drugs. Technique is easy to perform, it has lower risk for complications compared to other regional anesthesia techniques and lower risk to cause nausea and vomiting as well as urinary retention. For those reasons the level of satisfaction of patients is higher, hospital stay is shorter which reduces the total cost of hospital stay [7].

Ernst Wertheim laid founding stones of surgical treatment of cervical cancer when he published his paper in 1912 in the American Journal of Obstetrics and Diseases of Women and Children and presented the technique of radical abdominal hysterectomy [8]. In 1951 Meigs extended this procedure by adding en bloc pelvic lymph node dissection which has significantly improved survival after this procedure [9]. Being very extensive and radical, Wertheim-Meigs procedure causes significant intensity of pain in patients which is the cause for need for high levels of opioid analgesics in postoperative period with significant side effects.

Aim of the Study

The aim of this study was to determine the efficacy of wound infiltration with local anesthetic in providing postoperative analgesia and reducing the need for opioid analgesics after the Wertheim-Meigs procedure.

Methods

Prospective, randomised, double blind study was conducted at the National Cancer Research Center of Serbia in Belgrade from 01.01.2016-01.06.2017. Female patients scheduled for the elective Wertheim-Meigs operation due to the cancer of cervix, endometrium, and/or upper vagina were included. All the patients were American Society of Anesthesiologists (ASA) class I-III and between 25 and 69 years old. The study was approved by the Institutional Review Board and all patients signed the informed consent.

The criteria for inclusion of patients in the study were:

1. Patients scheduled for elective Wertheim-Meigs procedure
2. Patients 18 or more years old
3. Patients of ASA class I-III
4. Patients who have given consent to participate in the study.

The criteria to exclude patients from the study were:

1. Refusal of the patient to participate in the study
2. Patients who had an emergency procedure
3. Patient allergic to amid local anesthetics and/or tramadol.

The study included 28 patients who were randomised using randomization plan generated through software <http://www.randomization.com> into two groups, 14 patients in each group. All patients received the following drugs for premedication: intramuscular atropine 1 mg and midazolam 3 mg and then intravenous metoclopramide 10 mg, ranitidine 50 mg, ceftriaxone 50 mg/kg and metronidazole 500 mg 60 minutes before the start of operation. The operation was conducted using the balanced anesthesia technique. Induction in anes-

thetia was performed with intravenous administration of midazolam 2 mg, fentanyl 2 mcg/kg, propofol 1.5 - 2 mg/kg and rocuronium 0.6 mg/kg. All the patients were intubated. For maintenance of anesthesia sevoflurane 1 - 2% was used and for intraoperative analgesia bolus doses of fentanyl of 1 - 2 mcg/kg. For the antagonisation of neuromuscular blockade at the end of the procedure atropine 1 mg and neostigmine 2.5 mg were administered intravenously.

The first, study, group received wound infiltration with single shot technique of 20 ml of 0.25% levobupivacaine in the preperitoneal, subfascial and subcutaneous layer before the surgical suture of the abdomen. In the second, control, group wound was infiltrated with 20 ml of sterile saline. The surgeon performing the infiltration was unaware which solution was used for infiltration. Patients in both groups received paracetamol 1g intravenously 30 minutes before the end of operation.

Patients in both groups were administered intravenous diclofenac 75 mg every 12 hours. After the recovery from anesthesia and transfer to Post-anesthesia care unit (PACU), assessment of the severity of pain was done every 30 minutes for the first 2 hours and after that every hour for the first 24 hours after the operation. Patients assessed the intensity of pain they were experiencing using numeric scale which has values of 1 which represents no pain up to 10 which represents the worst possible pain. The significance of these values was explained to each patient and assessment was done by nurses of PACU which were unaware to which group the patients belonged. If the patients complained of pain outside the set hourly intervals these values were also recorded. The intensity of pain was also assessed during mobilisation at the same hourly intervals.

If the patients assessed the intensity of pain they were experiencing as 4 or less on the numeric scale they received intravenous paracetamol 1g in the intervals which were not shorter than 4 hours, up to maximal daily dose of paracetamol of 4g. If the patients estimated their intensity of pain as 5 or more they received intramuscular bolus dose of tramadol of 1 mg/kg in intervals no shorter than 4 hours, up to the maximal daily dose of tramadol of 400 mg. The occurrence of nausea and vomiting was estimated in the same hourly intervals as the pain as well as the need for the rescue antiemetics.

Kolmogorov-Smirnov test was used to test the normality of distribution. To compare the data of the two groups for which it was shown that they have normal distribution Student' t-test was used. If that was not the case, Mann-Whitney U test was used. P < 0.05 was considered statistically significant.

Results

28 patients were included in this study, 14 (50%) in each of the two groups. There was no statistically significant difference between the demographic characteristics of patients (age, weight, height, ASA class) of both groups (p > 0,05) (Table 1). There were no patients which were afterwards excluded from the study for any reason, including the appearance of previously not diagnosed allergic reaction to local anesthetic and/or analgesics used in this study. There were no patients with wound healing complications in any of the groups.

	Study group (n = 14)	Control group (n = 14)	P value
Mean age (in years)	47 ± 3.4	46 ± 4.1	0.314
Mean weight (kg)	69 ± 6.8	67 ± 5.4	0.245
Height (cm)	168 ± 9.3	170 ± 8.3	0.485
ASA class			
ASA class I	3 (21%)	4 (29%)	0.148
ASA class II	7 (50 %)	8 (57%)	0.162
ASA class III	4 (29%)	2 (14%)	0.172

Table 1: Demographic data of the patients.

The results are shown as mean values ± standard deviations or as an absolute number (%)

Mean value of the intensity of pain assessed using numeric scale was significantly lower during the whole period of follow-up of 24 hours in the study group compared to control group (3.64 ± 0.84 compared to 4.87 ± 1.01 ; $p < 0.05$). Mean value of the intensity of pain was significantly lower in the study group compared to control group in each hourly point of recoding (Table 2). Mean value of the intensity of pain was also significantly lower in the study group compared to control group during the mobilization of the patient (3.84 ± 0.78 compared to 5.87 ± 1.10 ; $p < 0.05$).

Mean value of the postoperative pain	Study group (n = 14)	Control group (n = 14)	P value
30 min	3.4 ± 1.4	5.7 ± 2.1	$P < 0.05$
60 min	2.9 ± 0.9	5.5 ± 1.0	$P < 0.05$
90 min	3.1 ± 1.1	5.4 ± 1.4	$P < 0.05$
120 min	3.6 ± 0.7	4.3 ± 1.2	$P < 0.05$
3 h	3.0 ± 0.6	4.4 ± 0.5	$P < 0.05$
4 h	3.1 ± 1.1	4.8 ± 0.5	$P < 0.05$
8 h	2.8 ± 1.2	4.6 ± 0.4	$P < 0.05$
12 h	3.9 ± 0.3	5.0 ± 0.7	$P < 0.05$
24 h	4.4 ± 0.4	5.2 ± 0.3	$P < 0.05$

Table 2: Assessment of the postoperative pain.

The results are shown as mean values \pm standard deviations.

During the whole period of follow-up mean total quantity of tramadol which the patients needed in the postoperative period was significantly lower in the study compared to control group (212.23 ± 29.47 mg compared to 335.04 ± 26.47 ; $p < 0.05$).

The appearance of nausea and vomiting and the need for rescue antiemetics was significantly lower in the study group compared to control group but the difference was not statistically significant ($p > 0.05$).

Discussion

Wound infiltration with local anesthetic is a simple, fairly safe and cost effective method of providing postoperative analgesia. This technique is based on prevention of inflammatory response and hyperalgesia [10]. Local anesthetics inhibit bradykinin induced activation of phospholipase D [11] and binding of substance P [12] and that way provide anti-inflammatory activity [13,14].

The most important advantage of this technique is the absence of systemic effects of local anesthetics which can occur during the central blocks like the presence of the motor block, delayed mobilization of the patient and urinary retention [10]. This technique facilitates the reduction of postoperative opioid doses as well as their systemic side effects.

Studies of this technique are very heterogeneous considering which local anesthetic was used, layer which was infiltrated by single shot technique or continuous infusion, whether the wound was infiltrated before the surgical incision or before surgical suture but most authors agree that this technique provides significant level of analgesia which enables the reduction of necessary opioid dosage.

Dierking, *et al.* (1992) [15] and Gill (2001) [16] have shown that preemptive wound infiltration with local anesthetic before the surgical incision significantly reduces postoperative intensity of pain.

Dierking, *et al.* (1994) [17] studied the effect of postoperative wound infiltration after inguinal herniorrhaphy. They infiltrated 0.25% bupivacaine 10 ml in internal fascia and another 15 ml of the same solution on both sides of the surgical wound compared to the infiltra-

tion of the same quantity of saline. Their results showed that pain at rest, during mobilisation and during cough was lower in the study group compared to the control group as well as the total consumption of morphine for the 24 hours after operation.

Quereshi, *et al.* (2016) got similar results with infiltration of 20 ml of 0.25% bupivacaine subfascially and in the deeper layers along the incision line before surgical closure during unilateral inguinal hernia repair regarding pain scores and postoperative tramadol consumption.

Results of this study are similar to the results of the other authors. No other study where local wound infiltration was used after Wertheim-Meigs procedure was found. It was decided to use levobupivacaine instead of lidocaine for infiltration since it has longer half-life than lidocaine which prolongs the postoperative analgesic effect. Tramadol was used for postoperative pain therapy instead of morphine because of less sedation and lower risk of respiratory depression [18,19].

Conclusion

This study showed that wound infiltration before surgical closure with 0.25% levobupivacaine is a simple, safe and cost-effective method of providing postoperative analgesia after Wertheim-Meigs procedure. The results of this study showed that mean pain scores during the first 24 hours after the operation were lower at rest as well as during mobilisation. The need for opioid analgesics as well as their total consumption was also lower when this method was used. Nausea and vomiting were also less frequent in the group which received wound infiltration with local anesthetic as well as the need for rescue antiemetics but the difference was not statistically significant. This method can be combined with different analgesics in postoperative period, to reduce the necessary dose of these drugs as well as their side effects.

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