CONTINUOUS PERIOPERATIVE INTRAVENOUS LIDOCAINE INFUSION IN GYNECOLOGIC ONCOLOGY SURGERY

Kontinuálna peroperačná intravenózna infúzia lidokaínu v gynekologickej onkologickej chirurgii

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Abstract
Aim: Evaluation of the efficacy of intravenous lidocaine administration during surgical interventions in gynecologic oncology.
Materials and Methods: A single-center randomized study. The study included 170 patients who underwent total hysterectomy or subtotal hysterectomy. The control group (Contr. Gr.) received anesthesia based on fentanyl, propofol, and atracurium. The intravenous lidocaine administration group (ILA Gr.) received 1 mg/kg/h lidocaine during anesthesia and 24 hs postoperatively. Final assessment: postoperative pain intensity (NRS), opioid requirement during surgery and postoperatively, stress response assessment, and postoperative sleep quality.
Results: 163 patients completed the study. Two patients in the IV lidocaine group and five patients in the control group were excluded from the analysis. At the time of surgery, the total fentanyl dose was 23 % lower in Contr. Gr. but the severity of the surgical stress response was more prominent in ILA Gr. ; blood glucose levels were 17 % higher in ILA Gr. at the end of surgery compared to Contr. Gr. In the postoperative period, pain intensity according to NRS was not statistically significantly different between the study groups 24 hs after surgery. The quality of sleep was better in ILA Gr. There were no significant differences in the dose of morphine for postoperative anesthesia between the study groups.
Conclusions: Intravenous administration in the perioperative period in patients after gynecologic oncology surgeries did not improve the quality of perioperative anesthesia and did not significantly reduce the dose of opioid analgesics during anesthesia and within a day of the postoperative period (Tab. 2, Fig. 6, Ref. 37). *Text in PDF www.lekarsky.herba.sk*.
KEY WORDS: intravenous lidocaine infusion, gynecologic oncology surgery, pain, stress response.
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Abstrakt
Cieľ: Hodnotenie účinnosti intravenóznej aplikácie lidokaínu počas chirurgických výkonov v gynekologickej onkológii.
Materiály a metódy: Jednocentrová randomizovaná štúdia, ktorá zahŕňala 170 pacientov. Pacienti podstúpili totálnu hysterektómiu alebo subtotálnu hysterektómiu. Kontrolná skupina (Contr. Gr.) dostala anestéziu na báze fentanylu, propofolu a atrakuria. Skupina s intravenóznym podávaním lidokaínu (ILA Gr.) dostávala 1 mg/kg/h lidokaínu počas anestézie a 24 hodín po operácii. Záverečné hodnotenie: intenzita pooperačnej bolesti (NRS), potreba opioidov počas operácie a po operácii, hodnotenie reakcie na stres a kvalita pooperačného spánku.
Výsledky: Štúdiu dokončilo 163 pacientov. Z analýzy boli vylúčení 2 pacienti v skupine s IV lidokaínom a 5 pacientov v kontrolnej skupine. V čase operácie bola celková dávka fentanylu o 23 % nižšia v Contr. Gr. , ale závažnosť reakcie na chirurgický stres bola výraznejšia v ILA Gr. ; koncentrácie glukózy v krvi boli o 17 % vyššie v ILA Gr. na konci operácie v porovnaní s Contr. Gr. V pooperačnom období sa intenzita bolesti podľa NRS medzi sledovanými skupinami 24 hodín po operácii štatisticky významne nelíšila. Kvalita spánku bola lepšia v ILA Gr. Medzi sledovanými skupinami neboli žiadne významné rozdiely v dávke morfínu pri pooperačnej anestézii.
Záver: Intravenózne podanie lidokaínu v perioperačnom období pacientkam po gynekologických onkologických operáciách nezlepšilo kvalitu peroperačnej anestézie a významne neznížilo dávku opioidových analgetík počas anestézie a do jedného dňa po pooperačnom období (tab. 2, obr. 6, lit. 37). *Text v PDF www.lekarsky.herba.sk.*
KĽÚČOVÉ SLOVÁ: intravenózna infúzia lidokaínu, gynekologická onkologická chirurgia, bolesť, stresová reakcia.

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Introduction

Despite the available recommendations and studies comparing different combinations of opioid and non-opioid analgesics, the problem of adequate perioperative analgesia is still not solved (13). Multimodal analgesia proposed by H. Kehlet (15) more than 20 years ago, unfortunately, could not finally resolve the problem of adequate postoperative analgesia. There are still many unresolved questions about the efficacy and safety of used combinations of analgesics, as well as the influence of such combinations on other parameters of adequate analgesia, such as the length of hospital stay, the effect on GI motility and on the consistency of intestinal anastomoses, etc. (5). The available data often lack sufficient evidence basis and sometimes present controversial results (14, 37). Prolonged intravenous infusion of lidocaine is proposed as one of the components of multimodal anesthesia/analgesia (2, 17, 30).

Over the past 15–20 years, there have been numerous randomized controlled trials that have examined the efficacy of prolonged IV lidocaine infusion in perioperative anesthesia, and a number of systematic reviews and meta-analyses (23, 24, 29) have been published on this technique (33, 34). One large meta-analysis, which included 4525 cases from 68 studies (35), unfortunately, did not reach a definite conclusion regarding these studies.

According to the Cochrane 2015 review (19), prolonged IV lidocaine infusion was shown to significantly reduce the intensity of postoperative pain, reducing the dose of opioid analgesics. The same Cochrane 2018 review showed (35) that prolonged IV lidocaine infusion in the postoperative period reduced the intensity of postoperative VAS level of pain only at rest and not on movement. Moreover, the analgesic effect is pronounced only on the first post-surgery day. The IASP Guidelines for the evaluation of analgesic efficacy, however, suggest that the evaluation of analgesic efficacy should be assessed in patients on movement. According to the Cochrane 2018 review, prolonged IV lidocaine infusion did not reduce pain intensity on movement compared to placebo (35). Other authors have concluded that prolonged IV lidocaine infusion might be an acceptable alternative to epidural analgesia with local anesthetics (30). The PROSPECT group guidelines also indicate that in the presence of contraindications to epidural analgesia, it is recommended to use prolonged IV lidocaine infusion for postoperative analgesia as an alternative (27). Although, if we refer to the Guidelines of the Australian and New Zealand College of Anaesthetists for the management of acute postoperative pain (22), we do not find recommendations for IV lidocaine administration as an option for postoperative pain management.

Therefore, the aim of the study was to compare the efficacy of perioperative analgesia with prolonged IV lidocaine infusion as a component of multimodal analgesia during surgical interventions in gynecologic oncology.

Materials and Methods

This is a prospective study of patients who underwent gynecologic oncology surgery at the National Cancer Institute (Kyjiv, Ukraine) for the period of 2019 – 2022. The study compared the efficacy of two groups of anesthesia: the prolonged perioperative lidocaine infusion group and analgesia without perioperative lidocaine infusion. All patients at the time of surgical resolution, were SARS-CoV-2 negative, anti-epidemic measures were followed. Patients with suspected infection until receiving the PCR test were managed according to the protocol of the management of the disease of COVID-19 (11, 12, 18). Pain management was also implemented taking into account possible post-covid complications (8 – 10).

Patients according to ASA I – III (American Society of Anesthesiologists) who were scheduled for total hysterectomy or subtotal hysterectomy were included in the study (Fig. 1).

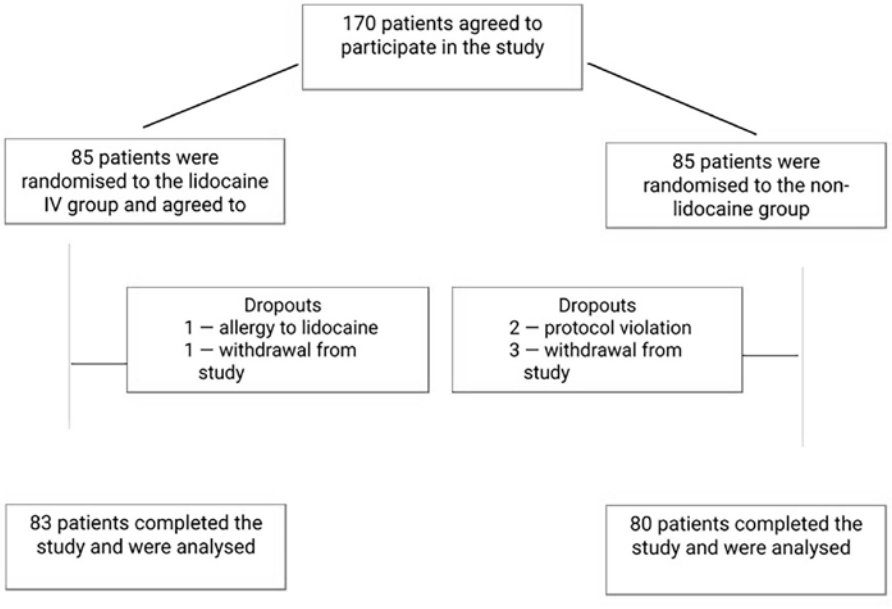


Figure 1. Study flowchart describing patients included in the study.

Exclusion criteria: patients under 18 years, emergency surgery, severe cardiopulmonary disease; myocardial infarction in the last 6 months; chronic obstructive pulmonary disease (COPD) [paO_2 < 60 mm Hg], neuropsychiatric disorders, and cardiac rhythm disturbances. Written informed consent was obtained from all study participants.

Anesthesia protocol

All patients did not receive premedication before surgery (neither opioids nor hypnotics) if they were emotionally stable. The patients were randomised into two groups according to the use of intravenous lidocaine during general anesthesia and postoperative analgesia. The patients were prospectively divided into two groups: Gr. Contr. (control group, 80 patients) in which anesthesia was inducted with propofol 2 mg/kg intravenously, atracurium 0.5 mg/kg, and fentanyl 1 – 2 μg/kg. After tracheal intubation, low-flow sevoflurane (1.5–2 v/%) inhalation anesthesia (1 – 1.5 L/min) was initiated. An additional dose of fentanyl (1 μg/kg) was administered when BP and HR increased above 20 % of preoperative values, atracurium (0.2 mg/kg) was administered when EMG (electromyography) values increased more than 30. In the IV lidocaine administration group (ILA Gr.), anesthesia was inducted with atracurium 0.5 mg/kg, fentanyl 1–2 μg/kg, and propofol 2 mg/kg. After tracheal intubation, low-flow sevoflurane (1.5–2 v/%) inhalation anesthesia (1–1.5 L/min) was initiated. An additional dose of fentanyl (1 μg/kg) was administered when BP and HR increased above 20 % of preoperative values, atracurium (0.2 mg/kg) was administered when EMG (electromyography) values increased more than 30. In Gr. IVL (intravenous lidocaine) was the component of anesthesia. A bolus dose of lidocaine (1 mg/kg, not more than 120 mg) was administered before induction of anesthesia and was continued at a dose of 1 mg/kg/h throughout the surgical intervention and for 24 hs postoperatively in the intensive care unit.

Standard monitoring during surgery included electrocardiography, non-invasive continuous monitoring of blood pressure, heart rate, capnography, BIS (which was maintained between 40 and 60). Infusion therapy was carried out according to the restrictive pattern (2 – 3 mL/kg/h with crystalloid solutions). Mean arterial pressure (MAP) was maintained at least 65 mm Hg, and if it decreased, 0.2 – 0.4 μg/kg/min norepinephrine infusion was used. A decrease in MAP to less than 20 % of baseline values was considered hypotension, an increase of 20 % in MAP from baseline values was considered hypertension, heart rate (HR) less than/more than 20 % of baseline values was considered bradycardia or tachycardia. Hemodynamic changes were recorded at the following stages: baseline (preoperative) and every 5 minutes during anesthesia and every 2 hs for 24 hs postoperatively.

Patients in both groups received IV dexketoprofen 50 mg and IV paracetamol 1000 mg prior to surgery intervention in the operating room. In the postoperative period as components of multimodal analgesia, patients of both groups received dexketoprofen 50 mg 3 times a day (daily dose not exceeding 150 mg) and paracetamol 1000 mg 3 – 4 times a day (daily dose not exceeding 4 g). In case of inadequate analgesia (NRS, numerical rating scale) in movement more than 4 points), patients were administered IM morphine 10 mg for additional analgesia.

Study endpoints

The primary endpoints assessed were fentanyl requirement during surgery and postoperative morphine requirement for analgesia, NRS postoperative pain intensity, where zero means no pain and 10 means worst pain at 2, 4, 6, 12 and 24 hs after surgery.

Secondary assessment points were changes in glucose levels at the end of surgery and 24 hs after surgery, incidence of hypotension, postoperative nausea and vomiting (PONV), time to appearance of intestinal motility after surgery, and postoperative quality of sleep. All patients receiving intravenous lidocaine were evaluated for changes in mental status and clinical manifestations of lidocaine toxicity. Mental status was assessed and categorized as follows: wakefulness/vigilance, confusion, drowsiness, and lack of response to stimuli. The following signs were considered to be manifestations of toxicity: facial/mouth numbness, dizziness, confusion, tinnitus, double vision, muscle twitching, seizures, arrhythmia, and numbness in the arms or legs.

Statistics

Statistical processing of the obtained results was carried out using the STATISTICA 8.0 software (StatSoft. Ink., 2008). The distribution of continuous data in the groups was assessed by plotting distribution diagrams and by the Kolmogorov – Smirnov's test. Given that if the distribution in the groups was not normal, a comparison between groups was made using non-parametric methods of data evaluation. Descriptive statistics included calculation of standard error of the mean and 95 % confidence interval (CI), standard deviation, median, and quadratic range (range between 25th and 75th percentile). Between-group comparison of quantitative indicators was performed using the Mann – Whitney U test, qualitative indicators – using two-tailed Fisher's criterion, and correlation between quantitative indicators was determined using Spearman's rank correlation. Differences were considered statistically significant when the type I error probability was less than 5 % ($p < 0.05$).

Results

A total of 170 patients were included in the study, of whom 163 completed the study and were included in the analysis. Both groups were well randomized, there were no statistically significant differences in the patient demographics (Tab. 1).

Table 1. Characterization of demographics in the study groups.

Characteristics	Gr. Contr/80	Gr. IVL/83	p
Age, years	**51.1±12.3**	**52.5±12.2**	**0.4599†**
BMI, kg/m²	**29.3±6.4**	**27.9±6.0**	**0.1144†**
Comorbidity:	n/%	n/%	
– Hypertensive disease	34/42.5	38/45.8	0.4521††
– IHD	25/31.3	33/39.8	0.2648††
– A history of CVA	3/3.8	2/2.4	0.4887††
– Type II diabetes mellitus	5/6.3	4/4.8	0.4853††
– ASA			
– I	14/17.5	19/22.9	0.3068††
– II	61/75	60/72.3	0.4593††
– III	5/6.3	4/4.8	0.4853††
Note: † Mann – Whitney U test, †† Fisher exact one-tailed test.			

The patients in the study groups did not differ statistically significantly by the presence of comorbidity and the degree of anesthesia risk.

The patients were equally distributed in the groups according to the scope of surgical intervention: uterine extirpation with appendages (UEA) was performed in 67.5 % of patients in the control group and in 66.3 % of patients in the lidocaine group (Tab. 2). According to the most traumatic surgical interventions in the scope of UEA with omentectomy and lymphadenectomy, patients also did not differ between the study groups, 12.5 % in the control group and 15.5 % in the IV lidocaine group, p = 0.3905.

Table 2. Characteristics of clinical data in the study groups during anesthesia.

Characteristics	Gr. Contr 80	Gr. IVL/83	p
Duration of surgery (min)	**119±36**	**120±45**	**0.8017†**
Type of surgical intervention:	**n/%**	**n/%**	
– UEA*	**54/67.5**	**55/66.3**	**0.5195††**
– UEA+omentectomy	**16/20**	**15/18.1**	**0.4749††**
– UEA+omentectomy+ lymphadenectomy	**10/12.5**	**13/15.6**	**0.3905 ††**
Blood loss (mL)	**141±111**	**115±53**	**0.0229†**
Intraoperative urine output (mL)	**193±264**	**226±251**	**0.1421†**
Infusion volume during surgery (crystalloids) (mL)	**908.7±245**	**890.3±194**	**0.9905†**
Infusion volume during surgery (colloid solutions) (mL)	**40.0±136**	**119.3±183**	**0.0003†**
Fentanyl (μg/kg)	**12.03±10.8**	**9.46±2.3**	**0.0001†**
Note: * UEA – uterine extirpation with appendages. † Mann – Whitney U test. †† Fisher exact one-tailed test.			

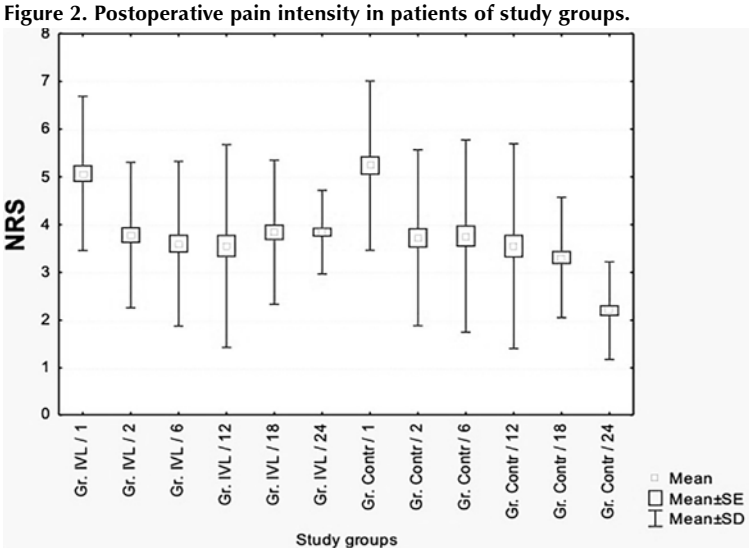
Duration of the surgery in Gr. Contr was 119±36 min, and in Gr. IVL it was 120±45 min, p = 0.8017. There were also no differences between the groups in the volume of intraoperative urine output, as well as the infusion volume of balanced solutions, but statistically significant differences were found in the volume of colloid solutions, in Gr. Contr. it was 40±136 mL, and in Gr. IVL it was 119.3±183 mL, p = 0.0003. In patients in Gr. Contr., the total dose of fentanyl during anaesthesia was 21 % higher compared to Gr. IVL (12.03±10.8 μg/kg in Gr. Contr vs 9.46±2.3 μg/kg in Gr. IVL, p = 0.0001).

Blood glucose level in Gr. Contr. patients increased from preoperative values from 5.61±1.27 mmol/L to 7.25±1.53 mmol/L at the end of the surgery and decreased to 6.12±1.44 mmol/L 24 hs post-surgery. In Gr. IVL these values were 5.56±1.02 mmol/L, 7.8±1.45 mmol/L and 6.63±1.38 mmol/L, (p = 0.0219, Gr. Contr vs Gr. IVL). Increasing of blood glucose level in patients after surgery in Contr. Gr. were 29 % at the end of the surgery, and in Gr. IVL were 40 % compared with preoperative values. One day after surgery, the blood glucose level had no significant differences in the two groups.

The total dose of fentanyl during anesthesia differed statistically significantly between groups and was 12.03±10.8 μg/kg in Gr. Contr and 9.46±2.3 μg/kg in Gr. IVL (p = 0.0001, Mann – Whitney U test). The blood loss during the surgery was 22 % greater in patients in Gr. Contr (141±111 mL) compared to Gr. IVL (115±53 mL), p = 0.0229. The urine output during the surgery had no significant differences in the two groups (Tab. 2).

The NRS score on movement in the IV lidocaine group 1 h after surgery was 5.1±1.6, after 2 hs 3.8±1.5, after 6 hs 3.6±1.7, after 12 hs 3.6±2.1, after 18 hs 3.8±1.5, and after 24 hs 3.8±0.9, whereas in the non-lidocaine group after one h it was 5.2±1.8, after 2 hs 3.7±1.8, after 6 hs 3.8±2.0, after 12 hs 3.5±2.1, after 18 hs 3.3±1.3, and after 24 hs 2.2±1.0 (Fig. 2).

Figure 2. Postoperative pain intensity in patients of study groups.



There were no statistically significant differences in postoperative pain intensity at 1, 2, 6 and 12 hs after surgery between the two groups, whereas at 18 and 24 hs after surgery, pain intensity was less in the control group, p = 0.0003 and p = 0.00001, respectively (Mann – Whitney U test). Number of pain scores of 5 or more during 24 hs of follow-up after surgery in Gr. Contr was 131, while in Gr. IVL it was 161, and was not statisti-

cally significantly different between the two groups, p = 0.1150 (Fisher exact one-tailed test).

The mean opioid dose (equivalent to morphine sulfate) during the first 24 hs after surgery was 23.73±6.76 mg in Gr. IVL, and in 27.96±5.0 mg in Gr. Contr p = 0.0001 (Mann – Whitney U test).

The number of patients reporting sleep disorders in the first 24 hs after surgery is presented in Table 3. In Gr. IVL sleep quality scores of 2 points were 0.05 % (4 patients), 3 points – 18.75 % (15 patients), 4 points – 58.75 % (47 patients) and 5 points – 21.25 % (17 patients), whereas in Gr. Contr these scores were as follows: 2 points – 1.25 % (1 patient), 3 points – 35.0 % (28 patients), 4 points – 37.5 % (30 patients) and 5 points – 2.5 % (2 patients). Statistically significant differences were found for sleep quality scores of 4 and 5, p = 0.0438 and p = 0.0009, respectively.

The number of patients reporting nausea and vomiting after surgery is presented in Table 3. One h after surgery, 21.25 % of patients in Gr. Contr experienced nausea, and at 2, 6, 12, 18, and 24 hs after surgery, 17.5 %, 11.25 %, 3.75 %, 1.25 %, and 0 %, respectively. In the lidocaine group, these figures were 14.45 %, 14.45 %, 14.45 %, 8.75 %, 1.2 %, and 0 %, respectively, and were not statistically different between the study groups.

In 4 patients (5 %) of Gr. Contr, intestinal peristalsis appeared 6 hs after surgery, in 23 patients (28.75 %) 12 hs, in 23 patients (28.75 %) 18 hs and in 21 patients (26.25 %) 24 hs after surgery. In patients in the IV lidocaine group, these values were: in 1 patient (1 %) one h after surgery, in 5 patients (6 %) 2 hs after surgery, in 28 patients (33.7 %) 6 hs after surgery, in 57 patients (67.8 %) 12 hs after surgery, in 67 patients (80.7 %) 18 hs after surgery, and in 72 patients (86.7 %) 24 hs after surgery. Statistically significant differences between groups were established at 2, 6, 12, 18 and 24 hs after surgery (Tab. 3).

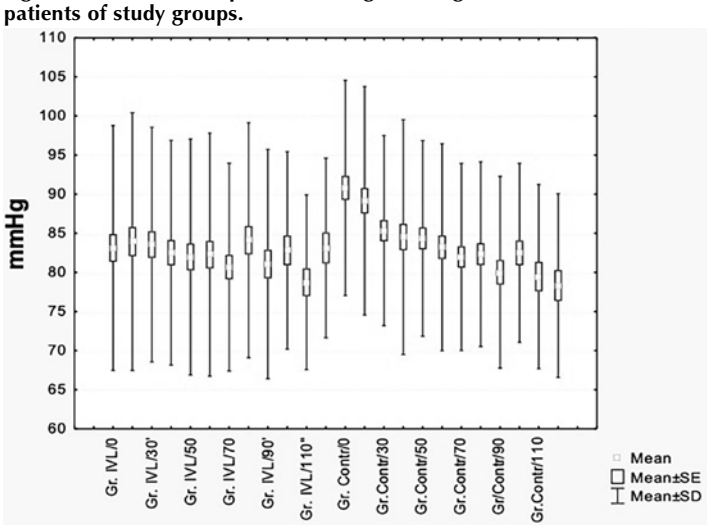
Table 3. Clinical changes identified during the study.

	1 h	2 hs	6 hs	12 hs	18 hs	24 hs
Peristalsis after surgery, n/%						
Gr. Contr	0/0	0/0	4/5	23/28.75	23/28.75	21/26.25
Gr. IVL	1/1	5/6	28/33.7	57/68.7	67/80.7	72/86.7
p*	0.5122	0.0373	0.0001	0.0018	0.0036	0.00001
Nausea after surgery, n/%						
Gr. Contr	17/21.25	14/17.5	9/11.25	3/3.75	1/1.25	0/0
Gr. IVL	12/14.45	12/14.45	12/14.45	7/8.75	1/1.2	0/0
p*	0.2283	0.4052	0.3812	0.1998	0.7424	1.000
Note: p* – Fisher exact one-tailed test.						

Evaluating of the effect of prolonged lidocaine infusion during surgery on mean arterial pressure (MAP) and heart rate (HR) demonstrated no statistically significant differences between the groups (Figs 2 and 3). Also, no statistically significant differences were found between the groups in hemodynamic parameters on the first day in the postoperative period (Figs 4 and 5).

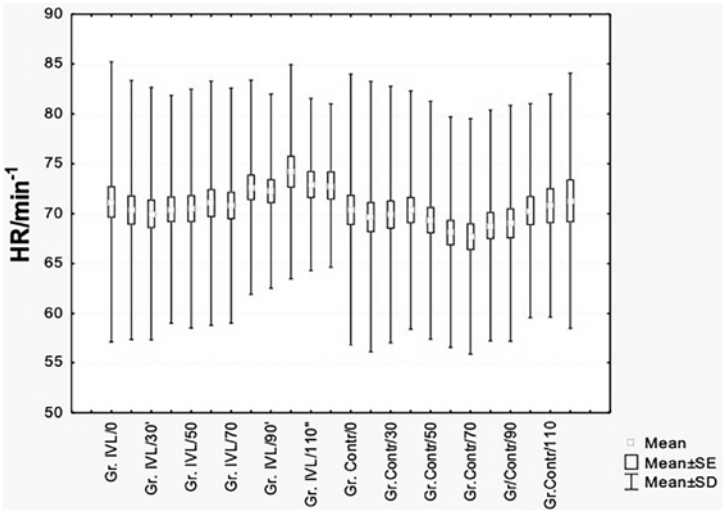
During anesthesia in Gr. IVL patients, MAP was in the range of 78 – 84 mm Hg, in Gr. Contr patients between 70 – 90 mm Hg with no significant difference between the study groups (Fig. 3).

Figure 3. Mean arterial pressure changes during anaesthesia in patients of study groups.



Heart rate in the IV lidocaine group during surgery did not exceed 74±10 bpm^{-1} and did not decrease below 69±12 bpm^{-1}. In control group patients, HR during surgery did not exceed 76±6 bpm^{-1} and did not decrease below 67±12 bpm^{-1} (Fig. 4).

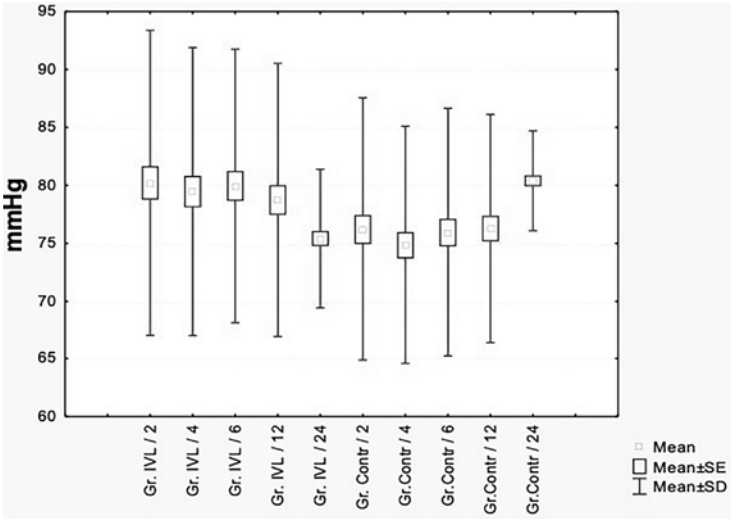
Figure 4. HR change during anesthesia in patients in the study groups.



Changes in MAP in the postoperative period in both groups were not clinically significant, but a statistically significant reduction of MAP by the end of the first postoperative day was found in Gr. IVL (p = 0.0001, Friedman ANOVA and Kendall Coeff.), whereas in Gr. Contr patients revealed an increase in MAP by the end

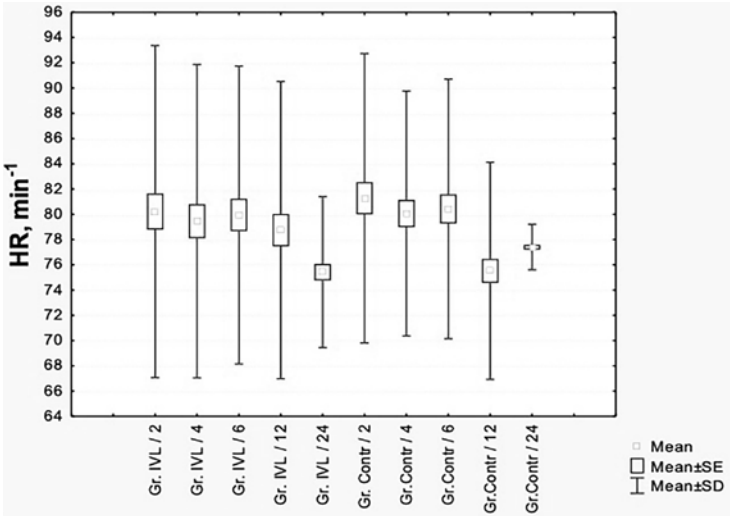
of the first day after surgery (p = 0.0001, Friedman ANOVA and Kendall Coeff.) (Fig. 5).

Figure 5. Change in mean blood pressure on the first postoperative day in patients in the study groups.



Changes in heart rate (HR) in the postoperative period in both groups were also not clinically significant, but statistically significant reduction of HR by the end of the first postoperative day was found in Gr. IVL (p = 0.0330, Friedman ANOVA and Kendall Coeff.), whereas in Gr. Contr patients revealed an increase in HR by the end of the first day after surgery, (p = 0.0001, Friedman ANOVA and Kendall Coeff.) (Fig. 6). By the end of the first post-surgery day, the HR in the lidocaine group was 75±6 bpm^{-1}, and in the control group 80±4 bpm^{-1}, p = 0.0001 (Mann – Whitney U test).

Figure 6. Change in heart rate on the first postoperative day in patients of the study groups.



Since no patient in the study had mental status disorder and LAST (local anesthetic systemic toxicity), measuring the plasma lidocaine levels wasn't performed.

Discussion

Current guidelines for perioperative pain management recommend a multimodal analgesia/anesthesia strategy. This approach helps to reduce doses of opioid analgesics in the perioperative period. Various adjuvant drugs including antidepressants, anticonvulsants, alpha-2 agonists, lidocaine, etc. have been proposed to achieve such non-opioid or low-opioid anesthesia and analgesia (2 – 4, 25, 26). This study wasn't demonstrated a beneficial effect of intravenous lidocaine infusion during surgery and in the postoperative period in patients who underwent gynecologic oncology surgery as a component of multimodal anesthesia and analgesia.

It was found that prolonged infusion of lidocaine during anesthesia reduced the total fentanyl dose by 23 % compared to the control group (9.46±2.3 vs 12.03±10.8 μg/kg). However, the extent to which this is clinically significant remains a rhetorical question. Similar results were obtained by Weibel et al. (35) who showed that IV infusion of lidocaine during surgery, while reducing opioid consumption, resulted in such differences that were not clinically relevant.

Despite the reduction of fentanyl dose during surgery in the lidocaine group, the severity of stress response was greater in patients of this group, which was manifested by an increase in blood glucose level after the end of surgery. This may suggest that quantitative reduction of the opioid analgesic dose due to IV administration of lidocaine during surgery does not reduce the severity of the surgical stress response on surgery trauma.

It was also founded that IV lidocaine infusion during anesthesia decreased fentanyl requirements but increased the infusion volume of colloid solutions during surgery, while the blood loss during surgery was greater in the control group. The volume of crystalloids during surgery did not differ between the two groups. Is the increase in volume of infusion and blood loss directly related to lidocaine infusion? A possible explanation for the differences in blood loss volume may be that lidocaine has a biphasic action on peripheral vascular smooth muscle, with vasoconstriction at low concentrations and vasodilation at higher concentrations (23). At higher concentrations, lidocaine exerts a dose-dependent vasodilating effect, which may have required an increase in colloid infusion volume to stabilize hemodynamics.

The study failed to show significant benefits in the quality of postoperative analgesia. The intensity of postoperative pain on movement differed only at 18 and 24 hs after surgery, and the number of pain scores of 5 or more at 24 hs did not differ between the study groups. In contrast to our results, several studies and meta-analyses have shown that lidocaine infusion in the perioperative period induces analgesia, which can vary significantly depending on the type of surgical intervention (4). The doses used during the study ranged from 1.5 to 3 mg/kg/h for open abdominal surgeries (1, 32). It should be noted that pain intensity in these studies de-

creased modestly 24 hs after surgery, noting that the reduction in opioid dose was clinically insignificant.

Abdominal hysterectomy is one of the most common gynecological surgeries in women. The incidence of severe postoperative pain can range from 5 % to 30 % (26). Preventive analgesia techniques have shown positive effects in various types of surgical interventions (21), which help in reducing the percentage of severe pain to a great extent. ERAS (Enhanced Recovery After Surgery) guidelines in gynaecology/gynaecologic oncology (updated in 2019) recommend intravenous lidocaine as a component of anesthesia (25). According to these guidelines, IV lidocaine infusion reduces intraoperative anesthetic requirements, improves the quality of analgesia, reduces the need for postoperative analgesics, and accelerates the recovery of bowel function with decreased length of hospital stay. The same revision of the protocol does not recommend the use of intravenous lidocaine as a component of multimodal analgesia in postoperative anesthesia. A possible reason for the lack of differences in analgesia between the two groups in our study was that we used a lidocaine dose of 1 mg/kg/h, whereas in studies by other authors that showed significant improvement in the quality of analgesia, lidocaine doses ranged from 1.5 to 3 mg/kg/h (1, 32).

During our study were estimated the difference in total morphine dose for analgesia between the control group and Gr. IVL The opioid-sparing effect of IV lidocaine was only 17 %. De Oliveira et al. (7) study showed an average 35 % reduction in hydromorphone dose, with patients receiving PCA with hydromorphone/ketamine, and the lidocaine dose was not specified in the study. Disappointing outcomes for IV lidocaine administration were also shown in another study in patients after mastectomy (31). Thus, different trials showed no significant effect of intravenous lidocaine administration during breast cancer surgery on opioid consumption and pain scores, suggesting that the benefit of this approach does not apply to all types of surgery.

It is possible that administration of lidocaine at a dose less than 2 mg/kg/h in patients after major abdominal surgery does not reduce opioid doses on the first day of the postoperative period. Similar results were also shown by Xu et al. (36).

In the postoperative period, the patients in the group of IV lidocaine infusion had hypotension during the first postoperative day, while the opposite trend was found in the patients of the control group. Such differences may also be explained by the vasodilating effect of lidocaine, which was enhanced by an accumulative effect due to prolonged administration of this anesthetic agent.

One of the few differences between the two study groups was better sleep quality on the first postoperative day and earlier onset of intestinal motility in patients who received lidocaine in the perioperative period. At the same time, the incidence of nausea did not differ between the groups. Our data confirmed the results obtained by other investigators. Thus, perioperative infusion of lidocaine shortened the time to recovery of intestinal peristalsis by an average of 8 hs (6). These benefits may be related to the reduced effect of opioids on GI motility. There have been enough studies about the positive effect of regional anesthetic techniques (20). However, there are quite contradictory data on the positive effect of IV lidocaine administration reported by other investigators. Thus, different investigations demonstrated faster recovery of gastrointestinal function, but the results were not statistically significant (16, 28).

Conclusion

It was founded no clinically significant reduction in pain or need for opioid analgesics with perioperative IV lidocaine infusion during gynecologic oncology surgeries, suggesting that this technique of lidocaine infusion does not have the same beneficial effect in all types of surgical interventions. Therefore, the positive results obtained with one type of surgery cannot be extrapolated to other types of surgery. This technique can only be effective for certain types of surgery.*

***Conflicts of Interest.** The authors declare that there is no conflict of interest.

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