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Perioperative regional anaesthesia in kidney transplantation

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Abstract

Background. *Postoperative analgesia in kidney transplant recipients is challenging due to potential nephrotoxicity of nonsteroidal anti-inflammatory drugs and the reduced clearance of opioid metabolites during transient renal impairment. Opioid-sparing multimodal postoperative analgesia using regional analgesia methods could provide better pain control and early activation after kidney transplantation.*

Aim. *To evaluate the clinical results of treatment using regional pain management methods in kidney transplant recipients.*

Material and methods. *A single-center study was conducted at Republican Research Center of Emergency Medicine from 2020 to 2022. The study included 97 patients who underwent heterotopic kidney transplantation from a living related donor. Patients were divided into 3 groups. In group 1 (31 patients), general anesthesia was used. For postoperative analgesia opioid analgesics in combination with metamizole 1000 mg were used. In group 2 (33 recipient patients), a combination of general anesthesia and open transversus abdominis plane block was used. In group 3 (33 recipient patients), a combination of general anesthesia and erector spine plane block was performed. Opioid*

analgesics were used as a "rescue analgesia" when necessary. The primary study end points were the pain intensity assessed by a visual analogue scale and opioid consumption on the first day after surgery. Secondary endpoints were the time of intestinal motility recovery, the presence of nausea and vomiting, the intensive care unit length of stay and the hospital length of stay.

Results. *Pain intensity 6 hours after surgery in patients of group 1 was 13.5% and 24.6% higher than in patients of group 2 and 3, respectively. In group 2, pain intensity was 12.8% higher compared to group 3 ($p=0.0017$). At 12 hours after surgery, the pain intensity was 42% higher in group 1 compared to group 2 and group 3 ($p<0.0001$). After 18 hours, the pain score in group 3 was 48.5% and 35.7% lower compared to groups 1 and 2, respectively ($p<0.0001$ and $p=0.0016$). 24 hours after surgery, the sensation of pain was 18.6% and 65.3% higher in group 1 compared to groups 2 and 3 ($p<0.0001$). The mean dose of narcotic analgesic equivalent to morphine in group 1 was 22.6±8.6 mg, which was 18.5% higher than in group 2 patients. In group 3, it was 12.0±4.3 mg and was 47% lower compared to group 1 ($p<0.0001$) and 34.7% lower compared to group 2 ($p<0.0001$) (all comparisons are statistically significant). The adequacy of analgesia and less opioid consumption contributed to the absence of postoperative nausea and vomiting in 75% of cases, early restoration of intestinal motility in 63% compared with the group of patients where opioid analgesics were used for postoperative pain relief.*

Conclusion. *The combined use of general anesthesia and erector spine plane block may be recommended as a method of effective perioperative analgesia in kidney transplantation.*

Keywords: kidney transplantation, preoperative analgesia, transverses abdominals plane block, erector spine plane block, visual analogue scale

Conflict of interests Authors declare no conflict of interest

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ASA, American Society of Anesthesiologists
CGN, chronic glomerulonephritis
CKD, chronic kidney disease
ESP block, erector spinae plane block
NAs, narcotic analgesics
PONV, postoperative nausea and vomiting
TAP block, transversus abdominis plane block
VAS, visual analogue scale

Introduction

Regional anesthesia methods as part of a perioperative pain management regimen have become increasingly popular today, especially with the development of ultrasound technology. The use of multimodal opioid-sparing anesthesia technology with the inclusion of regional blocks in the anesthesia and postoperative analgesia regimen promotes early extubation of patients reducing the consumption of narcotic analgesics (NAs) and reducing the negative effects inherent in narcotic analgesics therapy [1, 2].

The Enhanced Recovery After Surgery (ERAS®) Society has recommended the use of multimodal analgesia both to improve postoperative pain control, and also to facilitate early oral intake, mobilization, and accelerated surgical recovery. This approach is based on a combination of opioids, non-opioid analgesics and regional anesthesia techniques [3, 4]. Today, regional blocks under the ultrasound imaging guidance have become more commonly used in surgical interventions for kidney transplantation [5, 6]. Monotherapy with

systemic analgesics (opioids, paracetamol, non-narcotic analgesics) is insufficient to completely protect the operated patient from surgical stress [7]. It is necessary to take into account the possibly threats of using non-steroidal anti-inflammatory drugs and paracetamol in kidney transplant recipients [8]. More thoroughly designed studies are needed in the future to further evaluate the safety and efficacy of regional analgesia techniques in kidney transplant patients.

The objective was to assess the clinical results of treatment using regional pain management methods in kidney transplant recipients.

Material and methods

The study was conducted at the Republican Research Center of Emergency Medicine (Tashkent, Uzbekistan) in the period from 2020 to 2022. The study included 97 patients who underwent heterotopic living related donor kidney transplantation. The patient inclusion criteria for the study were kidney transplant recipients over the age of 18 years. The criteria of exclusion from the study were children, allergy to local anesthetics. Patients were assigned into three groups depending on the method of anesthesia and the method of postoperative pain management. The first and second groups consisted of patients who were included in the study retrospectively. In the first group (n=31), regional anesthesia methods were not used. In group 2 (n=33), at the end of the surgical intervention, the patients underwent transversus abdominis plane block (TAP block) under surgeon's visual control by using 20 ml of 0.25% bupivacaine solution *(Bupilong, Jurabek pharmaceuticals, Uzbekistan)* (50 mg) on the side of the surgical incision, with the addition of dexamethasone 4 mg as a local anesthetic adjuvant. In group 3, the patients (n=33) were included in the study prospectively; and before the induction in general anesthesia, in a sitting position, they underwent an

ultrasound-guided catheterization of the erector spinae plane (ESP) on the incision side at the level of T11. After the block had been performed with determining the level and area of anesthesia coverage, the induction in anesthesia was undertaken, which was similar to the 1st and 2nd groups. Intraoperative fentanyl administration in this group was performed in boluses of 50–100 mcg as needed (monitoring the increases in the heart rate, and mean arterial pressure). Postoperative pain management in this group of patients was performed with an extended erector spinae plane block (ESP block), as well as metamizole, similarly to the previous groups, 1000 mg every 8 hours intravenously.

The general anesthesia method was similar in all groups. The induction anesthesia included propofol (*Sayfol, Novell Pharmaceutical Laboratories, Indonesia)* 2–2.5 mg/kg; fentanyl *(Moscow Endocrine Plant, Russian Federation)* 2–5 mcg/kg; cisatracurium *(Mioxant, Liquor, Armenia)* 0.1 mg/kg. The maintenance anesthesia included isoflurane *(Izotroy, Troikaa pharmaceuticals, India)* 0.8–1.2 MAC (minimum alveolar concentration); fentanyl 5 μg/kg/h; cisatracurium 2.5–5 mg/h. All groups underwent postoperative baseline pain management with metamizole *(Analgin, Merry-Med, Uzbekistan)* 1000 mg intravenously every 8 hours; and, the "rescue analgesia" was administered on patient's demand, with morphine *(Morphine hydrochloride, Moscow Endocrine Plant, Russian Federation)* or trimepyridine *(Promedol, Moscow Endocrine Plant, Russian Federation).*

All 97 patients had chronic anemia, symptomatic arterial hypertension; all of them were on the maintenance hemodialysis and assigned ASA III level by American Society of Anesthesiologists (ASA) Physical Status Classification. Clinical and demographic data of patients are shown in the table.

Table. Clinical and demographic data of patients

Parameter	Group 1, without regional anesthesia (n=31)	Group 2, TAP block (n=33)	Group 3, ESP block (n=33)	p
Age, years	32.6±10.4	35.3±10.5	32.3±8.7	0.88*
Male/Female	23/8	23/10	23/10	0.21**
BMI	21.4 (19.4;23.3)	22.6 (20.6;24.9)	22.6 (20.1;24.2)	0.506***
CKD causes: CGN Urolithiasis	 31; 100% 0	 32; 97% 13%	 32; 97% 13%	 0.99**

Notes: Data are presented as mean (M) and standard deviation (±σ) or as a median with interquartile range, or as absolute number and percentage. * One way ANOVA; ** χ^2 test; *** Kruskal–Wallis test; BMI, body mass index; CKD, chronic kidney disease; CGN, chronic glomerulonephritis

The primary end points of the study were pain intensity as assessed on a visual analogue scale (VAS) and consumption of narcotic analgesic in morphine equivalent on the first day after surgery. VAS pain intensity was assessed at 6, 12, 18 and 24 hours after the surgery completion, and the mean value was recorded. The secondary endpoints were the timing of gastrointestinal motility recovery confirmed by the appearance of intestinal peristalsis on auscultation of the abdomen and(or) the passage of intestinal gases; the presence of nausea and vomiting; the intensive care unit length of stay and total hospital length of stay.

Statistical analysis was performed using the StatTech software, v. 3.1.6 (developed by Stattekh LLC, Russia) and the online resource https://www.sociostatistics.com/. Data were checked for normality of distribution using the Kolmogorov–Smirnov test. The parametric quantitative data are presented as means and standard deviation. The nonparametric data are presented as medians with interquartile range. Qualitative parameters are presented in the form of absolute numbers and percentages. For comparative analysis of parametric quantitative data, one-way analysis of variance was used. For nonparametric data, the Kruskal–Wallis test was used. For comparative analysis of qualitative parameters, the χ^2 test was used.

Results

Pain assessment using VAS revealed that at 6 hours after surgery, pain sensations in patients of group 1 were 13.5% and 24.6% higher than in patients of groups 2 and 3, respectively. A comparison of groups 2 and 3 revealed 12.8% higher pain intensity scores in group 2 compared to group 3 ($p=0.0017$, statistically significant). At 12 hours after surgery, pain intensity in group 1 was 41.6% higher compared to that of group 2 ($p=0.03$, statistically significant), and 41.5% higher than in group 3 ($p<0.0001$, statistically significant). Patients of groups 1 and 2 experienced moderate pain, and patients of group 3 felt mild pain although pain management in this group was limited to regional analgesia. At 18 hours after surgery, VAS pain scores in all three groups tended to further decrease. The VAS pain score in group 3 was statistically significantly lower by 48.5% and 35.7%, respectively, compared to groups 1 and 2 ($p<0.0001$ and $p=0.0016$). Comparison of data from groups 1 and 2 revealed that the pain intensity in group 2 was 20% lower than in group 1 ($p=0.0004$). At 24 hours after the surgery completion, pain sensations in group 1 were statistically significantly higher (by 65.3%) compared to group 3 and corresponded to severe pain, while the patients in group 3 experienced mild pain ($p<0.0001$). In group 2, the patients experienced moderate pain, but it was 57.3% higher than in group 3.

Comparison of data from groups 1 and 2 revealed that in the group where an open TAP block was used, pain sensations according to VAS were statistically significantly lower, by 18.6%, compared to group 1 ($p<0.0001$) where the regional anesthesia methods were not used (Fig. 1).

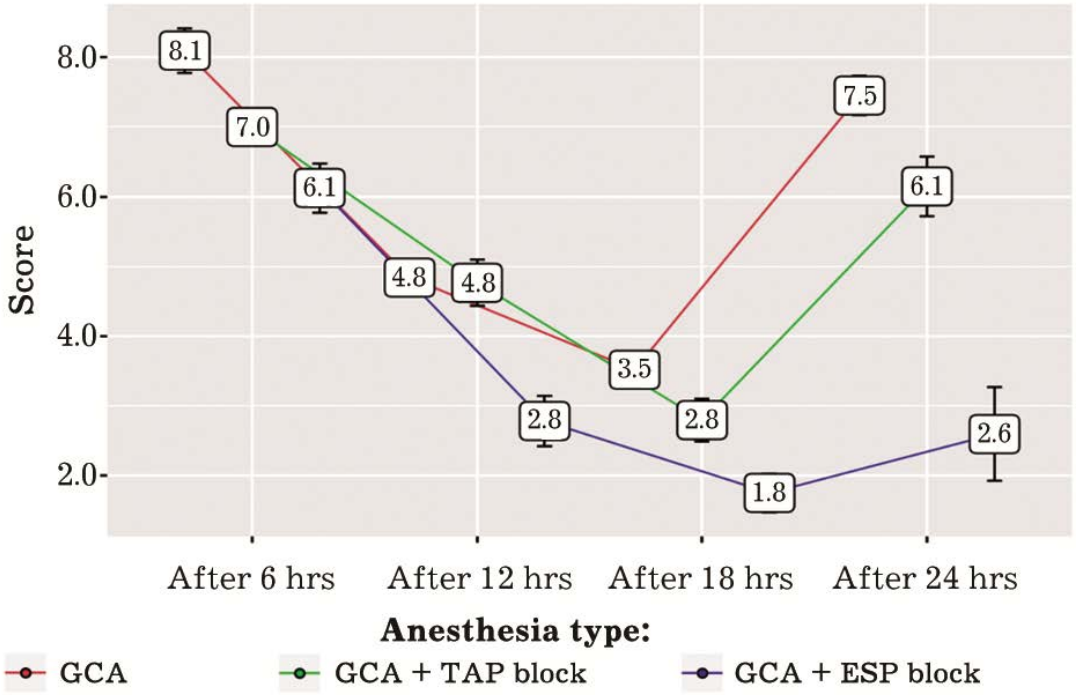

Fig. 1. Pain assessment using a visual analogue scale

In group 1, a narcotic analgesic drug was used in 100% of cases. The mean dose of NA equivalent to morphine was 22.6±8.6 mg, which was 18.5% statistically significantly higher than in the patients of group 2, of whom 94% required the NA use, and a mean dose equivalent to morphine in this group was 18.4±7.0 mg (p=0.036). In group 3, 78% of the total number of patients required the use of NA, while the mean dose of NA equivalent to morphine was 12.0±4.3 mg. The amount of NA consumed for postoperative pain relief in group 3 was statistically significantly lower (by 47%) compared to group 1 (p<0.0001) and by 34.7% lower compared to group 2 patients (p<0.0001) (Fig. 2).

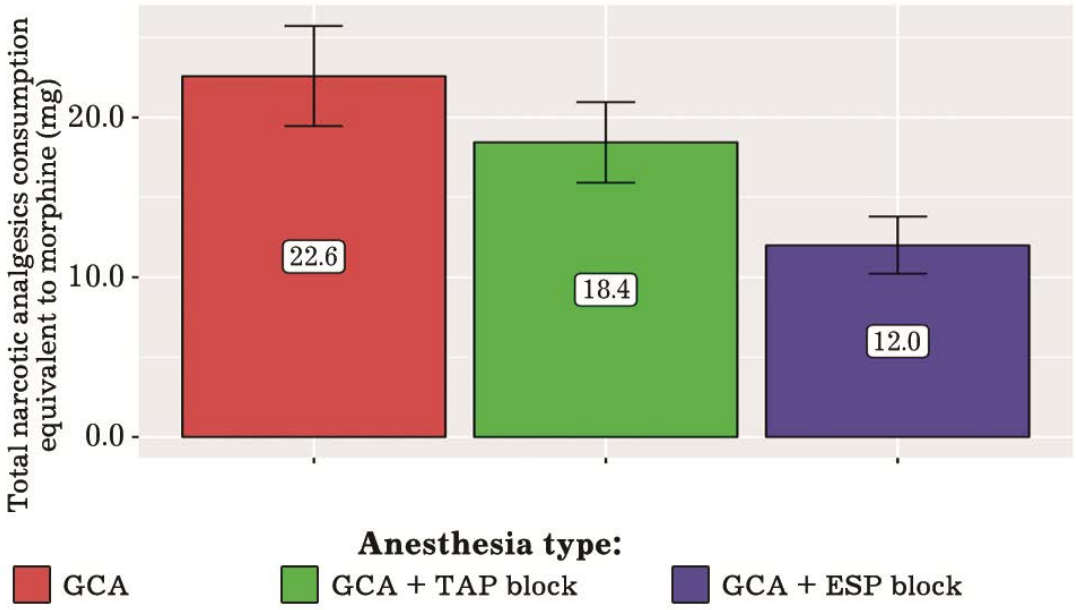

Fig. 2. Consumption of narcotic analgesics

The study analyzed the development of postoperative nausea and vomiting (PONV). Against the background of GCA and analgesia in the postoperative period, the PONV cases were seen more often in patients of group 1. Fifteen patients of group 1 had PONV symptoms, this amounted to 48.4%. The remaining 16 patients (51.6%) did not have PONV. In group 2, PONV phenomena were observed in 20.6% of cases (7 patients), which was statistically significantly lower (by 57.4%) compared to group 1. In the 3rd group, PONV was seen in 4 cases, amounting to 12.5%; that was statistically significantly lower (by 39.3%) compared to group 2 and by 74.1% compared to group 1 (Fig. 3).

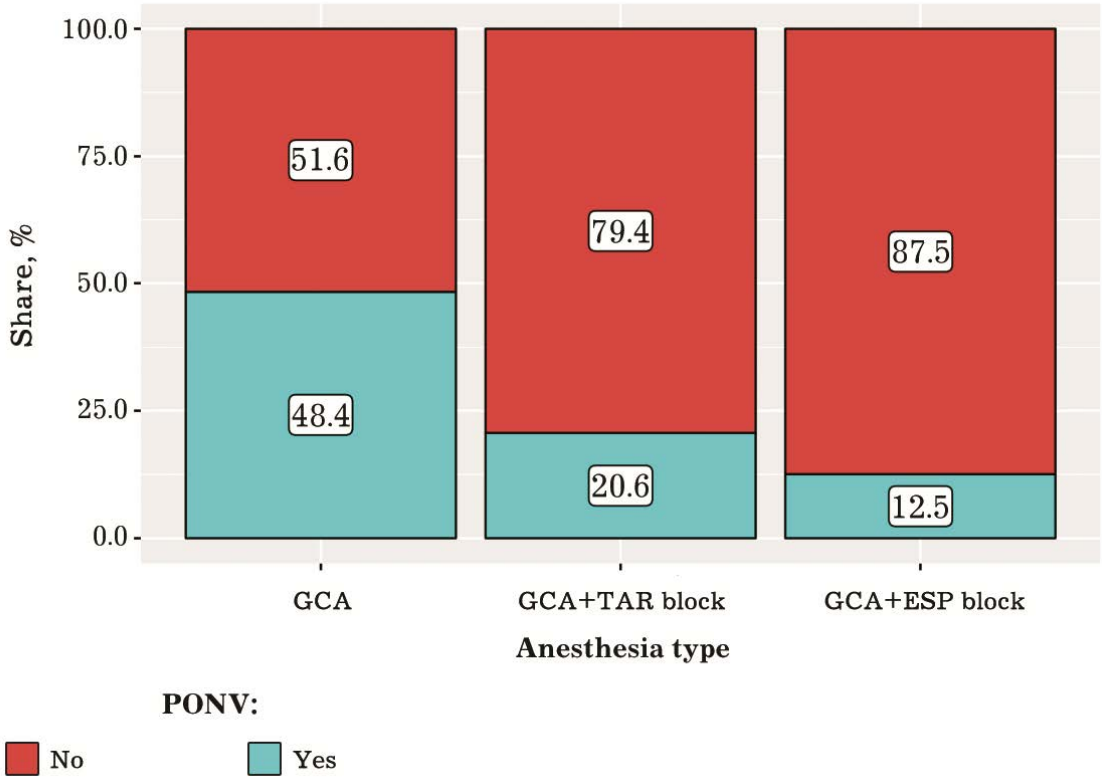

Fig. 3. Development of postoperative nausea and vomiting

An analysis was performed on the time to the intestinal motility recovery with respect to the type of anesthesia and postoperative pain management. The time till the intestinal motility recovery determined as the appearance of intestinal motility during auscultation of the abdomen and (or) the passage of intestinal gases, in group 1 was 24.2±3.1 hours (95% CI [23.1–25.3]), which was 36.3% statistically significantly longer than in group 2, where this parameter made 15.4±4.3 hours (95% CI [13.9–16.8]). The shortest time required to restore the intestinal motility in the postoperative period was observed in group 3 making 8.9±4.5 hours (95% CI [7.3–10.5]). A statistically significant difference was revealed in the timing of the intestinal motility recovery between the patients of the 1st and 3rd groups; the intestinal motility recovery took place 63.2% earlier in group 3 versus group 1. A comparison of groups 2

and 3 revealed a 42.2% earlier intestinal motility recovery in group 3 (Fig. 4).

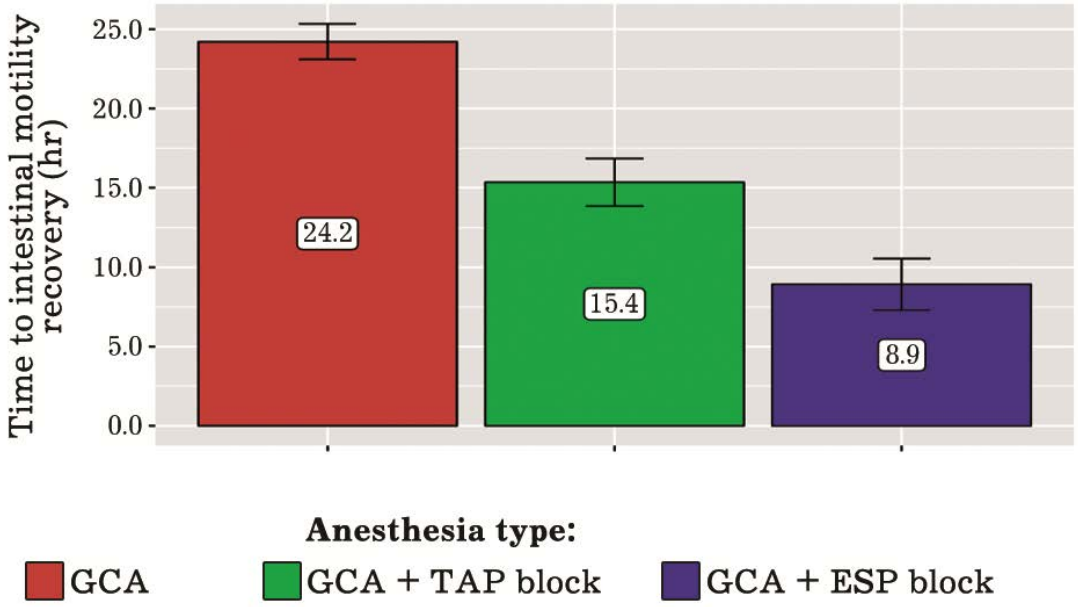

Fig. 4. Time frame for intestinal motility recovery

Given the lower NA consumption, better quality of postoperative pain management, earlier recovery of intestinal motility, absent PONV, the intensive care unit length of stay for patients of group 3 was shorter making 2.03±0.18 bed days (95% CI [1.97–2.09]), which was statistically significantly lower (by 28.5%) compared to the patients of group 1, where the intensive care unit length of stay was 2.84±0.90 bed days (95% CI [2.51–3.17], $p<0.0001$). In group 2 patients, intensive care unit length of stay was 2.21±0.41 bed days (95% CI [2.06–2.35], $p=0.028$). On account of lower NA consumption, the intensive care unit length of stay for patients of group 2 was statistically significantly lower (by 22.1%) compared to group 1. The best clinical outcomes of the early postoperative period in group 3 contributed to a statistically significantly

lower number of bed days (by 8.1%) compared to group 2 (p=0.0005) (Fig. 5).

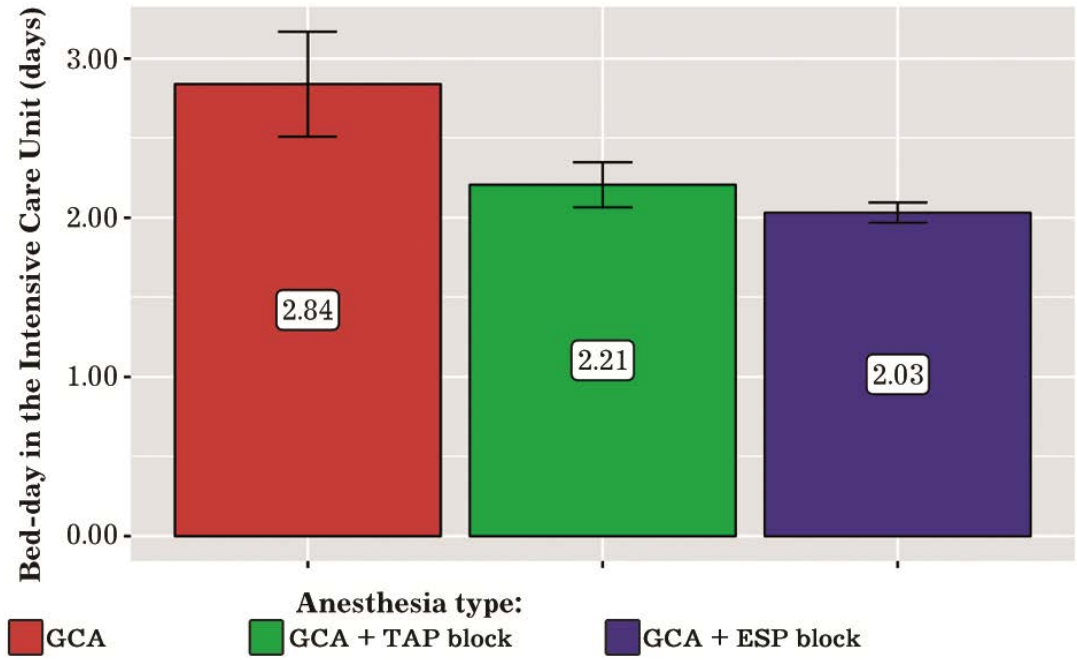

Fig. 5. Patients' length of stay in the Intensive Care Unit

The analysis the total hospital length stay revealed that the patients of group 1 stayed in hospital for a mean of 11.13±5.21 days (95% CI [9.22–13.04]), and the patients of group 2 stayed in hospital for a mean of 9.88±5.53 days (95% CI [7.95–11.81]), which was 11.2% shorter compared to patients in group 1 (p=0.35). Patients of group 3 stayed in hospital for 8.25±2.20 days (95% CI [7.46–9.04]), which was statistically significantly shorter (by 25.8%) compared to group 1 (p=0.047, statistically significant) and statistically significantly shorter (by 16.4%) compared to the patients of group 2 (p=0.12) (Fig. 6).

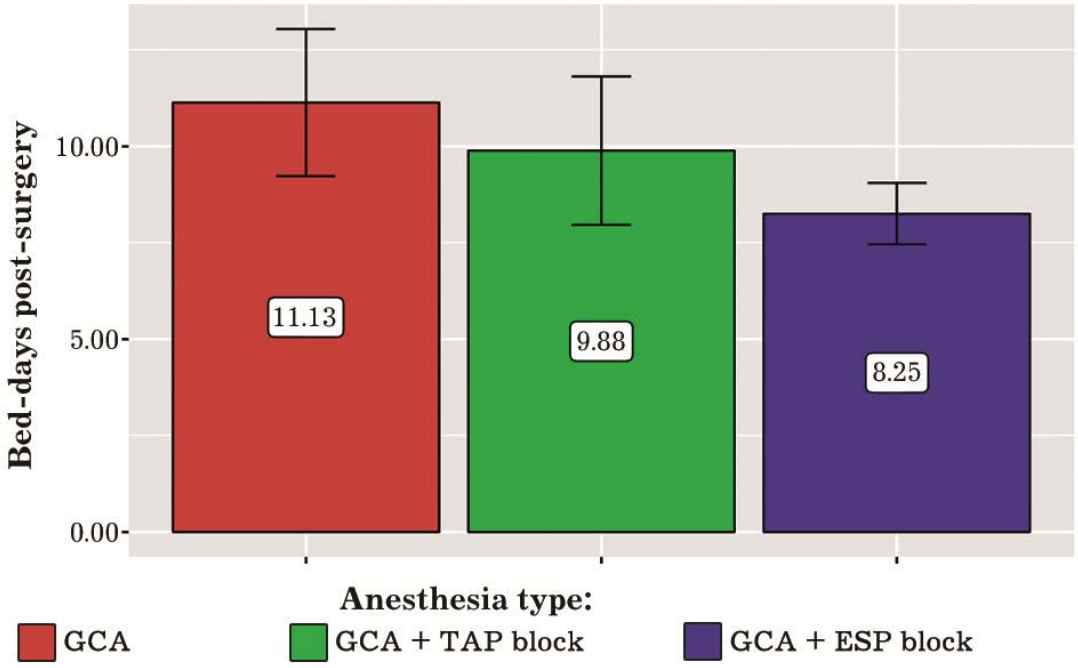

Fig. 6. Patients' length of stay in the intensive care unit

Discussion

The problems of pain management in patients after kidney transplantation are relevant today and require scientific research and evidence base. R. Chou et al. believe that the consequences of poorly controlled postoperative pain are significant, including cardiopulmonary complications, opioid-related side effects, unplanned hospitalization, longer hospital length of stay, and subsequent development of chronic pain or opioid dependence [9]. S.N. Davison et al. argue that despite advances in both surgical treatment and anesthesia techniques, postoperative pain remains an important problem in patients with chronic renal failure who undergoing kidney transplantation [6]. K.L. Lentine and K.C. Abbott, in independent studies, stated that the opioid analgesics consumption by the patients with the end-stage renal disease remains high, and previous studies show that 50% of opioid-naive patients continue to receive opioid analgesics in the postoperative period [8, 10]. S. Shruti et al. believe that the use of multimodal opioid-sparing

technology with the inclusion of regional anesthesia blocks helps reducing the NA consumption [2].

K. Mukhtar et al. were the first to study the efficacy of TAP block in kidney transplant recipients. Twenty selected patients were equally divided into study and control groups. The authors observed a statistically significant reduction in postoperative morphine requirements in the TAP block group. Pain scores were significantly lower in the TAP block group, and the incidence of nausea, vomiting, and sedation was significantly lower in the TAP block group compared to those in the control group [11]. B.K. Parikh et al. examined the efficacy of continuous TAP block in 40 kidney transplant recipients and obtained similar results, demonstrating in relieving pain as assessed by VAS, and a longer time till the first analgesic required [12]. E. Farag et al. used a continuous infusion of ropivacaine 0.5% for TAP block in kidney transplant recipients and reported on the reductions in opioid dosages and improvements in postoperative pain assessment scores, similar to the studies using bupivacaine [13].

In our study, the combination of regional anesthesia and on-demand use of NA contributed to a reduction by 18.2% in NA consumption for postoperative pain relief, and 20% lower subjective pain sensations by VAS assessment. There was also a 57.4% decrease in the PONV manifestations, a 36.3% earlier recovery of intestinal motility, a decrease by 22.1% in the intensive care unit length of stay, and by 11.2% in the hospital length of stay compared to the group where regional analgesia was not used, and NAs were routinely used for postoperative pain management. The greatest efficacy has been proven and confirmed by the scheme of extended erector spinae plane block in combination with NA as “rescue analgesia.” The duration and adequacy of pain relief with low NA consumption (47% lower than in the group with NA

monoanalgesia) contributed to the absence of postoperative nausea and vomiting in 75% of cases, early recovery of intestinal motility by 63% compared to the group of patients where NA was used for postoperative pain relief. Attributing to a better clinical course of the postoperative period, the intensive care unit length of stay reduced by 28.5%, and the hospital length of stay did by 25.8%.

Conclusions

1. The use of an open erector spinae plane block at the end of surgery contributes to a 20% lower sensation of pain, being statistically significant ($p=0.0004$) and a 20% reduction in the consumption of narcotic analgesics, being also statistically significant ($p=0.036$) on the first day after surgery compared to a standard pain relief with narcotic analgesics.

2. Extended erector spinae plane block contributes to a statistically significant reduction in pain intensity, being by 47% lower compared to standard analgesia ($p<0.0001$). The use of this method of regional anesthesia also contributes to the avoidance of postoperative nausea and vomiting in 75% of cases and to earlier recovery of intestinal motility than with standard analgesia.

3. Attributing to a better clinical course of the postoperative period compared to standard ananalgesia, the intensive care unit length of stay reduced by 28.5% ($p<0.0001$), and in the hospital length of stay did by 25.8% ($p=0.047$, statistically significant for both parameters).

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