

**Comparison of a combined general anesthesia to a combined
inhalational and epidural anesthesia for kidney and pancreas
transplantation**

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Objective: To assess the efficacy of epidural anesthesia as a component of a combined inhalation anesthesia in patients undergoing kidney and pancreas transplantation.

Material: A single-center retrospective study of anesthesia in 21 patients who underwent a simultaneous kidney and pancreas transplantation in N.V. Sklifosovsky Research Institute for Emergency Medicine.

Results: The use of the combined inhalational and epidural anesthesia allows early mobilization of patients after kidney and pancreas transplantation.

Keywords: epidural anesthesia, simultaneous kidney and pancreas transplantation, insulin-dependent diabetes mellitus.

Introduction

Currently, the main candidate population for a simultaneous kidney-pancreas transplantation (SKP Tx) includes: individuals suffering from insulin-dependent diabetes mellitus (IDDM) with end-stage chronic renal

failure (CRF) and/or other diabetic complications; patients with diabetic nephropathy in pre-uremic stage with associated diabetic complications; patients with complicated course of diabetes mellitus (DM); renal transplant recipients with DM after unsuccessful previous kidney transplantation [1, 2]. Despite such a wide range of individuals with indications to SKP Tx, this procedure is the operation of choice primarily for the patients with the end-stage CRF developed as an outcome of diabetic nephropathy [1-3, 8].

Type I diabetes mellitus mainly develops in childhood and adolescence [4, 9]. Mortality from renal failure is the highest, as a rule, among those aged 25-35 years, i.e. it affects young people of working-capable age [1, 5, 8, 11]. In this regard, diabetes and its renal complications have long ceased to be just a medical problem, but became social and economic challenge by nature [1, 4-6].

As far as the chronic renal failure develops into its end-stage in diabetic patients at the age of 25-30 years, the age of operated patients is commonly from 30 to 46 years old [1, 7, 11]. The initial severity of recipient's condition dictates specific requirements to anesthesiologic management that should ensure an effective protection of the human body from surgical trauma [8, 10, 11]. In the perioperative period, one of the main tasks is to maintain an optimal balance between the measures to correct the various components of homeostasis and the functional activity of the transplanted organ [11].

Objective: To assess the efficacy of epidural anesthesia in a comparative evaluation of the anesthetic protection in patients undergoing SKP Tx under a combined general anesthesia using sevoflurane with fentanyl

versus a inhalational anesthesia in combination with a dosed epidural infusion of naropin solution.

Material and methods. In the Sklifosovsky Research Institute for Emergency Medicine, a simultaneous kidney and pancreas transplantation (SKP Tx) was first performed in 2008. Since then over 35 such transplant procedures have been made.

Our study was based on a retrospective single-center clinical review of anesthesia in 21 patients: 12 men (57%) and 9 women (43%), who underwent a simultaneous kidney and pancreas transplantation (SKP Tx) in the Sklifosovsky Research Institute for Emergency Medicine. Patient's physical status in all patients was assessed as MNOAR¹ IV Degree according to the Operative and Anesthetic Risk Classification. The main pathology the SKP Tx was performed for was Type 1 DM (IDDM) with the end-stage CRF that had developed as a result of progressive diabetic nephropathy. Cardiovascular diseases were the most common existing comorbidities recorded in those patients. Specifically, 9 patients (47.3%) had the history of hypertension, 6 patients (31.6%) had the history of ischemic heart disease, including 3 with a stable angina (15.8%), 2 with cardiac arrhythmia (10.5%), and 1 with post-infarction atherosclerosis (5.3%).

The mean age of operated recipients was 35.1 ± 6.84 years old. Mean duration of surgery was 599.2 ± 103.42 minutes.

Patients were divided into two groups. Group 1 included 8 patients (35%) who were operated on under a multicomponent general anesthesia with mechanical lung ventilation (MLV) without epidural anesthesia. Group

¹ MNOAR: the Operative and Anesthetic Risk Classification developed by Moscow Scientific Society of Anesthesiologists and Critical Care Physicians, transliterated from Russian as MNOAR.

2 included 13 patients (65%) who were operated on under multicomponent general anesthesia with MLV and continuous epidural anesthesia.

In patients of Group 2, naropin in the mean dose of 87.5 ± 17.72 mg was used for intraoperative epidural anesthesia. A catheter was placed into the epidural space at the level of Th8-Th9, before the induction of anesthesia, the patient being in the seated or lateral lying position. The position was chosen dependent on the depth of sedation individually for each patient (midazolam, 0.03 ± 0.04 mg/kg). No complications associated with catheter insertion in the epidural space occurred.

The scheme of premedication (midazolam, 0.1 mg/kg), the induction of anesthesia (midazolam, 0.08 ± 0.004 mg/kg, propofol, 1.52 ± 0.16 mg/kg, fentanyl, 3.2 ± 0.14 μ g/kg), a muscle relaxation maintenance (cisatrakurium bromide, 0.16 ± 0.02 mg/kg) were similar in the two groups. Airway patency in both groups was maintained using standard orotracheal intubation. All patients were on MLV (Drager Primus) in the Volume Control mode using a fresh gas low flow (2 L/min). In both groups, the anesthesiologic maintenance included the fentanyl administration in a dose of 1.5-2.1 mg/kg x h, considering the operation stage and monitoring the adequacy of surgical anesthesia level, and the sevoflurane anesthetic inhalation with a target minimal alveolar concentration (MAC) of 0.7-1.0 vol/% (mean/average/range 0.8-2.7 vol%). Muscle relaxation was maintained by bolus infusion of cisatrakurium bromide at a dose of 0.07-0.09 mg/kg x h. After the ventilation parameters and hemodynamics had been stabilized, in patients of Group 2, the epidural infusion of 0.375% ropivacaine solution was started (the officinal 0.75% solution of local anesthetic naropin was diluted in 0.9% NaCl solution in 1:1 ratio). Ropivacaine was administered at a rate of 3 to 10 ml/h (from 0.16 to 0.54 mg/kg x h) using a dosing device. The ropivacaine

dose was selected to create an adequate sympathetic and segmental analgesic neuromuscular blocks at the levels of iliac vessels and the small intestine part designated for placement of transplant anastomoses. The total administered ropivacaine amount did not exceed the maximum [12] recommended dose and made 1.25 ± 0.25 mg/kg (0.25 ± 0.05 mg/kg/h).

We have defined the following main perioperative stages of the study:

- I. The start of anesthesia and surgical intervention;
- II. Renal reperfusion;
- III. Pancreas reperfusion;
- IV. Placement of intestinal anastomosis;
- V. Surgery completion.

The anesthesia efficacy was evaluated considering the following parameters: heart rate (HR); blood (systolic, mean and diastolic) pressure changes over time measured using an invasive arterial catheter introduced in the radial artery; core temperature; hemoglobin oxygen saturation; central venous pressure (CVP); blood acid-base balance. We also quantitated the amounts of anesthetics consumed, blood loss, fluid and transfusion therapy, urine output (before and after the kidney transplant inclusion in the systemic circulation), as well as the incidence of complications in the perioperative period, and the timing of extubation. In addition, patients of both groups were evaluated for glycemia before and after pancreas reperfusion.

Intraoperatively, an adequate hemodynamics was maintained by means of fluid and transfusion therapy, and, when necessary, by the infusion of sympathomimetic agents (dopamine at a dose of 4-10 mg/kg x min).

The surgery duration in Group 1, and 2 made 647.8 ± 130.1 , and 573.8 ± 107.8 minutes, respectively. The patients received cadaveric donor

transplants. Storage temperature, the method and duration of donor organ preservation made no differences between the groups.

Table 1. General characteristics of the study groups.

Group characteristics	Number of patients	Sex,%		Age, years	Body mass, kg	Type of anesthetics used	Duration of surgery, min
		male	female				
Group 1	8	57.14	42.86	37.42 ± 2.05	55.5 ± 11.4	Sevorane + Fentanyl + Nimbex	647.8 ± 130.1
Group 2	13	61.54	38.46	34.15 ± 2.40	63.4 ± 13.4	Sevorane +Fentanyl + Nimbex + CEA 0.3% Naropin solution	573.8 ± 107.8

CEA –continuous epidural anesthesia

Statistical data handling and analyses were performed using computer software packages (MS Excel 2007, StatSoft Statistica, version 10, and SPSS). The means, a standard deviation, and the standard error of the mean were calculated. Statistical significance of differences was studied by non-parametric statistical methods, using Mann-Whitney test (for intergroup differences) and Wilcoxon test (for intragroup differences). The difference was considered statistically significant at $P < 0.05$.

Results and Discussion

Table 2. The main intraoperative parameters of the study groups

Parameter	Group 1 (n = 8)	Group 2 (n = 13)
Volume of blood loss, ml	621.4 ± 42.1	415.3 ± 36.4
Fluid therapy and transfusions, ml	4142.9 ± 232.6	4193.1 ± 216.8

Intraoperative urine output, ml/h		
Prior to renal transplant reperfusion	10.6 ± 3.14	30.2 ± 9.23
After renal transplant reperfusion	84.6 ± 35.54	60.5 ± 24.3
Extubated in the operating room on surgery completion	2 (25%)	8 (61.5%) *
Incidence of intraoperative cardiac complications (ST segment depression, arrhythmias, hypo- and hypertension)	1 (12.5%)	2 (15.4%)

* P <0.05 compared to values in Group 1.

Table 2 demonstrates that the patients in Group 1 were extubated significantly less likely at surgery completion than the patients in Group 2, making 25% and 61.5% of the total number of extubations, respectively (Fig. 1).

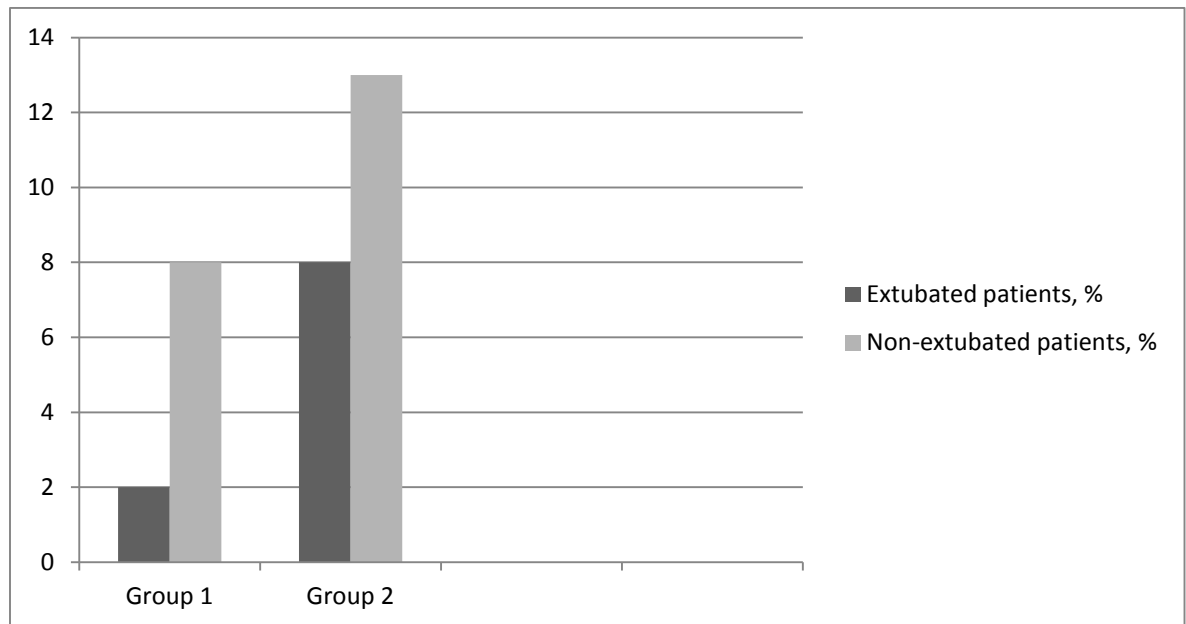


Figure 1. The proportion of the patients extubated in the operating room.

Table 3. Intraoperative consumption of main anesthetics.

Anesthetics	Group 1 (n = 8)	Group 2 (n = 13)
Fentanyl, mcg / kg x h	2.06 ± 0.32	1.5 ± 0.32*
Nimbex, mg/kg x h	0.09 ± 0.01	0.07 ± 0.01
Provive, mg	231.4 ± 34.8	125.3 ± 28.6*
0.375% Naropin solution, mg	-	87.5 ± 17.7

* P <0.05 compared to Group 1.

Table 3 clearly demonstrates the difference between the groups in the amounts of main anesthetics consumed. In Group 1, where the patients were operated on without epidural anesthesia, the mean consumed amount of each anesthetic presented was higher than that in Group 2. According to obtained data, in Group 2 the consumed amounts of fentanyl, nimbex, and propofol were 1.37 times (p <0.05), 1.29 times, and 1.85 times (p<0.02) lower, respectively, compared to data for Group 1 (without epidural analgesia component) (Fig.2). Probably, this might explain more common cases of postoperative postmedication and residual curarization in patients of Group 1 that impeded extubation in the operating room at surgery completion in a number of cases.

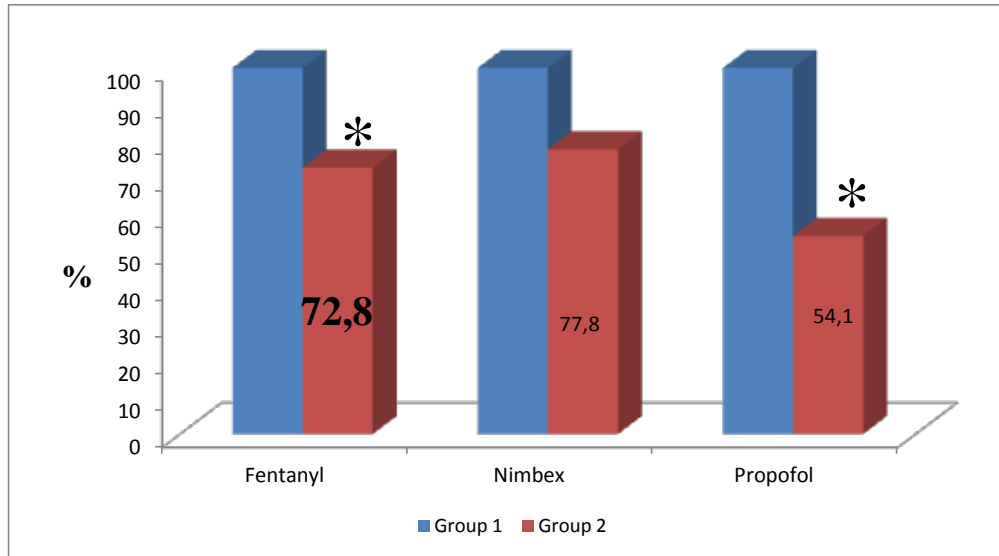


Figure 2. Mean requirements in anesthetics for patients in Group 1 and 2 (Group 1 consumption was defined as 100%)

* P < 0.05 between groups.

Table 4. Parameters of central hemodynamics, thermometry, and pulse oximetry at main stages of surgery

Groups	Stage	BP, systolic, mm Hg	BP, diastolic, mm Hg	BP, mean, mm Hg	Heart rate, beats per minute	CVP, cm of water
Group 1 (n = 8)	I	136 ± 9.2	87 ± 4.2	105 ± 7.1*	78 ± 2.1	8.5 ± 1.5
	II	140 ± 8.1	72.8 ± 5.6	95.1 ± 8.2*	79 ± 5.4*	7 ± 1.2*
	III	137 ± 6.1	68 ± 5.1	91 ± 7.7	82 ± 6.1	7.2 ± 1.4
	IV	135 ± 5.5	67.1 ± 6.2	89.7 ± 6.0	88 ± 6.8*	7.9 ± 1.4
	V	130 ± 8.1	67.8 ± 5.2	88.4 ± 6.1	92.1 ± 3.1	7.4 ± 1.2
Group 2 (n = 13)	I	125 ± 7.6	74 ± 5.2	89 ± 5.2	71 ± 2.2	7.7 ± 2.1
	II	130.3 ± 5.7	63.4 ± 9.4	85.9 ± 6.8	69 ± 3.1	8.6 ± 1.9
	III	133.1 ± 8.3	65.7 ± 6.3	88 ± 8.3	74 ± 5.2	8.2 ± 2.5
	IV	133 ± 5.2	68 ± 7.1	90 ± 7.2	78 ± 4.8	8.3 ± 2.1
	V	133 ± 8.4	65 ± 2.6	88 ± 3.6	86 ± 3.3	7.2 ± 1.7

* P < 0.05 compared to data of Group 2 in the same time period.

The efficacy of anesthetic protection in SKP Tx procedures was assessed by considering the following criteria: requirements in anesthetics, the level of drug-induced depression of consciousness, hemodynamic parameters measured. Reviewing the systemic hemodynamic parameters, we noted that BP remained stable in both groups at all stages of transplant surgery, however, at SKP Tx stages I, II, and III, Group 1 patients demonstrated a slight tendency to hypertension. Mean BP at initial two SKP Tx stages differed significantly between two groups: the mean BP appeared to be lower in the patients who received general anesthesia with epidural component (89 ± 5.2 mm Hg at stage I, and 85.9 ± 6.8 mm Hg at stage II). That could be explained by the presence of an epidural block. Heart rate values in both groups were within reference range, however, at stage V, Group 1 showed the tendency to tachycardia that could occur due to the start of awakening from anesthesia and emerging pain sensations. In general, hemodynamic parameters were within the reference range, but lower in Group 2 than in Group 1 at all stages of surgery.

Parameters of water-electrolyte status were measured in patients at all stages of surgery (Table.5).

Table 5. Parameters of water-electrolyte status and electrolyte shifts
in intraoperative period

Parameter	Group	Stage of the study				
		I	II	III	IV	V
pH	1	7.37 ± 0.04	7.33 ± 0.03	7.37 ± 0.03	7.37 ± 0.02	7.38 ± 0.06
	2	7.35 ± 0.05	7.35 ± 0.06	7.35 ± 0.05	7.36 ± 0.05	7.36 ± 0.06
PaO ₂	1	111.31 ± 16.5	120.6 ± 5.2 *	122.9 ± 6.7	113.6 ± 5.1	118.05 ± 10.6
	2	120.01 ± 11.4	130.09 ± 9.5**	119.37 ± 8.2	111.3 ± 5.6	128.9 ± 12.4**
Lac, mmol/L	1	0.7 ± 0.2	1.0 ± 0.4	1.4 ± 0.3	1.3 ± 0.2	1.5 ± 0.2
	2	0.9 ± 0.2	1.0 ± 0.5	1.4 ± 0.7**	1.4 ± 0.8**	1.31 ± 0.5
Na ⁺ , mmol/L	1	134.4 ± 4.7	134.2 ± 4.4	133.3 ± 3.2	132.8 ± 5.2	134.2 ± 4.1
	2	132.9 ± 3.4	132.8 ± 3.6	135.2 ± 4.5	134.8 ± 2.8	133.5 ± 3.7
Cl ⁻ , mmol/L	1	105.1 ± 5.0	103.9 ± 4.9	102.6 ± 4.5*	101 ± 2.8*	101.6 ± 3.2*
	2	104.1 ± 4.2	106.7 ± 3.2	107.8 ± 3.9	107.5 ± 4.5	106.5 ± 3.9
K ⁺ , mmol/L	1	4.02 ± 0.6	3.92 ± 0.54	3.8 ± 0.5	3.98 ± 0.13	3.92 ± 0.5
	2	4.8 ± 0.9	4.01 ± 0.6	3.95 ± 0.5	3.95 ± 0.6	4.19 ± 0.5
HCO ₃ ⁻ , mmol/L	1	22.1 ± 1.6	21.4 ± 2.5	23.12 ± 1.7	24.04 ± 0.9	24.4 ± 1.2
	2	22.9 ± 2.3	22.7 ± 2.0	22.3 ± 2.6	22.9 ± 2.5	23.5 ± 2.3

* P <0.05 compared to Group 2 at the stage.

** P <0.05 compared to the previous stage for the Group.

Data analysis demonstrated the presence of some statistically significant differences in blood electrolyte levels between two groups and

between stages of surgery, but all electrolyte parameters were within the reference ranges and were not affected by the epidural component of general anesthesia. That was also suggestive of adequate volume and proper composition of undertaken fluid and transfusion therapy in all patients operated on.

Glycemia levels were also monitored in patients of both groups at all stages of surgery. The decreased glucose level in group 2 was statistically significant (Table 6.)

Table 6. Intraoperative blood glucose levels and insulin doses

Group	Stage	Glucose level	Insulin dose
1	I	10.2 ± 2.8	4.6 ± 2.8
	II	9.5 ± 2.1	4 ± 2.3
	III	7.4 ± 2.1	2.7 ± 1.2
	IV	8.5 ± 1.8	4.25 ± 2.5
	V	7.3 ± 1.7	2.5 ± 0.7*
2	I	11.3 ± 2.7	6.1 ± 1.8
	II	8.7 ± 1.2	5.1 ± 1.5
	III	6.5 ± 2.2	2.7 ± 1.0
	IV	7.3 ± 1.9	2.5 ± 2.1*
	V	7.8 ± 1.8	1.5 ± 0.5*

* P <0.05 compared to the data at stage I for the same Group.

Prior to transplanted pancreas reperfusion, the mean blood glucose levels were 9.5 ± 2.1 mmol/L in Group I, and 8.7 ± 1.2 mmol/L in Group 2. The average dose of insulin to control hyperglycemia was 4±2.3 units in Group 1, and 5.1 ± 1.5 units in Group II. After pancreas reperfusion the mean glycemia level was 8.5 ± 1.8 mmol/L in Group 1, and 7.3 ± 1.9 mmol/L in Group 2. At this stage of surgery, the insulin therapy comprised

4.25 ± 2.5 units in Group I, and 2.5 ± 2.1 units in Group 2. Thus, the strong correlation between pancreas reperfusion and the reduction of glycemia level was clearly seen in both groups. There was no significant difference in insulin therapy between the groups. Administered insulin doses with regard to glycemia control in Group I were statistically insignificant between the stages of surgery. Group 2 showed statistically significant differences in the doses of insulin between stages I and IV, and also between stages I and V of surgery suggesting a better insulin production function of transplanted pancreas.

Thus, the multicomponent general anesthesia with mechanical ventilation using an inhaled anesthetic Sevoflurane provided an adequate surgical anesthesia level during SKP Tx in the studied patients.

Continuous epidural anesthesia in the complex of multicomponent general anesthesia with mechanical ventilation using an inhaled anesthetic Sevoflurane is a highly effective anesthesia technique for SKP Tx that affords to achieve a stable heart rate and blood pressure, as well as provides an adequate neuro-vegetative protection. This method allows the decrease in the total amount of anesthetics to be administered and an earlier mobilization of patients after surgery. A slight decrease in the heart rate and blood pressure during CEA posed no negative impact on the general condition of patients, since these parameters were within the range of physiological values at the level required for a good transplant reperfusion.

Conclusion

Both methods of anesthesia used for a SKP Tx procedure in patients with chronic renal failure and type I diabetes mellitus provide conditions to keep a stable electrolyte balance, acid-base status, ventilation, and oxygenation. Meanwhile, the use of continuous epidural infusion of 0.375% ropivacaine solution as a component of the combined sevoflurane-based general anesthesia reduces the anesthetics consumption. Specifically, the consumption of fentanyl, muscle relaxants, and Provive™ decreases by 1.37 (27%), 1.29 (22%), and 1.85 times (46%), respectively. Recovery of consciousness in the Operating Room occurs in 61.5% of patients that is 36.5% higher compared to the patients operated on under combined sevoflurane-based general anesthesia, but without continuous epidural anesthesia.

References

1. Khubutiya M.Sh., ed. *Transplantatsiya organov i tkaney v mnogoprofil'nom nauchnom tsentre* [Transplantation of organs and tissues in a multidisciplinary scientific center]. Moscow: AirArt Publ., 2011. 424 p. (In Russian).
2. Gruessner R.W.G., Sutherland D.E., eds. *Transplantation of the Pancreas*. New York: Springer-Verlag Publ., 2004. 349–380.
3. Cecka J. M., Terasaki P.I., eds. *Clinical transplants 2008*. Terasaki Foundation Laboratory, 2009. 550 p.
4. Dedov I.I., Shestakova M.V. Diabeticheskaya nefropatiya [Diabetic nephropathy]. Moscow: Universum Publ., 2000. 240 p. (In Russian).
5. Shestakova M.V., Yarek-Martynova I.Ya., Vikulova O.K., et al. Sakharnyy diabet i khronicheskaya bolezni' pochek: dostizheniya,

nereshennyye problemy i perspektivy lecheniya [Diabetes and chronic kidney disease: achievements, challenges and the prospect of a cure]. *Sakharnyy diabet*. 2011; 1: 81–87. (In Russian).

6. Got'e S.V., Arzumanov S.V., Tsiryul'nikova O.M., et al. Opyt sochetannoy transplantatsii podzheludochnoy zhelezy i pochki patsientam s sakharnym diabetom 1 tipa i terminal'noy khronicheskoy pochechnoy nedostatochnost'yu [Experience of co-transplantation of pancreas and kidney in patients with type 1 diabetes and terminal chronic renal failure] S.V. Got'e, ed. *Tezisy dokl. V Vseros. s"ezda transplantologov* [Abstracts. V Russian Congress of The Transplantation]. Moscow, October 8–10, 2010. *Vestnik transplantologii i iskusstvennykh organov*. 2010; Suppl. XII: 36–37. (In Russian).

7. Morath C., Schmied B., Mehrabi A., et al. Simultaneous pancreas-kidney transplantation in type 1 diabetes. *Clin. Transplant*. 2009; 23 (21): 115–120.

8. Kozlov I.A., Magilevets V.M., Krichevskiy L.A., Matveev Yu.G. Anesteziologicheskoe obespechenie transplantatsionnykh operatsiy [Anesthetic management of transplant operations]. V.I. Shumakov, ed. *Transplantologiya: ruk-vo dlya vrachey*. 2nd ed. Moscow: MIA Publ., 2006; 6: 116–160. (In Russian).

9. Beebe D.S., Belani K.G. Anesthetic management. In: Gruessner R.W.G., Sutherland D.E., eds. *Transplantation of the pancreas*. New-York: Springer-Verlag Publ., 2004. 143–149.

10. Kozlov I.A., Magilevets V.M., Shepelyuk A.N., Morev E.K. Nekotorye aspekty anesteziologicheskogo obespecheniya transplantatsii pochki [Some aspects of the anesthetic management of kidney transplantation]. *Vestnik intensivnoy terapii*. 2005; 3: 30–36. (In Russian).

11. Shumakov V.I., Tarabarko N.V. Peresadka podzheludochnoy zhelezy [Transplantation of the pancreas]. In: Shumakov V.I., ed. *Transplantologiya* [Transplantology]. Moscow: Meditsina Publ., 1995. 308–316. (In Russian).

12. Ovezov A.M., Likhvantsev V.V. Epidural'naya infuziya naropina v komplekse anesteziologicheskogo obespecheniya rezektsiy pecheni [Epidural infusion of naropina in the complex anesthetic management liver resections]. *Annaly khirurgicheskoy gepatologii*. 2004; 9 (2): 234. (In Russian).