

Questions to treat diarrhea caused by *Clostridium difficile* hitherto not fully developed. List of antibacterial drugs used in the treatment of intestinal infections caused by *Clostridium difficile*, including metronidazole, vancomycin, Bactrim, rifampicin and fluoroquinolones. Currently, the most promising direction in the treatment of this infection is the use of probiotics. In the treatment of moderate forms of the disease, we used metronidazole tablets in age dosage in the treatment of severe diseases include therapy metrogil i/v and rifampicin injections. To correct the identified dysbiotic shifts all children were assigned -immunobifidum. The control groups of 10 children were treated for 20 days standard bifidumbacterin (10 doses per day).

Domestic drug "Immunobifidum" manufactured by the original technology of "Orom-biological product" (Tashkent), consists of a complex of probiotic "Bifidobacterium bifidum" and extract fetal "immunoaktivina" does not contain artificial colors or preservatives. 1 tablet contains 10 doses of viable bifidumbacterin. The drug was administered to children under 1 year 1 tablet and aged 1 to 3 years 2 tablets before going to bed. The course of therapy was 20 days.

Upon completion of the full course of therapy normalization of stool, the disappearance of signs of inflammation in the intestines

scatological study and microbiological improvement was observed for all the children of the main group. After the event frequency of dysbiosis of III degree decreased by 3 times (68,0% – 26,6%) and II degree — 2 times (28% – 14,3%). The positive effect was observed in 62,5% of children.

Thus, clinical analysis showed that intestinal infections caused by *Clostridium difficile* is also characteristic symptoms of diarrhea and intoxication syndrome. The risk factors and the development of the disease is the early irrational use of antibiotics, prolonged hospital stay as a source of nosocomial infections, as well as age of the children.

Qualitative and quantitative changes in intestinal microflora are considered as one of the mechanisms that support and aggravating for the main disease

#### Conclusions:

1. The presented data give reason to treat an intestinal infection caused by *Clostridium difficile* as a serious problem that requires a specific approach to the diagnosis and the corresponding complex treatment

2. The obtained results allowed us to draw a reasonable conclusion about the usefulness of the drug "Immunobifidum" in the treatment of intestinal infection caused by *Clostridium difficile*.

#### References:

1. Асимова М. У. Диарея у детей: диагностика, клиника, лечение и профилактика: научное издание // Бюллетень ассоциации врачей Узбекистана. – Т., 2007. – № 2. – С. 103–106.
2. Ахмадеева Э. Н., Нижевич А. А., Амирова В. Р. Антибиотикассоциированная диарея у детей: Обзор // Российский педиатрический журнал. – М., 2010. – № 1. – С. 32–38.
3. Махмудов О. С. Диарейные заболевания у детей // Узбекистон тиббиёт журнали. – Ташкент. – 2005. – № 3. – С. 8–10.
4. Плоскирева А. А. Эффективность этиотропной терапии бактериальных острых кишечных инфекций у детей на современном этапе // Инфекционные болезни. – М., 2011. – № 4. – С. 79–83.
5. Циммерман Я. С. Синдром диареи: Современное состояние проблемы // Клиническая медицина. – 2009. – № 3. – С. 13–25.

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## Efficiency estimation of multi-modal approach to anesthetic management of long-term, abdominal operative interventions

**Abstract:** 86 patients has been examined and divided into 3 groups depending on the method of anesthesia have been investigated. Patients of 1<sup>st</sup> and 2<sup>nd</sup> groups were made traditional general anesthesia. Patients of 3<sup>rd</sup> group were made general anesthesia on the principle of multi-modal anesthesia.

Multi-modal approach to anesthetic management with the force to all parts of pain pathogenesis promotes the stability of hemodynamic indications in post-operative period, to minimum tension of homeostasis, less expressed reaction of sympathoadrenal system due to good neurovegetative protection.

**Keywords:** multi-modal analgesia, epidural analgesia, pain

#### Introduction

Multy-modal analgesia foresees the simaltenious usage

of 2 or more analgesics having different acting mechanisms and allowing to reach the adequate narcosis at minimum side-

effects typical for the big doses of one analgesic in the mono-therapy regimen [6; 9].

The background of narcosis is traditionally meant the system dosing of opiod analgesics. The opiod componet is the base of pain protection on the central (segmental and over-segmental) level. The medications of this group activate the endogenous anti-nociceptive system (central analgesia), but they cannot supply the full anesthetic protection. Opioid analgesics do not influence on peripheral and segmental non-opioid mechanisms of nociception and do not prevent the central sencitization and hyperalgia. That is why the general anesthetics in combination with the most powerful analgesics are not able to fully protect the patient from pain at the operating trauma. So, it should be the impact on the non-opioid mechanisms of pain development. [1; 4; 11].

The process of the central sencitization is connected with stimulating effect of neuro-transmitters (amino acids of aspartate and glutamate) on receptors and it leads to the fixing of hyperalgia. The general anesthetic ketamine in small doses is the antagonist of these neuro-transmitters receptors. The applying of the multy-modal central analgesia as the combination of opiod and ketamine in small doses allows to stop the process of the central sencitization. [6; 10; 12].

One of the key-moments of multy-modal central analgesia is the choice of the anesthesia's method during the operation. It is determined on the base of modern clinical and experimental investigations that the general anesthasias

disposing the perception of pain do not supply the blockade of passing nociceptive impulses even on supra-segmental level let alone the spinal level. The general dosage of opioid analgesics inputting into the system bloodstream do not supply the enough blockade of opiate receptors of back horns of spinal corde. Weakly anesthetized spinal cord is exposed to the strong struck by damaging stimules and it provokes above mentioned plastic changes of the central nervous system. So, the adequacy level of anesthesia is determined by the quality of the spinal cord protection. That is why the regional anesthesia with the full blockade of afferent nociceptive impulsation in this or that type must be the obligatory and main component of intra-operative protection [14; 16].

#### Aim

The aim of our investigation is the collation of the anesthesia course in patients with using multi-modal approach to anesthetic management and to traditional general anesthesia at long-term operative interventions.

#### Materials and methods

86 patients has been examined and divided into 3 groups depending on anesthesia and postoperative pain relief ways. There were no differences on age, gender and types of operations and concomitant pathology among patients of three groups (tables 1; 2; 3). The presence of concomitant pathology did not limit the using of multimodal anesthesia at the condition of elimination of hypovolemia and anemia correction.

Table 1. – Distribution of patients by sex, abs %

Sex	1 <sup>st</sup> group	2 <sup>nd</sup> group	3 <sup>rd</sup> group	Totally
Females	9 (34,5)	8 (30,7)	10 (29,4)	27 (31,4)
Males	17 (65,3)	18 (69,3)	24 (70,6)	59 (68,6)
Totally/average age	26 (100)/51,6±	26 (100)/46,2±	34 (100)/55±	86 (100)

Ways of premedication, anesthesia and post-operative pain-relief are given in Table 4.

Table 2. – Distribution of patients in groups due to performed operations, abs%

Operations	1 <sup>st</sup> group	2 <sup>nd</sup> group	3 <sup>rd</sup> group	Totally
Gastrectomy	8 (30,8)	8 (30,8)	14 (41,2)	30 (34,8)
Subtotal stomach resection	14 (53,8)	15 (57,7)	11 (32,4)	40 (46,5)
Extirpation of gullet with following pactics	3 (11,6)	2 (7,7)	4 (11,7)	9 (10,5)
Pancreatoduodenal resection	1 (3,8)	1 (3,8)	5 (14,7)	7 (8,2)
Totally	26 (100)	26 (100)	34 (100)	86 (100)

Table 3. Distribution of patients by nature of concomitant pathology at abdominal operations, abs%

Concomitant pathology	1 <sup>st</sup> group (26)	2 <sup>nd</sup> group (26)	3 <sup>rd</sup> group (34)	Totally (86)
Hypertensive disease	6 (23)	7 (27)	14 (41,4)	27 (31,3)
Diabetes	3 (11,5)	1 (3,7)	2 (5,8)	6 (7)
Anaemia	9 (35)	8 (30,7)	8 (23,5)	25 (29)
Cachexia	5 (19,2)	5 (19,4)	5 (14,7)	15 (17,5)
Chronic bronchitis	1 (3,7)	1 (3,7)	2 (5,8)	4 (4,6)
HD+D+ CB	2 (7,6)	4 (15,5)	3 (8,8)	9 (10,6)

Such type of patients admitted to hospital with emergency pathology connected with surgical problem (hemorrhage,

3<sup>rd</sup> level dysphagy, cachexia and etc.) and was operated after correction of general condition medicamentous or endo-

scopic hemostasis, hypovolemia, water-electrolytic violations elimination. According to condition and revealed nature of

disorders patients referred to II–III E class by ASA.

Table 4. – Ways of premedication, anesthesia and post-operative pain-relief in patients with abdominal operations (n=86)

Level	1 <sup>st</sup> group	2 <sup>nd</sup> group	3 <sup>rd</sup> group
Premedication	promedol 20 mg, dimedrol 10 mg, atropine 0,5 mg. H <sub>2</sub> blocker nevo-fam 20 mg i\m (4,4± 0,2 h)	promedol 20 mg, dimedrol 10 mg, atropine 0,5 mg. H <sub>2</sub> blocker nevo-fam 20 mg i\m (4,3± 0,3 h)	promedol 20 mg, dimedrol 10 mg, atropine 0,5 mg. H <sub>2</sub> blocker nevo-fam 20 mg i\m (4,5± 0,4 h)
Anesthesia maintenance	combined general anesthesia with use of fentanil 5–8 mkg/kg/hour, ketamin 1,5–2 mg/kg/hour	combined general anesthesia with use of izofluran 1,5–2 v\% and fentanil 5–8 mkg/kg/hour	Izofluran 0,8–1 v\%, ketamin 0,8 mg/kg — block of NMDA receptors, analgetic component EDA + bolus dosing of fentanil in traumatic moments of operation by 0,1mg i\m.
Post-operative pain relief	morphine 30–50 mg\day i\m	morphine 30–50 mg\day i\m	NSAID ketonal 300mg; EDA bupivacaine 0,25%-50mg each 5–6 hours (or lidokain 1%-200 mg each 3–4 hours); morphine 10 mg i\m at necessity

Ways of investigation:

- ECG for estimation of data of central hemodynamics (Hitachi –500);
- Average blood pressure (ABP), general peripheral vascular resistance (GPVR), left ventricular work index (LVWI), cardiac index (CI) were counted by calculating methods;
- ABP monitoring, heart rate frequency (HRF), ECG, saturation (SpO<sub>2</sub>) with Nikon-Kohden (Japan) monitor.
- Blood analysis:
  - glucosae level, stress hormone level (cortisol);
- Kidney secretory function:
  - minute diuresis (MD);
  - glomerular filtration (GF);
  - tubular reabsorption (TR);
- Temperature gradient
- Extubation time;

**Results.** At initial level of intra-operative period there were no differences in hemodynamics, glucose and cortisol indications between groups. Investigations of acid-base balance of blood at all levels did not reveal disorders. Reliable differences between groups were determined in pH and BE indexes.

At the 2<sup>nd</sup> level investigation in the 2<sup>nd</sup> and 3<sup>rd</sup> groups there were pointed reliable differences in hemodynamics indexes in compare with the 1<sup>st</sup> one. Decreasing of ABP on 13% in the 3<sup>rd</sup> group in compare with the 1<sup>st</sup> one was pointed. LVWI index was reliably higher in the 1<sup>st</sup> group for 21% in compare with the 3<sup>rd</sup> one. There was revealed a reliable difference of LVWI on 13,1% at comparing of groups 2 and 3 (pict.1).

Glucose index at comparing of groups 1 and 3 was higher on 17,2% in 1<sup>st</sup> group and at comparing groups 2 and 3 there was revealed reliable difference equal 15,5%. Cortisol index did not have reliable differences in all groups.

At a comparative estimation of the main parameters of hemodynamics at traumatic moment of operation (3<sup>rd</sup> level) between groups 1 and 2 was pointed that HRF in patients of 1<sup>st</sup> group was 13% higher in compare with 2<sup>nd</sup> group patients. Correspondingly to HR changes there was a reliable difference in LVWI index which was 19,6% higher in 1<sup>st</sup> group than in the 2<sup>nd</sup> one. Humoral indexes of stress — cortisol and glucose were also measured according to hemodynamic indexes (pict.2,3) and were 24% higher in 1<sup>st</sup> group than in the 2<sup>nd</sup> one. Comparing groups 1 and 3 we revealed that ABP index was higher in group 1 for 19,6%, HRF was higher for 34%. Patients from group 1 had EF lower for 10,2%, LVWI was higher for 45,2%, and index CI reliably increased for 21,8%. Glucose index in group 1 was higher for 56% and cortisol — was higher for 81%.

The comparison of patients from groups 2 and 3 at traumatic part of operative intervention was interesting. In spite of extra use of inhalation anesthetics in group 2 there was a difference in hemodynamic and humoral indexes in compare with the patients of group 3. ABP in group 2 was higher for 14,8%, HRF — for 24,9%. CI and EF did not have reliable differences. LVWI increased in patients of group 2 for 21,4% in compare with group 3. Cortisol index in group 2 was higher for 45,2% and glucose index was 56% higher in compare with group 3.

Only by the end of operation hemodynamics indexes approached to normodynamia and did not have reliable differences between groups. Comparing groups 1 and 2 it was revealed that glucose index was 22% higher in group 1 and cortisol index was normal. Comparing groups 1 and 2 we revealed reliable increasing of cortisol index in group 1 34,4% and glucose — for 59,6%. Comparing groups 2 and 3 we revealed reliable increasing of glucose for 30% in group and cortisol — for 26% in group 2.

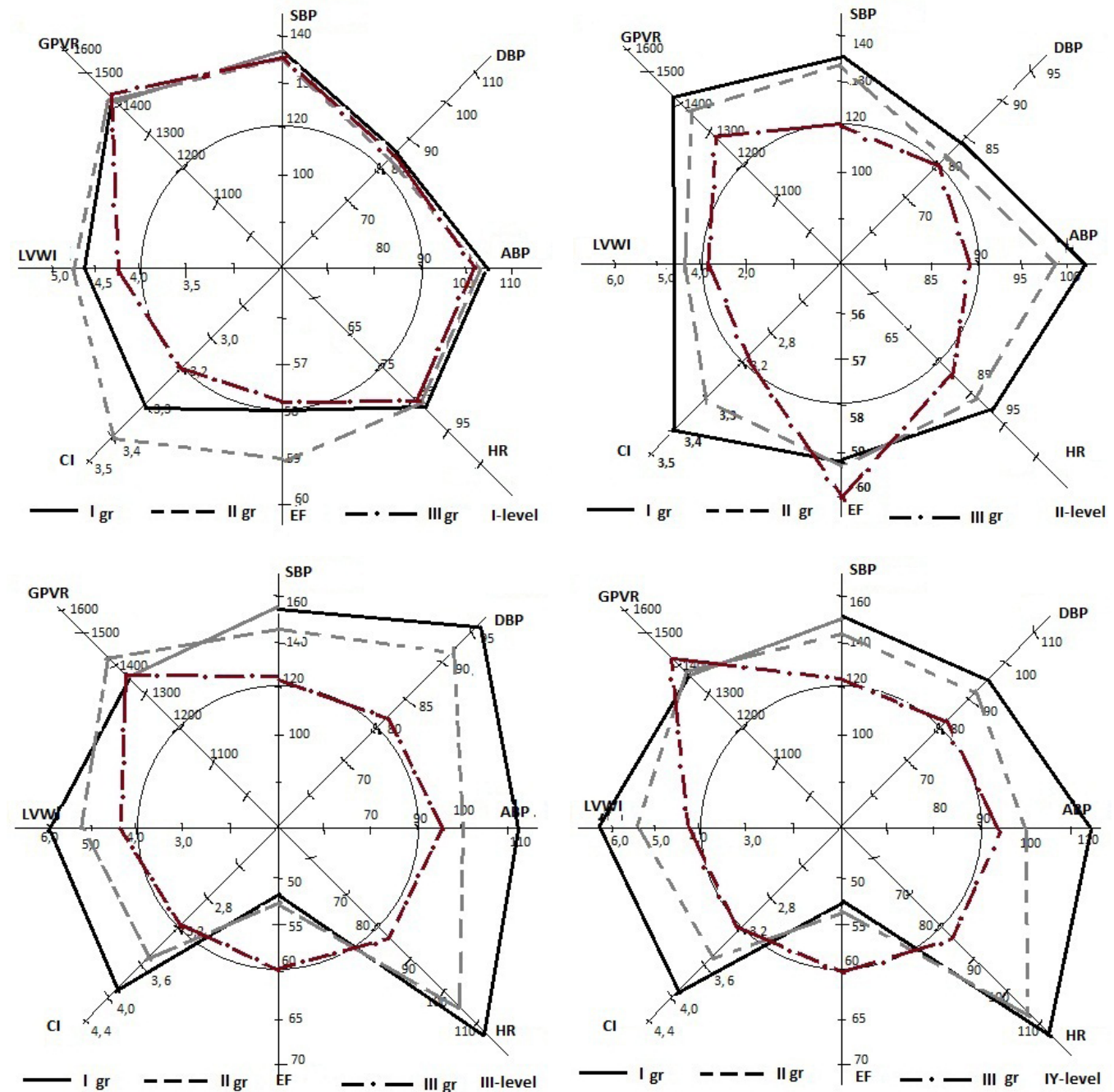


Figure 1. – Hemodynamics indexes in intra-operative period in compare between groups at abdominal operative intervention

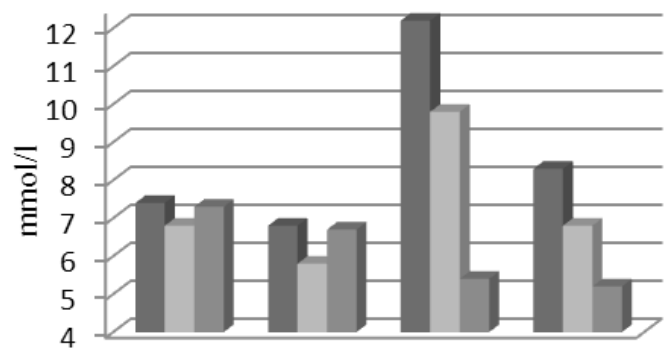


Figure 2. – Glucosae indexes

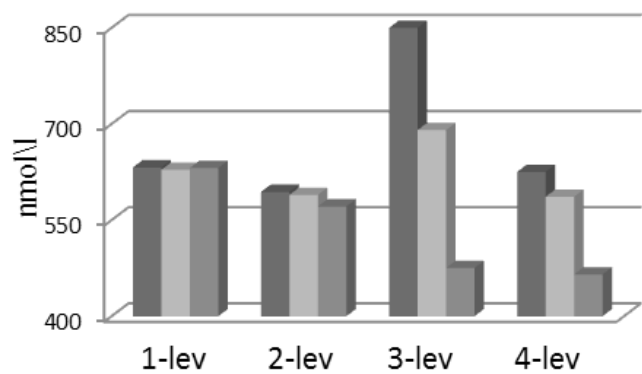


Figure 3. – Cortisol indexes

Investigation of kidney excretory function (table 5) detected following: in group 3 with the use of multimodal analgesia minute diuresis remained normal. In 1<sup>st</sup> group this index was

26,8% lower and in group 2 was 22,3% lower than in group 3. GF index in 1<sup>st</sup> group decreased 17,4% than in group 3 and in a 2<sup>nd</sup> group this index was decreased on 19,6% than in group 3.

Table 5. – Kidney excretory function at long traumatic operations in intra-operative period

Indexes	Group	1 <sup>st</sup> stage	2 <sup>nd</sup> stage	3 <sup>rd</sup> stage	4 <sup>th</sup> stage
MD, ml\min	1	1,03±0,02	0,92±0,04	0,82±0,01 <sup>a</sup>	0,76±0,01 <sup>a</sup>
	2	1,12±0,08	0,93±0,01	0,87±0,02 <sup>b</sup>	0,77±0,03 <sup>b</sup>
	3	1,13±0,09	1,04±0,08	1,12±0,01	1,14±0,09
GF, ml\min	1	97,5±2,5	90,3±2,4	84,5±2,5 <sup>a</sup>	80,3±2,4 <sup>a</sup>
	2	98,2±3,2	91,4±2,3	82,2±3,2 <sup>b</sup>	81,2±2,2 <sup>b</sup>
	3	106,1±4,2	104,4±5,3	102,3±4,2	104,2±4,2
TR,%	1	98,9±0,2	98,3±1,4	99,0±1,3	99,0±1,3
	2	98,8±1,1	98,6±1,2	98,2±1,4	99,1±1,4
	3	98,6±1,4	98,4±1,3	98,6±1,1	98,5±1,2

Note.  $p < 0,05$ : a- comparison groups 1 and 3; b- comparison groups 2 and 3.

Comparing temperature gradient index (table 6) between groups we detected that temperature gradient in the group

with multimodal analgesia was 65,2% lower in compare with group 1 and was 62,2% lower in compare with group 2.

Table 6. – Temperature index in intra-operative period at long traumatic operative interventions

Indexes	Group	1 <sup>st</sup> stage	2 <sup>nd</sup> stage	3 <sup>rd</sup> stage	4 <sup>th</sup> stage
t cutaneous, °C	1	36,62±0,12	36,73±0,08	36,12±0,14	36,02±0,15
	2	36,71±0,11	36,63±0,07	36,13±0,13	36,03±0,14
	3	36,63±0,09	36,74±0,05	36,82±0,09	36,81±0,05
t rectal, °C	1	37,12±0,13	37,31±0,16	37,32±0,13	37,24±0,14
	2	37,21±0,14	37,21±0,11	37,23±0,16	37,31±0,13
	3	37,13±0,12	37,23±0,17	37,21±0,12	37,23±0,11
Temperature gradient, °C	1	0,51±0,05	0,63±0,07	1,21±0,04 <sup>ab</sup>	1,22±0,01 <sup>b</sup>
	2	0,53±0,04	0,64±0,03	1,12±0,01 <sup>a</sup>	1,31±0,05
	3	0,52±0,03	0,51±0,06	0,42±0,04 <sup>c</sup>	0,43±0,06 <sup>c</sup>

Note.  $p < 0,05$ : a — comparison groups 1 and 2; b — comparison groups 1 and 3; c — comparison groups 2 and 3.

Use of inhalation anesthetics in scheme of general anesthesia in group 2 allowed to reduce consumption of narcotic analgetics for 35% in compare with 1<sup>st</sup> patients group. Combined use of general anesthesia and EDA in intra-operative period in patients of group 3 allowed to reduce reliably fentanyl consumption to 60,8% in compare with the 1<sup>st</sup> one. Comparing groups 2 and 3 revealed reducing fentanyl in group with the use of multimodal anesthesia on 40%.

Paying attention on duration and traumacity of operation patients of three groups were performed prolonged artificial lung ventilation (PALV). Extubation period of patients from group 1 was 31% higher than in the 2<sup>nd</sup> one. In group 3 extubation period was 52,3% lower than in group 2 and 67% lower than in group 1.

## Conclusion

1. At emergency traumatic long abdominal operative interventions use of perioperative multimodal anesthesia promotes stability of central and peripheral hemodynamics indexes, temperature gradient, sympato-adrenal system, ABB, kidney secretory function in compare with traditional analgesia.

2. Use of multimodal analgesia at volumetric abdominal operations promotes reducing of narcotic analgetics consumption in intraoperative period to 60,8% in compare with traditional one.

3. It is recommended to use the following protocol of multimodal anesthesia and postoperative pain relief with the aim of increasing the quality of anesthesia at emergency, long-term, traumatic, abdominal operative interventions:

Premedication	NSAID -ketonal 100 mg (principle of preemptive analgesia), promedol 20 mg, dimedrol 10 mg, atropine 0,5 mg, nevofam 20 mg i.m.
Type of regional block	Puncture and catheterization of epidural area at the level Th7–Th8, catheter is conducted cranially at 5–6 sm, test-dose — lydocaine 2%-40 mg. Main dose — 0,5% bupivacaine 50–60 mg + fentanyl 0,05 mg (or lydocaine 2% –200 mg + fentanyl 0,05 mg).

Induction into anesthesia	dormicum 0,15–0,2 mg/kg, fentanyl 3 mkg/kg, ketamin 0,8–1mg/kg with the aime of NMDA receptors block. Myoplegia — arcuronium 0,08–0,1 mg/kg, dithylin 1–1,5 mg/kg.
Anesthesia maintenance	Hypnotic component- isophluran approx. 0,8–1 o6%; Analgetic component EDA (bupivacaine 0,5% 15–25 mg or lydocaine 2%- 80 mg) + bolus dosing of fentanyl into traumatic periods of operation 0,1 mg. i\ v. Myoplegia — arcuronium 0,025 mg/kg\h
Postoperative period	NSAID ketonal 300 mg i\ m; EDA bupivacaine 0,25%-50 mg each 5–6 hours (or lydocaine 1%-100 mg each 3–4 hours); Morphine 10 mg i\ m at necessity

### References:

1. Volchkov V. A., Ignatov Yu. D., Strashnov V. I. Pain syndromes in anesthesiology and reanimatology. M 2006; 166–186.
2. Andrae MH, Andrae DA. Regional anaesthesia to prevent chronic pain after surgery: a Cochrane systematic review and meta-analysis. Br J Anaesth. 2013.111: 711–20.
3. Barratt S., Smith R., Kee J. Multimodal analgesia and intravenous nutrition preserves total body protein following major abdominal surgery. Red. Anesth. Pain. Med. 2008. 27: 15–22.
4. Bernucci F., Carli F. Functional outcome after major orthopedic surgery: the role of regional anesthesia rederned. Curr Opin Anaesthesiol. 2012. 25: 621–628.
5. Bolivar M., Bolivar A., Vargas G. Multimodal postoperative analgesia with nonsteroidal anti-inflammatory drugs and the epidural hematoma “myth” // Book Abstr. 9<sup>th</sup> World Congress on Pain, Vienna, Austria, 2009. – P.439.
6. Duale C., Sibaud F., Guastella V., Vallet L., Gimbert YA., Taheri H., Filaire M., Schoeffler P., Dubray C. Perioperative ketamine does not prevent chronic pain after thoracotomy. Eur J Pain. 2009.13:497–505.
7. Eric B., Rosero et al. Preemptive, Preventive, Multimodal Analgesia: What Do They Really Mean? Plastic and Reconstructive Surgery. 2014. 134 (4S-2): 85–93.
8. Fabian O. Kooij, Wolfgang S. Does Regional Analgesia for Major Surgery Improve Outcome? Focus on Epidural Analgesia. Anesthesia & Analgesia. September 2014. 119 (3): 740–744.
9. McDaid C., Maund E., Rice S., Wright K., Jenkins B., Woolacott N. Paracetamol and selective and non-selective non-steroidal antiinflammatory drugs (NSAIDs) for the reduction of morphine-related side effects after major surgery: a systematic review. Health Technol Assess. 2010. 14: 1.153.
10. Sigtermans M., van Hilten J., Bauer M. et al. Ketamine produces effective and long-term pain relief in patients with complex regional pain syndrome type 1. Pain. 2009.145: 304–11.

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## Transcultural aspects of opium addiction in the Republic of Uzbekistan

**Abstract:** Ethno-cultural and socio-economic factors have an effect both on the prevalence of the disease in question across given territory and on peculiarities of its clinical dynamics. Many studies demonstrated direct relationship between various ethnic and socio-cultural characteristics, clinical structure, and dynamics of mental disorders. The work was initiated to study transcultural characteristics of opium addicts among Uzbek indigenous inhabitants and Slavs born and residing in Uzbekistan.

**Keywords:** ethno-cultural peculiarities, opium addiction, transcultural aspects

### 1. Introduction

Opium addiction is a potentially life-threatening condition (UNODC, World Drug Report, 2010) bringing about adverse social consequences, such as an addict's low social integration, economic dependence, and criminal activity. On the one hand, globalization of economic and public relations characterizes the present stage of humanity's development; on the other hand, cultural diversity and ethnic heterogeneity of population can be seen in many countries.

Up-to-datedness of transcultural aspects of addiction is corroborated by the necessity to understand mechanisms of addictive attraction and its essential characteristics. Findings from considerable number of studies addressing various aspects of drug addiction demonstrated that its epidemiological and clinical peculiarities are determined by a number of factors. Ethno-cultural and socio-economic factors have an effect both on the prevalence of the disease in question across given territory, and on peculiarities of its clinical dynamics