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CLINICAL PHARMACOLOGY IN ADAPTIVE REGULATION OF STRESS PATHWAYS IN MEGACOLON INTENSIVE CARE

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Abstract

Aim of the study: Analysis and optimization of anesthetic management and intensive care during intra-abdominal resection in children with Hirschsprung disease to improve treatment efficacy and reduce postoperative risks.

Materials and Methods: The study examined the performance of 65 children (aged 3 to 14 years) who underwent elective abdominal surgery (abdominoperineal proctoplasty) with various modifications: gastroentero-entero anastomoses, entero-entero anastomoses, and intestinal ulcer resections with various signs of perioperative pain. In the operating room of the Tashkent Pediatric Medical Institute from 2021 to 2024.

Results: After premedication, a comparative analysis of heart rate assessments at baseline revealed no significant differences between the two clinical comparison groups ($p>0.05$). During the run-in period, a significant decrease in heart rate was recorded: 15.2% in Group 2 compared to Group 1 ($p<0.05$). During the maintenance period, heart rate decreased by 9% in both groups. A non-significant increase was recorded during the awakening period, by 10% ($p<0.005$), and by 8.3% in Group 1. Extubation was performed early after surgery, with a statistically significant 11.9% higher prevalence in Group 2 than in Group 1.

Children with Hirschsprung disease (congenital aganglionosis) often experience severe postoperative complications, such as enterocolitis, sepsis, abdominal compartment syndrome, and multiple organ dysfunction. These conditions are associated with excessive activation of the stress response, necessitating the development of new approaches to its control. [1, 3].

Stress-limiting mechanisms (antioxidant, anti-inflammatory, and neuroprotective) play a key role in adaptation to surgical trauma. Their targeted stimulation (e.g., through pharmacological agents or neuromodulation) can accelerate recovery and reduce the risk of complications. [5, 6, 8] This minimum of adverse effects is achieved through the use of low doses of administered drugs. This technique provides better early results in surgical correction of intra-abdominal resections in abdominal surgery and fewer complications [2, 4, 7].

Introduction

Analyzing the available literature, it can be noted that many issues and problems of anesthesia during abdominal surgery with intra-abdominal resection in children remain far from resolved. The search for improved anesthetic protection for patients during surgical interventions remains a pressing issue.

The aim of the study:

Was to develop a personalized algorithm for modulating stress-limiting systems to optimize intensive care after intra-abdominal resections in children with Hirschsprung disease.

Materials and Methods:

The study examined the performance of 65 children (aged 3 to 17 years) undergoing elective abdominal surgery, including abdominoperineal proctoplasty (APP), with various modifications, including gastroentero-entero anastomoses, entero-entero anastomoses, and intestinal ulcer resections, with varying signs of perioperative pain (Table 1).

The following epidural puncture levels were used to numb pain: jejunum and ileum (T8-T10), cecum, ascending colon (T8-T11), descending colon, sigmoid colon (T10-L2), and rectum and perineum (T11-L4). EA was performed preoperatively and used as the primary anesthetic during the procedure, and then continued in the postoperative period.

Table № 1 Classification of abdominal surgical interventions based on perioperative pain severity.

Pain severity	Variations of abdominal interventions for STIs, according to Hirschsprung's modifications
Surgeries with mild pain.	Soave-Lenishkin
Surgeries with moderate pain.	Romualdi-Rebeira Soave-Balle
Surgeries with severe pain (very painful)	Della Terre procedure

In Group 1 (control), 25 children underwent neuroleptanalgesia, a traditional method. In Group 2 (40 children), primary anesthesia was combined multimodal anesthesia with epidural analgesia (EA) and bupivacaine. All patients met ASA physical status classes I–III. The study stages included preoperative, premedication, induction period, maintenance period, and recovery period. Data on premedication, anesthesia, and postoperative analgesia are presented in Table 2. Pain levels were assessed using a visual analog scale (VAS) (twice: 1 and 6 hours after surgery), and complications were recorded for 24 hours after surgery.

Statistical processing of the results was performed using parametric analysis methods. Data are presented as the arithmetic mean (M) with the standard error of the mean (m). Student's t-test was used to assess the reliability and significance of differences in the analyzed parameter between the compared groups. The significance level of the coefficient was assessed using the standard method and was considered acceptable at $p \leq 0.05$.

Results and Discussion

After premedication, a comparative analysis of heart rate assessment at baseline revealed no significant differences between the two clinical comparison groups ($p > 0.05$). During the

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introductory period, a significant decrease in heart rate was recorded: 15.2% in Group 2, compared to Group 1 ($p < 0.05$). During the maintenance period, heart rate decreased by 9% in both groups. A non-significant increase was recorded during the awakening period, by 10% ($p < 0.005$), and by 8.3% in Group 1. Extubation was performed early after surgery; the number of patients in Group 2 was statistically significantly higher by 11.9% compared to Group 1 (Table 3).

Table 3. Dynamics of central and peripheral hemodynamic parameters during the intraoperative period (M ± m)

	Dynamics of parameters during the study									
	1- stage		2- stage		3- stage		4- stage		5- stage	
	1-gr.	2- gr.	1- gr..	2- gr.	1-гр.	2-гр.	1-гр.	2-гр	1-гр.	2-гр
heart rate contractions	118,1 ±3,8	116,4 ±3,1	100,5 ±3,2	96.2 ±2,8	98,5 ±1,9	82,3 ±4,5	110,4 ±4,4	109,1 ±3,7’’	101,6 ±3,1	97.1 ±2,8
average blood pressure	105,4 ±3,2	108,5 ±4,3	77,2 ±3,7	96,4 ±3,7	82,3 ±4,5	95,1 ±4,4	81,9 ±4,1	97,3 ±2,9’’	79,2 ±3,6	95,1 ±3,7
impact volume	54,9 ±3,6	55,1 ±2,8	52,2 ±2,2	68,3 ±2,3	56,2 ±3,4	76,1 ±1,4’’	51,3 ±2,1	62,4 ±1,5¯ ¯	51,2 ±2,1	69,1 ±2,3
heart index	3,0 ±1,2	3,1 ±0,4	2,5 ±2,3	3,5 ±1,2	3,1 ±0,5	3,8 ±0,5	2,9 ±1,3	3,4 ±1,8¯ ’	2,4 ±2,3	3,9 ±1,2
general peripheral vascular contraction	2148,3 ±42,4	2137 ±55,5	1792 ±48,1	1531 ±50,1¯	1705 ±51,2	1503 ±47,8¯	1856 ±50,4	1720 ±48,5¯	1772 ±46,1	1581 ±51,1¯
arterial pressure	86 ±9	91 10±	72 ±9	79 ±10	83±10	87±9	85 ±15	90 ±10	75 ±9	78 ±10
arterial pressure central venous pressure	6,8±2	6,1±3	4,4 ±1,8	5,2±2	5±4	6,1±2	5,1±9	6,3±2	4,9 ±1,8	5,1±2

Note: *p<0.05 from the norm: **p<0.01 from the norm: from the initial values: ’’ p<0.01 from the initial values: ¯p<0.05 between (1) and (2): ¯ ¯p<0.01 between (1) and (2). * — when comparing data of patients in groups 1 and 2; BPsr — mean arterial pressure; TPR — total peripheral vascular resistance; SI — cardiac index; HR — heart rate.

When comparing TPR at the second stage, a significant decrease in TPR by 2.4% was noted between the main group of children and the groups, and at stage 3 by 6.5%, as well as at stage 4 by (8.8%). At the awakening stage of the study, TPR decreased by (7.4%). A comparative analysis of the total peripheral vascular resistance (TPVR) values between the first and second clinical comparison groups revealed significant differences, with a 2.2% decrease in total peripheral vascular resistance (TPVR), respectively. When comparing the data at stage 5 of awakening, a 3.5% decrease in total peripheral vascular resistance (TPVR) was observed in the control group.

Hemodynamic parameters in the first group of patients were not significantly different from those in the second group of patients. However, in the third stage of the study, patients in the first group showed a 1.7% increase in stroke volume, while in the second group, a 9.1%

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decrease in stroke volume was observed. Average arterial pressure (ABP) decreased by 4.6% in the same stage and by 6.8% in the second group, while CI decreased by 11.3% and 14.4%, respectively, with a decrease in CI and stroke volume (to 52.2 ± 2.2 ml). It can be noted that combined multimodal anesthesia in combination with EA effectively improves the quality of pain relief, as evidenced by the dynamics of pain intensity and the quality of analgesia.

It was noted that already on the first day of pain treatment, patients demonstrated stable hemodynamic parameters (heart rate, blood pressure, CI, and total peripheral vascular resistance).

In the second group (up to 2.5 ± 2.3 L/min x m²), central venous pressure decreased to 4.4 ± 1.8. In the first group of patients, changes in central hemodynamic parameters were consistent with hypodynamic circulation. Furthermore, total peripheral vascular resistance remained high. Analysis of analgesia showed that hemodynamic disturbances were due to insufficient antinociceptive protection against the surgical aggression of pain syndrome. The persistent flow of nociceptive impulses from the injury site leads to sensitization of nociceptive neurons in the spinal cord and the formation of hyperalgesic zones, which leads to stress-induced circulatory restructuring.

Blood loss was replenished with packed red blood cells (10 ml/kg) and infusion therapy (15-30 ml/kg). In a single case of massive blood loss, infusion therapy was doubled, with a 1:2 colloid ratio between the first and second groups (HES 130/0.4 - Voluven®). Postoperatively, a statistically significant difference of 32.3% was recorded between groups 1 and 2 in terms of initial analgesia, with initial analgesia in group 1 being lower than in group 2, demonstrating the long-lasting effect of EA (bupivacaine) and validating the concept of multimodal analgesia used intraoperatively.

The study concluded that combined multimodal anesthesia effectively improves the quality of pain relief, as evidenced by central hemodynamic parameters and analgesia. They also point to the advantages of using bupivacaine as a component of EA in patients in the first group compared to those in the second group, allowing for earlier tracheal extubation. In the second group, hemodynamic disturbances are caused by insufficient antinociceptive defense against aggression during abdominal surgery, and the persistent flow of nociceptive impulses from the injury site leads to sensitization of nociceptive neurons in the spinal cord, which causes stress-induced circulatory changes.

When assessing the severity of pain using a visual analog scale 6 hours after surgery, the following results were obtained. Thus, the severity of pain syndrome less than 3 points on the VAS in Group 1 patients with analgesia and postoperative intramuscular administration of promedol was 67%. In Group 2, only intramuscular administration of 0.8% ketoprofen was required. Children over 12 years of age required postoperative analgesia. Similar data were obtained when analyzing pain intensity using a visual analog scale 12 hours after surgery. Pain intensity of less than 3 points on the VAS was 55.5% in the first group of patients, compared to 18.3% in the second group. Furthermore, no cases of arterial hypotension were recorded in patients in the second group who used multimodal analgesia (Fig. 1).

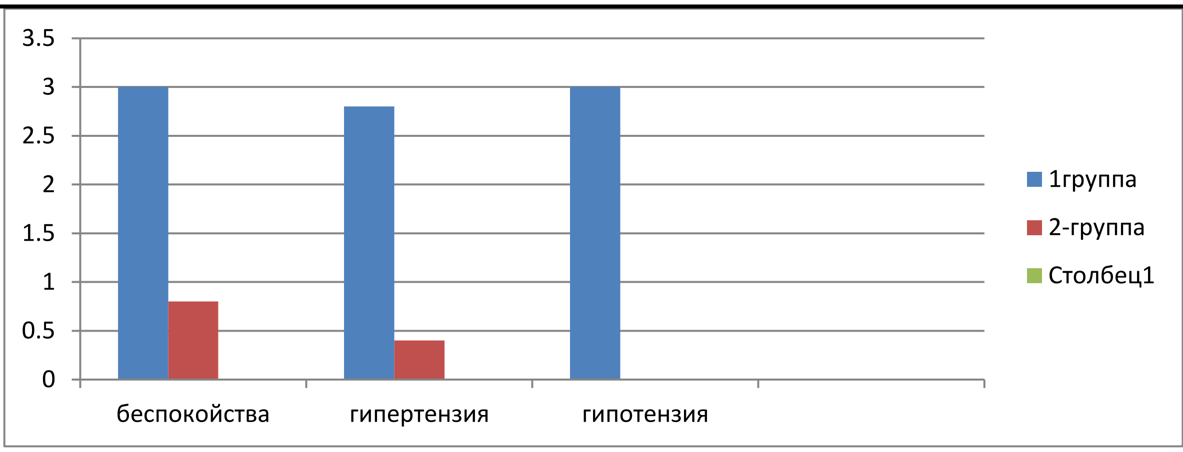

Figure 1. Comparative Rate of Postoperative Complications

Figure 1 shows the rate of postoperative complications in the study groups. The study revealed that the incidence of postoperative nausea and vomiting in the neuroleptanalgesia group was 25.8%, compared to 1.3% in the multimodal group. Postoperative hypertension occurred in 15% of patients in Group 1, compared to 0.5% in Group 2. Hypotension was observed only in Group 1 patients, with a rate of 37.5%, with a reduction in systolic blood pressure of 18–25% from baseline.

Thus, it can be concluded that the vast majority of children in the study group tolerated abdominal interventions quite well, likely due to the chosen method. From this perspective, the positive impact of a combined multimodal anesthesia method on central hemodynamic parameters during abdominal surgery with intra-abdominal resections in children is of particular interest.

Conclusions

1. Personalized modulation of stress-limiting pathways is a new approach in intensive care that can significantly improve the outcomes of surgical treatment of megacolon in children. The relevance of this topic is determined by the need to reduce postoperative mortality, optimize rehabilitation, and implement individualized approaches in pediatric practice.
2. The presented results indicate that the most effective method for pain relief in children is combined multimodal analgesia based on EA, bupivacaine, and propofol, which effectively blocks nociceptive impulses and improves the quality of anesthesia.
3. The use of multimodal analgesia for abdominal interventions provides a 2-fold lower subjective pain intensity according to the VAS scale, thereby improving the quality of the postoperative period in children compared to traditional analgesia with narcotic analgesics.

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