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## NECROTIZING ENTEROCOLITIS OF NEWBORNS. DO WE DO EVERYTHING TO SAVE OUR PATIENTS?

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## НЕКРОТИЧЕСКИЙ ЭНТЕРОКОЛИТ НОВОРОЖДЕННЫХ. ВСЁ ЛИ МЫ ДЕЛАЕМ ДЛЯ СПАСЕНИЯ СВОИХ БОЛЬНЫХ?

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The aim of the study was to compare the efficacy of anesthesia in infants with NEC presacral during anesthesia with different preparations.

We were treated 19 infants with NEC from 1B to 3A stages, during the double-blind controlled prospective randomized study and the period from 2012 to 2014. Boys were 12, girls – 7. Body weigh was 1996±0.2 grams. The group 1 of 10 infants was assigned the complex treatment technique, developed by us, presacral anesthesia 0.5% sol. ropivacaine of 0.1ml/kg. The group 2 was 9 infants, was assigned with the traditional methods of complex intensive care the blockade of procaine solution 0.25% the rate of 0.5ml per administration. Determined by the concentration of substance P, cardiac output and peripheral vascular resistance at diagnosis, after 2,4,8 and 16 hours after initiation of treatment. Assessed the extent and severity of pain on a scale CHEOPS. The control group consisted of 20 healthy newborns without evidence of NEC.

After 16 hours from the start of treatment, despite the additional analgesic therapy was undertaken in a group 2, level of pain on a scale CHEOPS was significantly higher than in the same period of observation in the group 1. It was 9.5±0.2 and 6.0±0.5 points, respectively, with p=0.001. The concentration of substance P in serum of blood of newborns with NEC corresponded to the severity of pain and was significantly higher in the group 2 compared to the group 1 to 16 hour of therapy.

Presacral analgesia with ropivacaine is more efficiently and reduces the number of surgical interventions in newborns with NEC probably by reducing circulatory disorders of internal organs and systems.

*Key words: necrotizing enterocolitis, treatment, anesthesia, pain, scale CHEOPS, newborns*

Рассмотрена проблема лечения новорожденных с некротическим энтероколитом (НЭК). Пациенты были случайным образом распределены на две группы, сопоставимые по гестационному возрасту, весу и полу. Первую группу составили 10 новорожденных с НЭК 1–3 стадии, у которых в комплексе лечения проводили пресакральные блокады с ропивакаином. Вторая группа была представлена 9 пациентами с НЭК 1–3 стадии, которым проводили пресакральные блокады с прокаином. Определяли концентрации субстанции Р в пуповинной крови, сердечный выброс и перифери-

ческое сопротивление сосудов при установлении диагноза, через 2, 4, 8 и 16 часов после начала лечения. Установлена статистически значимая разница по группам наблюдения начиная со 2 часа терапии. Через 16 часов от начала лечения в первой группе по отношению ко второй отмечалось достоверное снижение уровня болевого ощущения по шкале CHEOPS (6,0±0,5 и 9,5±0,28 баллов соответственно,  $p=0,001$ ). Таким образом, проведение пресакральных блокад с ропивакаином является эффективным методом лечения новорожденных с НЭК, приводящим к уменьшению количества осложнений и замедлению прогрессирования заболевания.

*Ключевые слова: некротический энтероколит, лечение, анестезия, шкала CHEOPS, новорожденные*

**D**agnosis and treatment of necrotizing enterocolitis in infants remain an urgent problem in modern pediatric surgery [1]. This is due to the high percentage of septic complications and high mortality in this group of patients [2].

Modern understanding of the pathogenesis of this disease recognizes its multiple etiologic [3]. However, the authors note the high importance of the processes of circulatory disorders in the intestinal wall of the newborns [4]. Some believe that these disorders take place even in utero, contributing to the subsequent translocation of flora from the intestinal lumen into the thickness of the bowel wall, and then leading to the development of local or systemic septic complications [5]. Particularly interesting works, confirming the relationship between pain level and vasoconstriction of internal organs, including intestine, in rats and other laboratory animals [6]. The early biochemical markers of NEC are not completely defined, but it is noticed the increasing level of stress markers in the child's blood serum [7].

Taking into account the determining role of circulatory disorders of the newborns intestine in the pathogenesis of the NEC development, it must be think that effective anesthetizing can reduce the number of complications and mortality risk in patients with developing necrotizing enterocolitis [8]. Simultaneously works, proving the harmful effects of opiates on the developing brain of infants appeared [9].

Traditional anesthetic approaches are that combined methods of analgesia are more effective than monotherapy [10]. It is offered to use as components of analgesia narcotic analgetics, combining them with non-steroidal anti-inflammatory agents in some cases. Only in exceptional cases (Stage 3 NEC, after surgery) it is offered to use presacral blockades of the local anesthetics solution. Procaine is used most for this purpose. To monitor the degree of pain is difficult, and most of the studies are recommended specially designed scales for this purpose [11, 12].

We believe that a single injection of a short acting local anesthetic can not adequately cut short the pain syndrome in newborns with NEC. We have developed a technique of presacral blockades in newborns with NEC with the use of ropivacaine differentially depending on the stage of the disease.

The aim of the study was to compare the effectiveness of anesthesia in infants with NEC during presacral anesthesia with different drugs.

**Material and Methods.** We were treated 19 infants with NEC during the double-blind controlled prospective randomized study and the period from 2012 to 2014. The severity of the disease varied from 1B to 3A stages on clinical data and depending on the measuring thickness of the bowel wall by ultrasound. Available data on allocation of infants depending on the NEC severity are shown in Table 1.

Table 1

Comparison of groups by NEC stage

Group	NEC 1b	NEC 2a-2b	NEC 3a
Group 1 (n=10)	3 (30%)	5 (50%)	2 (20%)
Group 2 (n=9)	3 (33.3%)	4 (44.4%)	2 (22.2%)

Randomly (using a statistical software package «Statistica 6.0» by method of generating of random numbers) infants were allocated in groups of observation. The Group 1 was 10 infants with NEC. They were treated with the use of, technique, developed by us of, presacral anesthesia by 0.5% sol. ropivacaine of 0.1 ml/kg in complex treatment. The Group 2 was 9 infants, which were held with the traditional methods of complex intensive care the blockades procaine solution 0.25% the rate of 0.5 ml per administration. The extent and severity of pain were assessed on a scale CHEOPS at admission, in 2, 4, 8, 16 hours after the presacral anesthesia. In the same period, the state of cardiac output, total peripheral resistance according to echocardiography were determined. The concentration of the neuropeptide – substance P was determined before and after 16 hours after the presacral blockade. Mortality and the number of complications requiring surgical intervention (perforation of a hollow organ or the development of peritonitis) by the end of third day from the time of diagnosis NEC were study endpoints. The Control Group consisted of 20 healthy newborns without evidence of NEC. All groups were matched by age, weight and gender (Table 2).

Table 2

Comparison of investigation groups by gestation age, gender and body weight

Index	Control Group (n=20)	Group 1 (n=10)	Group 2 (n=9)
Gestation Age in weeks (averg.)	35±1.1	34.6±0.9	35.1±1.1
Boys	15 (75%)	6 (60%)	6 (66.6%)
Girls	5 (25%)	4 (40%)	3 (33.4%)
Body weigh, gramm (avrg.)	2019±0.132	1998±0.137	1995±0.142

Statistically significant difference in the groups was assessed by the criterion of Mann-Whitney, considering significant differences in the groups with  $p < 0.05$

**Results.** When establishing the diagnosis NEC the level of pain in patients in the Group 1 and group 2 was significantly higher than in the Control Group of infants. The estimate on a scale CHEOPS between Group 1 and Group 2 did not differ significantly and was, respectively, in average  $11.7 \pm 0.028$  and  $12.0 \pm 0.01$  points ( $p = 1.0$ ). Against the background of the treatment in the Group 1 in 2 hours statistically significant differences, compared to the original data in the severity of pain, were indicated. These differences persisted for a long time. It was characterized by the consistent trend to a decrease of the severity of pain and the approximation of the value of determination on a scale CHEOPS to the indicators of the control group to 16 hour of starting treatment.

In the Group 2, the differences were not significant. Statistically significant differences from baseline were observed only during the first 2 hours from the start of therapy. After 4 and 8 hours statistically significant differences from baseline were not observed. After 16 hours from the start of treatment, despite the additional analgesic therapy, in the Group 2, level of pain on a scale CHEOPS was significantly higher than in the same period of observation in the group 1. It was  $9.5 \pm 0.2$  and  $6.0 \pm 0.5$  points, respectively, with  $p = 0.001$  (Table 3).

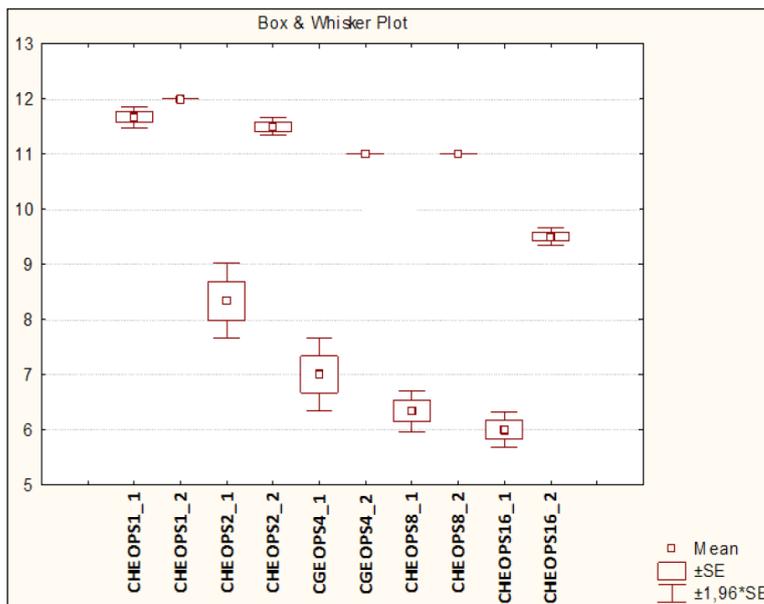


Fig. 1. CHEOPS' levels by groups in different time points

During the statistical analysis, there was no difference between groups in determining cardiac output in different observation periods. Simultaneously peripheral vascular resistance in patient's from Group 1 after 8 hours from the start of treatment was significantly decreased in comparison with the patients of the Group 2.

The concentration of substance P in serum of blood of newborns with NEC corresponded to the severity of pain and was significantly higher in the group 2 comparison with to the Group 1 to 16 hours of therapy.

**Discussion.** As we expected, and it was shown in the course of the study, the effectiveness of procaine analgesia in the development of NEC in newborns is precarious. Significant differences in comparison with the initial high values on the scale of assessment CHEOPS persist only for a few hours. Starting from the 4th hour of therapy, statistically significant differences compared with the original data are not available. At the same time, the differences between groups by this time become statistically significant. In the future, the emerging trend of changes in indicators only persists. In the group of infants with NEC where anesthesia was used in complex with procaine, the severity of pain on a scale CHEOPS, the concentration of substance P significantly higher than those in group, where ropivacaine was used as a local anaesthetic. By 16 hours from the beginning of the intensive care, differences between the groups are still valid.

An interesting fact is that during adequate anesthesia peripheral vascular resistance in newborns Group 1 significantly reduced compared with patients' data of Group 2. This fact may indirectly support the theory that pain impulses contributes to circulatory disorders of the intestine in newborns, initiating the most necrotic changes in the intestinal wall.

As it turned out, the newborn Group 1 had less complications (perforation of a hollow organ, perito-

**CHEOPS' scale levels in patients from different groups**

Time in hours from treatment	Control Group (n=20)	Group 1 (n=10)	Group 2 (n=9)
Initial assessment	5,8±1,1	11.66±0.29 *	12.00±0.001 *
After 2 hours	-	8.33±1.04 **\***	11.5±0.25 *
After 4 hours	-	7.0±1.0 **\***	11.0±0.02 *
After 8 hours	-	6.3±0.57 **\***	11.0±0.01 *
After 16 hours	-	6.0±0.5 **\***	9.5±0.25 *\**

\* –  $p < 0.05$  in comparison with Control Group.

\*\* –  $p < 0.05$  in comparison with initial assessment from the same group.

\*\*\* –  $p < 0.05$  in comparison with the same time from the Group 2.

Dynamics of the pain sensations of both droup is reflected in Fig. 1. It is clearly visible that in the Group 1 the duration and severity of the analgesic effect is significantly higher than in the Group 2. It appears authentic, and significant reduction of measure pain on a scale CHEOPS approaching it to the normal values to 16 hour of therapy NEC.

nitis and others), which required much less surgical intervention in the first 3 days from the time of diagnosis NEC (Fig. 2). The mortality rate in the groups did not differ significantly, however, in our opinion this pattern is due to the short observation period (3 days) and a small amount of the sample population, which requires further research in this area.

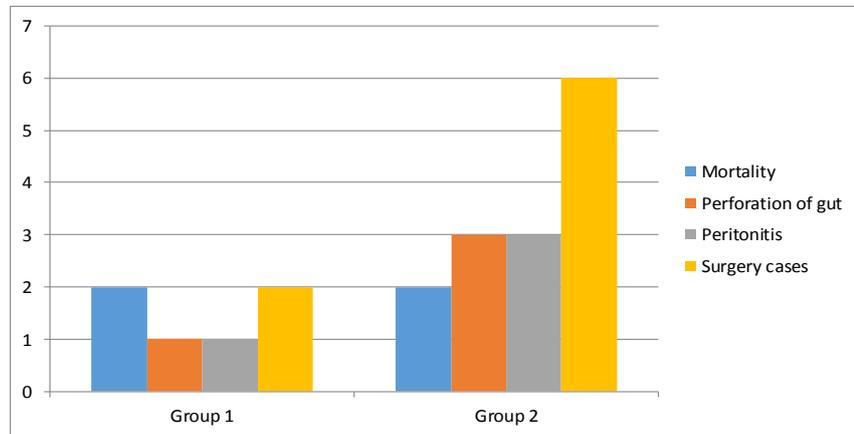


Fig. 2. Mortality levels and amount of surgical cases by groups

An essential component of maintaining necrotic processes in the wall of the intestine in the newborn can be a pain syndrome, which leads to the development of vascular spasm and increase peripheral vascular resistance, however, this requires further study.

### Conclusions

1. In the complex treatment of newborns with NEC should be widely used Presacral blockade with ropivacaine solution as an effective and safe method of analgesia in newborns with the indicated pathology.

2. Using the purpose of analgesia in a single injection solution Presacral space procaine undesirable because short duration of action (less than 4 hours) and low efficiency.

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