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CLINICAL EFFICACY OF GASTRIC FEEDING WITH ANTIREFLUX MIXTURE IN PREMATURE INFANTS ON MECHANICAL VENTILATION

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Abstract. *Introduction.* Gastroesophageal reflux is a common pathological condition in critically ill premature infants. *The aim of the study* was to analyze the incidence of gastroesophageal reflux (GER) in premature infants and to evaluate the effectiveness of gastric feeding with antireflux mixture in children on artificial ventilation in the presence of GER. *Materials and methods.* A retrospective study was conducted on the basis of the Irkutsk Municipal Pediatric Clinical Hospital (Irkutsk) in the period from 2018 to 2020, which included the medical histories of 73 premature infants. In the course of the study, the frequency of GER, the frequency of use of antireflux drugs, changes in body weight during the period of stay in intensive care, the duration of ventilation, the duration of stay in intensive care and changes in laboratory parameters at the time of admission and 10 days after the start of intensive care were evaluated. *Results and discussion.* A retrospective analysis showed that 69.8% of the total number of children in the medical history had any records of manifestations of gastroesophageal reflux. When clinical manifestations of GER occurred, the frequency of transfer to an antireflux mixture was in 100% of cases, of which 52.4% received medication (motilium, omeprazole) during hospitalization in intensive care, and 19.6% continued to receive it after transfer to the department. Among those who received antireflux mixtures, GER was diagnosed in only 47% of patients. Among all newborns who received the drugs, 62.7% of patients received motilium and 35.2% omeprazole. With the ineffectiveness of conservative antireflux therapy, surgical fundoplication was performed in 17.6% of patients. *Conclusion.* Conservative antireflux therapy for gastric feeding in premature infants with low and very low body weight, with pneumonia, on artificial lung ventilation does not provide sufficient effectiveness of child nutrition.

Keywords: *intensive care in neonatology, enteral feeding, antireflux therapy*

КЛИНИЧЕСКАЯ ЭФФЕКТИВНОСТЬ ГАСТРАЛЬНОГО КОРМЛЕНИЯ АНТИРЕФЛЮКСНОЙ СМЕСЬЮ У НЕДОНОШЕННЫХ ДЕТЕЙ НА ИСКУССТВЕННОЙ ВЕНТИЛЯЦИИ ЛЕГКИХ

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Резюме. *Введение.* Гастроэзофагеальный рефлюкс — часто возникающее патологическое состояние у недоношенных новорожденных детей в критическом состоянии. *Цель исследования* — проанализировать

частоту развития гастроэзофагеального рефлюкса (ГЭР) у недоношенных детей и оценить эффективность гастрального кормления антирефлюксной смесью у детей на искусственной вентиляции легких при наличии ГЭР. *Материалы и методы.* На базе Областного государственного автономного учреждения здравоохранения «Городская Ивано-Матрёнинская детская клиническая больница» (г. Иркутск) в период с 2018 по 2020 гг. было проведено ретроспективное исследование, в которое были включены истории болезни 73 недоношенных детей. В процессе исследования оценили частоту ГЭР, частоту использования антирефлюксных препаратов, изменение массы тела за период нахождения в реанимации, длительность ИВЛ, продолжительность пребывания в реанимации и изменения лабораторных показателей на момент поступления и через 10 дней после начала интенсивной терапии. *Результаты и обсуждение.* Проведенный ретроспективный анализ показал, что у 69,8% детей в истории болезни были какие-либо записи о проявлениях гастроэзофагеального рефлюкса. Все пациенты при возникновении клинических проявлений ГЭР получали антирефлюксную смесь, из них у 52,4% проводили медикаментозное лечение (мотилиум, омепразол) во время госпитализации в реанимации, а 19,6% продолжали получать их и после перевода в отделение патологии новорожденных. Среди тех, кто получал антирефлюксные смеси, ГЭР был диагностирован только у 47% пациентов. Из всех новорожденных, получавших препараты, 62,7% пациентов получали мотилиум и 35,2% омепразол. При неэффективности консервативной антирефлюксной терапии 17,6% пациентов была выполнена оперативная фундопликация. *Заключение.* Проведение консервативной антирефлюксной терапии при гастральном кормлении у недоношенных детей с низкой и очень низкой массой тела, с пневмонией, на искусственной вентиляции легких не обеспечивает достаточной эффективности питания ребенка.

Ключевые слова: *интенсивная терапия в неонатологии, энтеральное кормление, антирефлюксная терапия*

INTRODUCTION

Gastroesophageal reflux (GER) is a pathologic condition that often occurs in premature infants in critical condition. A number of factors contribute to this condition: a relatively large volume of liquid food intake, functional "immaturity" of the lower esophageal sphincter, and the position of the child's body when feeding — the child lying on the back [1]. Determining the exact prevalence of GER versus gastroesophageal reflux disease (GERD) is a difficult task because of the unclear distinction between physiologic and pathologic reflux.

Conservative treatment should be considered as first-line therapy in infants without clinical complications [2]. Based on the available data, body positioning can be considered a well-established and safe method for the treatment of preterm infants with symptoms of uncomplicated GER. A reduction in GER manifestations is observed in the left lateral position with the head elevated, whereas the supine and right side positions provoke reflux [3]. In addition, certain benefits can be achieved by modifying the diet and/or duration of feeding, such as reducing the feeding rate and using hydrolyzed formula [4]. The use of transpyloric feeding is an effective feeding method, allows faster stabilization of nutritional balance and substantial weight gain [4]. Gum used to thicken the food clump has been found to impede the absorption of a number of nutrients [5, 6]. There have also been concerns about a possible association between formula thickener and the development of necrotizing enterocolitis [7]. Antireflux medications, including histamine-2 receptor antagonists and proton pump inhibitors, are not licensed for use in newborns in the Russian Federation (RF) and many other countries, although *off label* use (use of medications for indications not mentioned in the instructions for use) is often reported [8]. Antacids and other acid-suppressing drugs can reduce gastric acidity but do not affect the signs/symptoms of GER, and their use is associated with an increased risk of adverse outcomes, including necrotizing enterocolitis (NEC) and infections [9]. A number of researchers recommend the use of antireflux medications with caution (if it is possible) in preterm infants because of the lack of evidence of efficacy and possible harm [10].

AIM

To analyze the incidence of gastroesophageal reflux (GER) in preterm infants and to evaluate the efficacy of gastric feeding with antireflux formula in infants on artificial lung ventilation in the presence of GER.

MATERIALS AND METHODS

A retrospective study was conducted. It included 73 case histories of premature infants treated

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in the neonatal intensive care unit of the Ivano-Matryoninsky Children's Clinical Hospital (Irkutsk city) in the period from 2018 to 2020. Patients included in the study were born prematurely at 28–35 weeks of gestation with low and very low weight, required ventilatory support and had a confirmed diagnosis of pneumonia.

The patients in the generated sample were divided into two groups. The first group consisted of 51 patients with confirmed gastroesophageal reflux. The second group consisted of 22 patients without GER. Respiratory therapy in the intensive care unit was performed in the PCV (pressure-controlled ventilation) mode using a MAQUET Servo-i ventilator (Germany).

In the course of the study, we evaluated the frequency of GER, ALV and changes in laboratory parameters at the time of admission and 10 days after the start of intensive care.

Statistical processing of the obtained data was performed using STATISTICA 10.0 program. The results are presented as median and quartiles (25–75%). Statistical analysis of significance of differences between quantitative signs for two independent groups was performed using the Mann–Whitney criterion. The Kraskell-Wallis test was used to assess the statistical significance of differences between several signs in dynamics. The p value <0.05 was taken as the level of statistical significance.

RESULTS

Retrospective analysis of medical records showed that 69.8% (n=51) of children had any records of gastroesophageal reflux manifestations in their medical history. Gestational age in the group of children with GER was 31 (28–35) weeks and in the group without GER it was 32 (28–36) weeks. Age at the time of admission was 19 (10–77) days in the group with GER and 17 (9–65) days in the group without GER. At the onset of clinical manifestations of GER, 100% of patients received antireflux medication, of which 27 patients (52.4%) received medication (motilium, omeprazole) during ICU hospitalization, and 19.6% (n=10) continued to receive them even after transfer from the ICU. Among those who received therapeutic (antireflux) formula, GER was diagnosed in 47% (n=24) of patients. Among all neonates receiving medication, 62.7% (n=32) of patients received motilium and 35.2% (n=18) received omeprazole. If conservative antireflux therapy was ineffective, 9 (17.6%) patients underwent surgical fundoplication (Fig. 1).

In analyzing of the weight dynamics on the 10th day from the beginning of conservative antireflux therapy it was found that children diagnosed with GER had a lower weight gain of 11 (9–14) g compared to patients without reflux 17 (14.5–18) g (p_U <0.01). When analyzing the weight of patients on the 10th day of conservative antireflux therapy

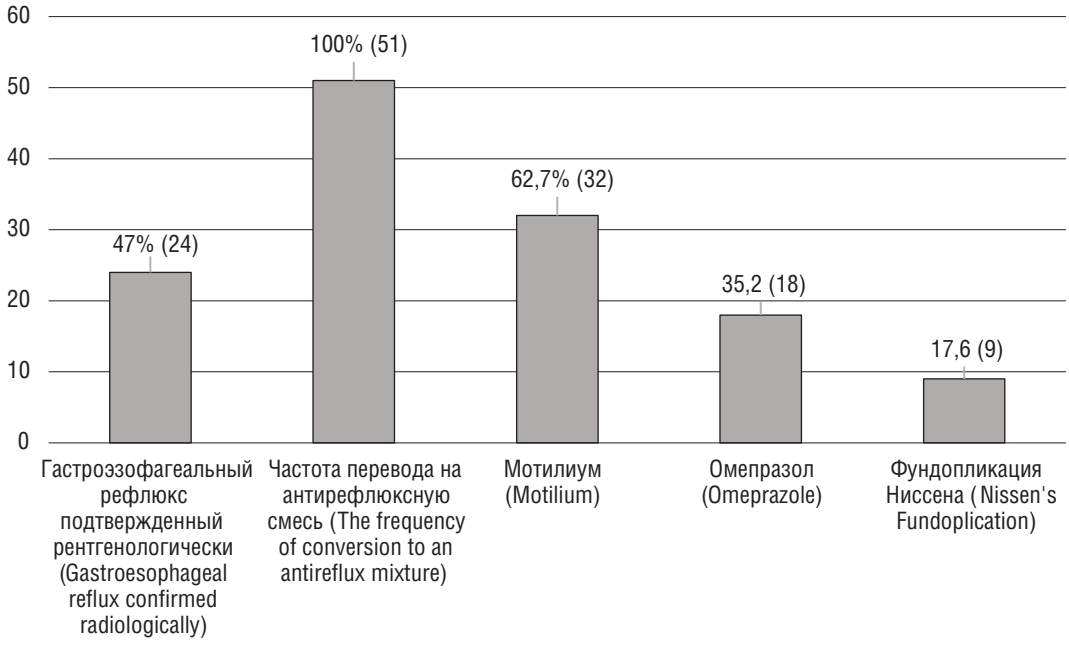

Fig. 1. Retrospective analysis

Рис. 1. Ретроспективный анализ

we managed to reveal statistically significant differences. Thus, weight in children with GER was 1979 (1759–2100) g, in patients without gastroesophageal reflux it was 2247 (2090–2337.5) g (p_U <0.01) (Fig. 2). Intensive care stay time in children diagnosed with GER was significantly higher than in children without GER, 12 (9.5–14.5) days versus 17 (15–20) days (p_U <0.01).

The rates of length of hospital stay in children with GER were 49 (34–74) days versus 37 (34–46) days in children without GER (p_U <0.01). The level of total protein in patients with GER on the first day was 39.2 (35.3–53.3) g/L. Control of this parameter on the 10th day revealed a decrease in the concentration of total protein to 34.1 (30.9–48.2) g/L. Total protein in the group of children without GER on the first day was 40.2 (38.1–51.3) g/L, on the 10th day in the group of children without GER the level of total protein was 46.9 (42.2–50.8) g/L (Fig. 3).

Creatinine in children with GER on the first day was at the level of 54.4 (28.2–56.5) μmol/L. In the group of children without gastroesophageal reflux it was 49.1 (33.3–58.7) μmol/L. On the 10th day of the study there were also no significant changes in the studied groups. Thus, the creatinine level in the group with GER — was 50.5 (30.3–53.9) μmol/L, in the group of children without GER it was 54.3 (30.2–52.6) μmol/L. Comparable results were obtained when analyzing urea levels. In the group of children with reflux in the first day of stay in the Department of Anesthesiology, Reanimation and Intensive Care urea was 3.0 (2.2–3.5) mmol/L, on the 10th day of observation it was 4.0 (3.0–4.8) mmol/L. In the group of children without GER it was 3.2 (2.5–3.9) mmol/L, on the 10th day of observation it was 4.1 (3.2–5.4) mmol/L. Glucose level in the group of children with GER on the first day was 4.2 (3.6–7.1) mmol/L, in the group of children without GER it was 4.9 (3.8–5.1) mmol/L. Thus, in the group of children with GER the glucose level was 5.9 (3.3–7.8) mmol/L, in the group without GER it was 5.3 (4.5–6.9) mmol/L. The level of K^+ in the group of children with gastroesophageal reflux on admission was 4.1 (3.5–4.5) mmol/L, in the group of children without GER it was 3.9 (3.4–4.2) mmol/L. The study of K^+ level in dynamics did not reveal statistically significant changes: on the 10th day of the study in the group of children with gastroesophageal reflux the level of K^+ was 3.8 (3.5–4.2) mmol/L, in the group of children without GER it was 4.1 (4.0–5.3) mmol/L. Na^+ concentration in the group of children with gastroesophageal reflux on admission was 137.5 (136.0–142.6) mmol/L, in the group of children without GER it was 139.3 (137.0–141.6) mmol/L. When studying the level of Na^+ concentration in dynamics, no statistically significant differences were found: on the 10th day of the study in the group of children with GER the Na^+ level was 138.10 (136.4–141.6) mmol/L, in the group without GER it was 138.1 (136.6–140.9) mmol/L. Plasma Ca^{2+} concentration in the group of children with GER at admission was 1.15 (1.1–1.5) mmol/L, in the group without GER it was 1.3 (1.1–1.4) mmol/L. On the 10th day of the study, in the group of children with gastroesophageal reflux the Ca^{2+} level was 1.1 (1.1–1.3) mmol/L, in the group of children without GER it was 1.3 (1.0–1.4) mmol/L.

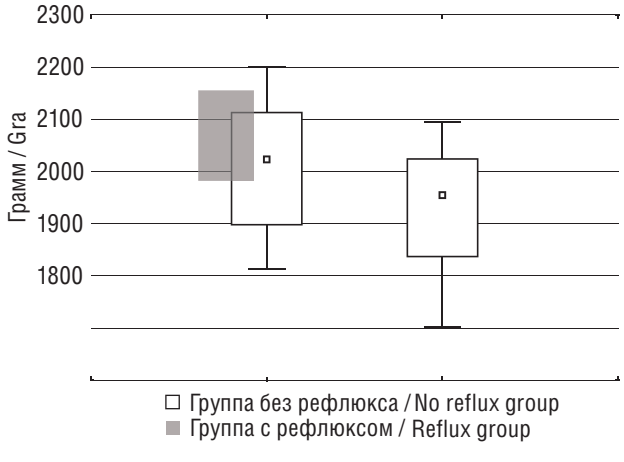

Fig. 2. Weight on the 10th day of antireflux therapy

Рис. 2. Масса тела на 10-й день проводимой антирефлюксной терапии

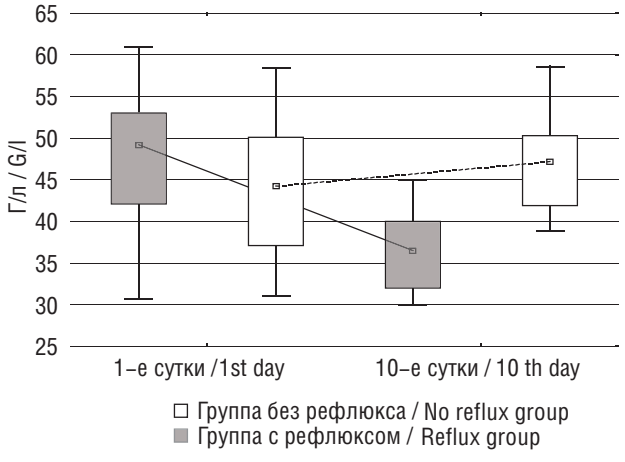

Fig. 3. Total protein level

Рис. 3. Изменения уровня общего белка

DISCUSSION

It was found that children with reflux had lower birth weight and gestational age during comparing patients with gastroesophageal reflux with patients without GER. This may be due to the fact that transient relaxation of the lower esophageal sphincter is more common in preterm infants. An interesting finding was that the incidence of using drugs for conservative therapy of GER was higher than the incidence of documented GER. This indicates that drugs for conservative therapy of GER are prescribed without a confirmed diagnosis. In our analysis, we found that manifestations of GER occurred in 69.8% of patients, while the rate of switching to antireflux formula was 100% of cases. However, among infants receiving antireflux treatment, gastroesophageal reflux was confirmed radiologically in only 39.6%. In 36.9% of cases, infants received medication during hospitalization in the intensive care unit, and 18.2% of patients continued to receive medication after they were transferred. We noted a high level of use of drug therapy in preterm infants: in 57% of cases motilium was prescribed, in 45.4% of cases children received proton pump inhibitors (omeprazole). When analyzing weight dynamics, it was found that the average daily weight gain in children with reflux was 32.2% less than in children without GER. The concentration of total protein in children with GER was also 14.2% lower than in children without GER. Due to ineffectiveness of conservative therapy, 17.6% of patients underwent fundoplication.

CONCLUSION

Conservative antireflux therapy with gastral feeding in premature infants with low and very low weight, with pneumonia, on artificial lung ventilation does not provide sufficient effectiveness of feeding the child.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

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Consent for publication. Written consent was obtained from legal representatives of the patients for publication of relevant medical information within the manuscript.

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