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Original Article

The Comparison of Growth and Developmental Status in Surgical Necrotizing Enterocolitis with the Control Group

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Abstract

Background: Surgery in premature neonates following Necrotizing Enterocolitis (NEC) is an awful event. There are many concerns regarding the future of these neonates. Releasing inflammatory substances following perforation can have a significant impact on the premature brain. Based on the ASQ questionnaire, we aimed at finding out whether there is any neurodevelopmental delay following NEC surgery.

Methods: We compared developmental aspects of neonates who underwent NEC surgery with control using the Ages and Stages Questionnaire (ASQ II).

Results: We compared 29 children that had surgical NEC in their neonatal period with their premature peers. They were homogeneous in age, sex, head circumference, weight, and Apgar count at birth in the neonatal period; they had no significant difference in the incidence of sepsis and ventilation-requiring days and cerebral incidence hemorrhage. At the study time, there was a significant difference in growth parameters, weight ($p<0.001$), and height ($p=0.014$). Also, there was no significant difference in head circumference and developmental parameters such as communication, motor, and problem-solving domains.

Conclusion: This study indicates that if these patients do not develop severe neurological complications in the neonatal period, their abilities are close to their premature peers in arrival to community and school. However, we still recommend close monitoring of these cases due to the possibility of impaired central nervous-gastrointestinal coordination.

Keywords: Brain, Child, Communication, Hemorrhage, Humans, Infant, Newborn, Schools, Sepsis, Surveys and Questionnaires

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Introduction

Necrotizing Enterocolitis (NEC) is a prevalent global surgical emergency of the gastrointestinal tract in newborn infants. Up to 5% of patients are admitted to the Neonatal Intensive Care Units (NICUs). Peritonitis occurs in critically ill premature infants with a limited physiological reserve (1,2). It results in severe changes in various body systems, leading to a very high mortality rate (1,3). Despite advances in healthcare, the mortality rate is currently around 30% (4,5). Several studies show that premature infants are at high risk of cognitive and psychomotor disorders than term children. The neural developmental disorder is a primary complication of NEC (6-8). At present, about 30% of these patients die at the earliest stages of care, but the others' fate and their life adequacies remain unclear (7,9). Surveys have revealed that many premature children's lives are close to that of their peers; however, in these cases, peritonitis and surgery seem to separately affect the patient's physical and neural development (3,6,10). These patients sometimes require frequent admissions due to gastrointestinal complications such as short bowel syndrome, malnutrition, various infections, and other complications. These conditions can also affect the growth and development of these patients. This study's main objective was to investigate the effect of surgical complications and subsequent stresses on these patients' growth and development.

Materials and Methods

This survey is an analytic cross-sectional study performed in the developmental clinic of the Children's Hospital of Tabriz University of Medical Sciences from October 2013 until October 2017. Developmental aspects and growth of all premature neonates with surgical NEC were compared with their control group. The developmental status of participants was evaluated using the Ages and Stages Questionnaire II (ASQ II). We compared them with the cutoff points related to each area (11,12). We used the ASQII (third year of life) for comparing both groups. The implemented ASQ was adapted to the culture of Iranian patients. The control group was premature neonates without a history of surgery based on inclusion and exclusion criteria.

Inclusion criteria

1. Premature neonates less than 34 weeks gestational age with NEC who underwent surgery and survived until the end of the study.
2. The control group included premature neonates less than 34 weeks gestational age.

Exclusion criteria

1. Anomalies of CNS or brain damage unrelated to NEC
2. Congenital anomalies
3. Presence of malnutrition for reasons unrelated to NEC
4. Parents granted no consent for participation in the study and follow-up
5. Deafness
6. Visual disturbances.

We extracted the required data from the files based on the data collection form. The children were invited and thoroughly examined after obtaining their parents' informed consent. We measured height and weight with a weight and size measuring scale (Seca) and the head circumference with a tape measure. Developmental status of infants was assessed using ASQ II. We extracted other data such as gestational age, birth weight, labor complications, the location of anomalies, length of stay, and types of treatments from the patients' files. In case a patient did not attend the office, we called them to decrease the missing data. Our interviewer was a development expert, thus the history and physical examination were observed, decreasing the parents' errors during the interview.

Statistical analysis

The statistical analysis was performed through a descriptive method (frequency, percentage, mean, and standard deviation), and Chi-square and the mean difference tests were used for comparison. The Kolmogorov-Smirnov test was utilized to assign the normality assumption. Based on the statistical formulae, 30 patients were sufficient in each group for this study with a significance level of 0.05 and a power of 0.80. All statistical analyses were performed by SPSS17 for Windows (SPSS Inc., Chicago, IL, USA), and $p<0.05$ in all cases were considered significant.

Results

This study included 29 patients with surgical NEC and 29 preterm patients as the control group born from October 2013 to October 2016.

At birth, patients were homogeneous in gestational age, weight, sex, head circumference, and height. These parameters were not significantly different from each other (Table 1). The Kolmogorov-Smirnov test held the normality assumption between both groups. Sixty-two percent of the children (18 patients) with NEC and Fifty-five percent of the children (16 patients) without NEC were delivered via cesarean section route. At birth, 13 patients (45%) from the case group needed ventilation support. In the control group, it was 31 % (nine patients). Patients' age at the time of surgery was 7.00±10.82 days (2-45 days). Four patients had Spontaneous Intestinal Perforation (SIP). Ten patients (34%) had stage 3A of modified Bell's staging in NEC's staging, and 19 patients (66%) had stage Bell 3B. The surgery resulted in short bowel syndrome in two patients (7%) managed by total parenteral nutrition. We evaluated patients for growth and development parameters, height, weight, and head circumference. Patients with surgical NEC had delay comparing to the control group in two parameters of height (p=0.014) and weight (p<0.001) at the time of the study (Table 2). ASQ II evaluated the developmental staging. This section failed to show any significant difference between these patients and their peers. These patients had an acceptable score, above the cutoff point (ASQ: SE-2 age interval cutoff score at three years old is 105), and they did not need complementary tests.

Discussion

Patient caregivers are always concerned about patients' primary care and future surgical NEC status (13). This disease's potential risks are prematurity, peritonitis, surgical stress, neonatal anesthesia, and the probability of short bowel syndrome (14). Prematurity alone causes several complications, including brain problems (such as cerebral hemorrhage and leukoencephalopathy) and an increased risk of infection. Due to multiple issues, the probability of these patients' long-term survival may decrease (15,16). All of these problems can lead to serious long-term harm to the baby. These concerns include impairments in patients' growth retardation,

Table 1. Displays demographic information

At birth	NEC	Premature	p-value
GA (week)	31.83±4.81	30.16±3.78	N/S
Sex (male)	47%	53%	N/S
Birth weight (gr)	778±1843	1687±488	N/S
Head circumference(*cm*)	3.97±31.05	93.99±29.23	N/S
Height (*cm*)	40.36±6.76	39.58±6.61	N/S
Apgar	8.43±0.81	8.26±0.87	N/S

N/S: Not significant.

Table 2. Growth parameters at three years of age

At three years old	NEC	Premature	p-value
Birth weight (*kg*)	11.23±23	14.33±3.9	0.001
Head circumference (*cm*)	46.43±1.87	46.65±0.97	N/S
Height (*cm*)	89.86±9.95	92.93±8.52	0.014

N/S: Not significant.

psychomotor development, and mental abilities (17). The mentioned concerns caused these patients to be monitored for long-term physical development and evaluated for psychomotor development (18). Complications decreased with recent advances in NICU care and individualized development (19). It has always been a concern for parents and caregivers that they can enter school, grow, learn well after a very stressful period, and tolerate various therapeutic interventions at the beginning of their lives. We designed this study in two aspects of physical growth and development. Can severe stress and the need for special care interfere with a child's brain development and learning routine? Does inhalation anesthesia at birth harm the patients' mental development?

In premature infants with enterocolitis, severe inflammation and ischemia and the products of oxidative cycles and severe damage to the intestines are significant stressors. Shortening the absorption level of the premature infants' intestine causes severe damage to the digestive process. Intestinal damage and anatomical changes can lead to disruption of the intestinal microbial flora. These factors can lead to impaired physical growth, especially in the short term (18). Does this condition persist for a long time, and can it interfere with central nervous system-gastrointestinal coordination? We have no answers to these questions (20,21). Many studies reported the possibility of delayed physical growth in patients with enterocolitis requiring surgery (15,22,23). In some studies, growth retardation was not significant (24,25). In 2018, Hong *et al* showed that patients with necrotizing enterocolitis had severe growth retardation at discharge. However, by 18 to 22 months of age, this growth retardation is almost caught up than their control peers (18).

In this study, patients with surgical NEC were significantly behind in weight gain and height growth compared to their predecessors. No significant differences were observed in head circumference between the two groups. They may receive fewer calories than their peers that probably indicate a disorder of central nervous system-gastrointestinal coordination. These patients' care plans should include proper physical growth monitoring and treatment to prevent this condition. The Ages and Stages Questionnaire (ASQ II) can be filled out by parents or caregivers quickly. It is a suitable and trustable screening instrument for developmental delay. It is translated into Persian and showed its reliability and validity in many studies (11,12).

Numerous studies have shown warnings with regard to neurodevelopmental growth in patients with surgical necrotizing enterocolitis. Patients' families are always concerned about their entry into society and their ability to compete with their peers. This issue is considered in many studies, thus reducing these abilities has been shown (15,17,22,24). In contrast, in many studies, the problems caused by this situation have not been significant compared to their peers (16,25,26). In a review article, Mutanen *et al*, in two areas of physical growth and neurodevelopment, reported delay in surgical NEC patients (15). They also stated that one of the causes of these disorders is anesthesia in infancy, although there is not much agreement about it (27). In this study, we could not show a significant difference between patients in the two groups. The patients' communication, problem-solving, motor, and personal-social skills were similar to the control group. One of the critical reasons in this study could be eliminating patients with severe complications and severe brain complications in infancy (based on the exclusion of criteria). However, this indicates that if these patients do not develop severe neurological complications in infancy, their abilities are close to their peers.

Study limitations

As the hospital is a tertiary level and the patients are referred from other hospital centers, we have little information regarding their previous care and its impact on the development. We suggest that for further studies, maybe it is better to calculate SNAPPE2 criteria at the beginning of admission of each neonate.

Conclusion

In total, there are two significant concerns for patients with necrotizing enterocolitis requiring surgery. The concerns include their physical and nervous development. In the current study, a disturbance was found in weighting parameters and a smaller amount in the patients' height growth. In head circumference and neurodevelopment, we failed to show a disorder

compared to their pre-matched counterparts. However, we still recommend monitoring these patients, and due to the possibility of impaired central nervous-gastrointestinal coordination, these patients need more attention.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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