



## Transpyloric Feeding of Gastroesophageal Reflux of Preterm Infants

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### Abstract

Optimizing nutritional support is essential for critically ill children, and preterm infants are particularly vulnerable to the effects of prolonged fasting. There is a lot of evidence in the scientific literature for the benefits of enteral nutrition. It is known that premature infants need an individual approach to nutrition due to the prevalence of catabolic processes, while treatment in the intensive care unit requires a surplus of calories. Timely introduction of enteral nutrition helps to reduce morbidity and mortality in this population. Gastroesophageal reflux (GER) is common in preterm infants. The decreasing tolerance to enteral feeding makes doctors usually prefer parenteral nutrition. However, its use can be associated with metabolic, infectious and iatrogenic complications. A step-by-step therapeutic approach is recommended in the treatment of GER in preterm infants. Conservative treatment should be considered as first-line therapy in children without clinical complications. Feeding through a gastric tube is not always well tolerated by seriously ill patients. As for the treatment of complicated GER, studies show that the use of transpyloric feeding is comparable in effectiveness to fundoplication. Transpyloric feeding tube can be justified as a strategy for treating GER that is refractory to conservative therapy.

**Keywords:** Enteral Nutrition; Transpyloric Feeding; Preterm Infants; Gastroesophageal Reflux; Nutritional Support

### Introduction

Prematurity is the leading cause of infant morbidity and mortality. In the structure of infant mortality, 40% occurs in the early neonatal period and 30% in the post-neonatal period [1-3]. Providing nutritional support for the care of seriously ill patients in the intensive care unit is an extremely important and very complex task facing neonatologists [4-6]. For patients who need nutritional support, early feeding can be provided enterally or parenterally. According to European guidelines, enteral nutrition is the preferred method of feeding for patients with a functioning gastrointestinal tract. Gastroesophageal reflux (GER) is common in preterm infants. At the World Congress of Gastroenterologists

in 2006 (Montreal), a definition of gastroesophageal reflux disease was proposed as a condition that develops when throwing stomach contents into the esophagus causes disturbing symptoms and/or leads to the development of corresponding complications [7]. Infants with gastroesophageal reflux should be managed in a step-wise fashion using non-pharmacological measures where possible and pharmacological measures where necessary [8]. The causes of the development of GER in premature infants are the presence of antral hypomotor activity, altered tone of the inferior esophageal sphincter, and delayed gastric emptying [9]. A large residual volume of the stomach often leads to interruption of feeding, forcing the use of parenteral nutrition. Reduced peristaltic activity in the duodenum is probably less significant than impaired peristalsis in

the stomach. Placing the tube after the pylorus should overcome the risk of developing gastroesophageal reflux, since the pylorus acts as a protective barrier, excluding reflux of contents back into the stomach [10]. Methods of feeding a critically ill patient are still a goal of debate, as is the determination of the best way to provide enteral nutrition [11]. Postpyloric feeding is associated with a significant reduction in the residual volume of the stomach, which can ensure the intake of sufficient nutrients. It is successfully used to maintain enteral nutrition in patients who would otherwise require parenteral nutrition [12].

### Problems of feeding in preterm infants

The incidence of GER among infants born before 34 weeks of pregnancy is approximately 22% [13,14]. In premature infants, gastroesophageal reflux should be considered as a pathological phenomenon that can be promoted by a number of physiological factors. First of all, they include the "supine" position of the body, which increases the migration of liquid gastric contents [15]. In addition, factors contributing to the development of gastroesophageal reflux include immature esophageal motility, delayed gastric emptying, which gives more time for reflux to occur [16]. The shorter inferior esophageal sphincter, which is located slightly above rather than below the diaphragm, serves as a less effective barrier to gastric contents [17]. After birth the esophagus lengthens, and the inferior esophageal sphincter moves deeper into the abdominal cavity, increasing the barrier effect. During development, the inferior esophageal sphincter functionally "matures", leading to a decrease in transient relaxations [18]. At the same time, the nature of infant feeding contributes to an increase in the frequency of GER development. The diet of preterm infants and the liquid consistency of food facilitates gastroesophageal regurgitation. In addition, to achieve normal growth, premature infants should get more calories than older babies. The need for the necessary calories creates a significant burden on the stomach. There is some supporting evidence for the theory that delayed gastric emptying leads to increased episodes of inferior esophageal sphincter relaxation that cause reflux [19]. Other evidence suggests that reflux in infants is mainly the result of inferior esophageal sphincter dysfunction, rather than delayed gastric emptying [20]. There are also external factors that contribute to the development of GER in infants. Some medications, such as theophylline and caffeine, often used to treat apnea and bronchopulmonary dysplasia in premature

infants, have a number of gastrointestinal side effects. Methylxanthines lead to smooth muscle relaxation, increased gastric secretion, and may be associated with increased episodes of reflux. Nasogastric tubes are often used to feed infants who have reduced or no sucking and swallowing reflexes. However, there are data indicating an increase in GER episodes when nasogastric tubes are standing [6]. In addition, some clinical conditions and syndromes commonly seen in the intensive care unit also put infants at increased risk of developing gastroesophageal reflux. The association between apnea, gastroesophageal reflux, and bronchopulmonary dysplasia remains controversial [21-23]. However, in some cases, gastroesophageal reflux may be associated with complications such as feeding problems, growth retardation, esophagitis, and aspiration [24,25]. Conservative treatment of gastroesophageal reflux is still a subject of debate. A non-pharmacological approach, such as changing the body position [19], changing the feeding regimen, and using anti-reflux formulas for feeding, is currently considered the recommended strategy in the treatment of premature infants [26]. The use of inhibitors of gastric acid secretion, such as H<sub>2</sub>-receptor blockers and proton pump inhibitors, is associated with an increase in the number of cases of necrotic enterocolitis and infection [27]. There is evidence that oral domperidone administration causes prolongation of the QT interval [13]. Therefore, before starting pharmacological therapy, the prospects for risk and benefit should be carefully evaluated. GER is usually suspected based on the development of a number of clinical symptoms, but it can also be confirmed by special diagnostic methods. Esophageal pH measurement is generally recognized as a standard diagnostic method [19]. pH-metry also allows you to detect episodes of acid reflux. However, a significant limitation of this method is its inability to detect neutral refluxes. Thus, since the acidity of gastric juice depends on age, feeding mixtures buffer the pH of the stomach contents, therefore, the pH-metric may be erroneous when used in premature infants [17,15]. Another method for diagnosing gastroesophageal reflux is monitoring multiple intraluminal impedance [14]. This method analyzes variations in the electrical impedance of the esophagus through several intraluminal electrodes [19,28]. Because of its specific ability to detect non-acid refluxes, intraluminal impedance monitoring is considered a sensitive diagnostic tool, especially useful in the postprandial period [29]. A step-by-step therapeutic approach is recommended in the treatment of GER in preterm infants. Conservative treatment

should be considered as first-line therapy in children without clinical complications [30]. Based on the available data, body position can be considered a well-proven and safe treatment for premature infants with symptoms of uncomplicated GER. A decrease in GER manifestations is observed in the left side position with an elevated head end, while the position on the back and right side provokes reflux [31]. In addition, certain benefits can be achieved by changing the diet, for example, reducing the feeding rate or using a hydrolyzed mixture [9]. Antireflux drugs have been found to be ineffective in the treatment of gastroesophageal reflux in preterm infants, and gum used to thicken the food lump makes it difficult to absorb a number of nutrients [15,32]. There was also concern about a possible linking between the milk thickener and the development of necrotic enterocolitis [33]. According to many experts, the goal of feeding preterm infants should be to achieve a “catch-up” growth rate that is close to the normal growth rate of a fetus of the same gestational age. Unfortunately, the majority of premature babies, born with very - and extremely low weight, do not receive enough nutrients to ensure normal development rates, and, as a result, have stunted growth during their hospital stay. Restricting nutrition after birth “until the baby is stable” ignores the understanding that without nutrition, the baby goes into a catabolic state of metabolism. Catabolism does not contribute to normal growth, development, and even more so to recovery. At this stage, it is important to define a strategy for improving nutritional status preterm infants, to eliminate the negative effects of poor growth associated with insufficient nutrient intake. Parenteral feeding and lack of enteral nutrition has many adverse consequences. Parenteral nutrition is associated with a significant loss of biodiversity and changes in the colonization pattern of gut microbes over time [34]. Studies conducted in animal models have shown that prolonged parenteral nutrition contributes to changes in bacterial colonization of the gut, changes in the microbiota, and the development of NEC. [35]. Nine randomized controlled trials of transpyloric feeding versus gastric tube feeding in preterm infants conducted in the 1970s and 1980s concluded that there was no evidence of improved “feeding tolerance” or growth but found an increased risk of gastrointestinal disorders and an increased risk of death. However, the study that showed an increased risk of death had unequal baseline characteristics that could explain the difference in the compared groups: the average gestational age was 27.7 weeks in the transpyloric feeding group versus 28.5 weeks in the gastric feeding

group. Also, in the group with transpyloric feeding, children had an initially low Apgar score, which is known to be a very unfavorable criterion [36]. After excluding this study from the Cochrane Analysis, no significant differences were found between these groups in mortality, weight gain, height, head circumference, necrotizing enterocolitis, and intestinal perforation. Studies evaluated transpyloric feeding as an initial feeding strategy compared to gastric tube feeding to improve growth and feeding tolerance, whereas transpyloric feeding was not evaluated as a treatment for gastroesophageal reflux in critically ill preterm infants. As for the treatment of complicated GER, extensive studies show that the use of transpyloric feeding is comparable in effectiveness to fundoplication [37,38]. Since transpyloric feeding or fundoplication does not affect swallowing function, aspiration pneumonia may persist due to swallowing dysfunction in children with severe neurological deficits. Studies conducted in newborns with apnea and bradycardia have shown that transpyloric feeding may have some benefit in reducing the frequency of both apnea and bradycardia, compared to gastric feeding [39,40]. Aspiration is a recognized factor of lung damage and is widespread among premature infants, which contributes to the development of bronchopulmonary diseases [22]. Transpyloric feeding is known to reduce the risk of aspiration and is safe in premature infants [41,42]. Early transpyloric feeding is associated with a reduced risk of death in BPD among infants with ENMT [43]. A study conducted in 2020 did not reveal an increase in the frequency of hypoxemia during transpyloric feeding compared to gastric feeding [23]. Refractory paresis of the stomach is a consequence of damage to the vagus nerve after surgery on the upper abdominal cavity. These studies have shown that the transpyloric probe is a safe, effective, and less invasive alternative for patients with postoperative gastroparesis [10]. It is also known that transpyloric feeding does not lead to changes in the hormonal profile of infants [41]. The risk of perforation of the intestinal wall during post-pyloric feeding is minimal [44-46]. Thus, transpyloric nutrition is an effective strategy for feeding seriously ill patients, eliminating complications of parenteral nutrition and reducing the risk of aspiration. Post-pyloric feeding in children in critical condition at the earliest possible time allows you to start effective enteral nutrition, minimize the number of possible gastrointestinal complications, which ultimately contributes to optimizing the quality of treatment for children [47]. According to various sources, half-element is osmolar formulas were used for post-pyloric nutrition

[10,48]. The lack of evidence base on the possibility of using breast milk as a substrate for feeding limits the therapeutic potential of transpyloric nutrition. Indications for installing a postpyloric tube in newborns in critical condition are: the inability of gastric enteral nutrition, when the volume of stagnant gastric discharge is  $\geq 6$  ml per day [10]. Severe gastro-esophageal reflux with a risk of aspiration. Aerophagia, gastric distension, and intolerance to enteral feeding during noninvasive mechanical ventilation. Violation of gastric motility or gastric paresis [48].

## Conclusion

Based on the analysis literature, the usage of postpyloric feeding in premature infants, if gastral feeding is not possible, minimizes the risks of complications associated with the usage of parenteral nutrition, as well as with the absence of enteral feeding. Transpyloric feeding reduces the rate of aspiration in premature infants who need artificial ventilation. Feeding through a transpyloric tube can be justified as a strategy for treating enteral insufficiency caused by paresis of the upper gastrointestinal tract. In neonatal intensive care unit, the method of transpyloric feeding is underappreciated and underutilized.

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