

## Fundoplication in Neonates and Infants with Primary Gastroesophageal Reflux

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**Purpose:** Gastroesophageal reflux in infant is a physiological process. However, surgery is performed in high risk infants with severe gastroesophageal reflux disease (GERD) when medical management fails. This study focuses on efficacy and safety of Nissen fundoplication for GERD in infants under age 12 months.

**Methods:** This study was a retrospective case analysis of 11 neonates and infants under 12 months of age who underwent Nissen fundoplication following a failure of medical treatment between June 2010 and June 2013 at Pusan National University Children's Hospital. The records were reviewed to determine the effect of fundoplication on symptoms and post-operative complications.

**Results:** A total of 11 infants consist of four males and seven females. Mean birth weight was 2,305.5±558.6 g (1,390-3,130 g). They had some underlying disease, which are not related with GERD such as congenital heart disease (54.5%), prematurity (45.5%), neurologic disease (18.2%), respiratory disease (18.2%), and other gastrointestinal disease. Mean body weight at surgery was 3,803.6±1,864.9 g (1,938.7-5,668.5 g). Mean age at operation was 99.9±107.6 days (17-276 days). Duration from operation to full enteral feeding was 10.9 days. Symptoms related GERD disappeared in all patients including one who got reoperation. One infant died of congenital heart disease unrelated to surgery. There were no complications related to fundoplication.

**Conclusion:** Fundoplication is effective and safe treatment in the neonates and infants with severe GERD.

**Key Words:** Gastroesophageal reflux, Fundoplication, Infant

### INTRODUCTION

Gastroesophageal reflux (GER) is a well-recognized condition in infants, which usually resolves af-

ter physiological maturation of the lower esophageal sphincter and lengthening of the intra-abdominal esophagus in the first few months after birth [1]. The incidence of GER in infants is 85%, occurring 1.6

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times more frequently in males than in females [2]. Prevalence of GER decreases to 18% in childhood [2]. However, symptoms of gastroesophageal reflux disease (GERD) in infants include coughing or choking, vomiting, chronic respiratory problems, growth failure, sleeping problems, and apnea. GERD can also be life-threatening and affect the quality of life [2,3].

In majority of patients with GERD, therapy including dietary thickeners, head-up positioning, prokinetic agents, and histamine type-2 receptor antagonists is effective. However, anti-reflux surgery such as Nissen fundoplication is needed in case of treatment failure [4]. Nissen fundoplication is a well-established treatment option in children with GERD. Indications for fundoplication include recurrent aspiration pneumonia, apneic episodes, bradycardia, apparent life-threatening events, bronchopulmonary dysplasia, severe vomiting, growth failure, esophagitis, and esophageal stricture [2,5].

According to a larger scale US study [6], fundoplication effectively improved symptoms of GERD in 94% of the 7,000 children with GERD. However, few studies have been performed in infants, and the benefits of surgery for those aged < 12 months are not clearly defined [7,8]. In many studies, surgery was performed in high-risk infants with underlying diseases such as neurologic impairment [9-11], congenital diaphragmatic hernia [12], chronic respiratory conditions, or repaired esophageal atresia [13].

Because of the low incidence of this disease, only few studies on fundoplication have been performed in children with primary and secondary GERD in Korea [14-16]. Our study focused on the efficacy and safety of Nissen fundoplication in infants with GERD aged < 12 months.

## MATERIALS AND METHODS

This retrospective case analysis included 11 neonates and infants aged < 12 months who underwent Nissen fundoplication for severe GERD following failed medical treatment between June 2010 and June 2013 at Pusan National University Children's Hospital.

GERD was defined by a combination of clinical symptoms and the results of barium swallow esophagography and endoscopy. Gastrointestinal symptoms (vomiting, hematemesis, dysphagia, feeding intolerance, growth failure) and respiratory symptoms (cough, choking, aspiration pneumonia, apneic episodes, and dyspnea) were assessed. Barium swallow esophagography was performed in all patients and endoscopy was performed in 5 of 11 patients. Free reflux of gastric content through the gastroesophageal junction into the upper esophagus was observed during barium esophagography. The diagnosis of GERD was confirmed in all patients by barium swallow esophagography. Endoscopy was performed to identify reflux esophagitis and exclude other gastrointestinal disorders causing GERD.

Twenty infants were diagnosed with GERD and underwent Nissen fundoplication following failed medical treatment between June 2010 and June 2013. Nine patients were excluded based on the following exclusion criteria: 1) prophylactic fundoplication with neurologic deficit, 2) accompanying hiatal hernia, and 3) accompanying congenital esophageal defects. A total of 11 infants were included in this study. Medical treatment failure was defined by life-threatening events associated with GERD, ongoing ventilator-dependence secondary to recurrent aspiration, recurrent aspiration pneumonia, or growth failure secondary to recurrent vomiting.

On admission, all patients underwent clinical examination by a pediatrician. Age (at symptom onset, diagnosis, and fundoplication), sex, birth history (gestational age, birth weight), underlying disease (prematurity, congenital heart disease, neurologic/pulmonary/gastrointestinal disease) were investigated.

Medical records were reviewed to determine the effect of fundoplication on symptoms, particularly on the occurrence of life-threatening events and need for intensive care, and on the success of enteral feeding and subsequent growth for 3 months after surgery. Postoperative complications (bowel obstruction, wound infection, respiratory compromise, pneumonia, tight Nissen, loose Nissen, ventral her-

nia, and dumping syndrome) were also assessed for 3 months post surgery.

## RESULTS

Eleven patients (4 boys, 7 girls) were included in this study. Five patients (45.5%) were born prematurely, one patient (9.1%) had hypoxic brain injury, and one (18.2%) underwent simultaneous gastrostomy for accompanying velopalatal insufficiency and cricopharyngeal incoordination. Median birth weight was 22,104 (1,390-3,130) g. Median age at symptom onset was 15 (13-82) days. Median age at first visit was 30 (1-272) days (Table 1).

Six (54.5%) had congenital heart disease. Two (18.2%) had neurologic disease, two (18.2%) had respiratory disease, and two (18.2) had other gastrointestinal disease. Four patients (36.4%) had multiple accompanying diseases (Table 2).

Common indicating symptoms or signs for fundoplication in infants with GERD aged < 1 year are vomiting (n=9, 81.8%), feeding intolerance (n=6,

54.5%), apneic episodes or desaturation events (n=6, 54.5%), growth failure (n=3, 20.0%), and cough (n=2, 18.2%) (Table 3).

Median body weight at surgery was 2,800 (1,938.7-5,668.5) g, with six infants weighing < 3,000 g. Median age at surgery was 50 (17-276) days. Duration between symptom onset and surgery was 65.4±74.6 (9.2-140) days.

Postoperative time taken to establish full enteral feeding was 10.9 days (n=10). No complications related to fundoplication were noted. Nine out of 11 patients (81.8%) had favorable outcomes after fundoplication. Symptoms persisted in 1 patient (9.1%) after fundoplication, but disappeared after reoperation. One patient with congenital heart disease died of unrelated causes.

## DISCUSSION

Surgery for GERD during infancy is a contentious issue. Only infants in whom medical treatment has failed or those with life-threatening complications of GERD underwent the surgery [2,17], probably because of perceived technical challenge and the potential for significant postoperative morbidity. In this study, infants with GERD aged < 12 months with persistent life-threatening episodes associated with GERD, ongoing ventilator-dependence secondary to recurrent aspiration, recurrent aspiration pneumonia, or growth failure secondary to recurrent vomiting despite medical treatment were included.

Few reports on fundoplication in infants have

**Table 1.** Clinical Data and Initial Assessment in 11 Infants

Variable	Value
Male : female	4 : 7 (36.4/63.6)
Birth weight (g)	2,305.5±558.6 (1,390-3,130)
Age at first symptom onset (day)	34.5±47.5 (13-82)
Age at first visit (day)	50.7±78.5 (1-272)
Prematurity	5 (45.5)
Hypoxic brain injury	1 (9.1)
Simultaneous gastrostomy	1 (9.1)

Values are presented as number (%) or mean±standard deviation (range).

**Table 2.** Accompanying Diseases of 11 Infants

Disease	Number (%)
Congenital heart disease	6 (54.5)
Prematurity	5 (45.5)
Neurologic disease*	2 (18.2)
Respiratory disease <sup>†</sup>	2 (18.2)
Other gastrointestinal disease <sup>‡</sup>	2 (18.2)
Multiple accompanying disease	4 (36.4)

\*Epilepsy, developmental delay, <sup>†</sup>laryngomalacia, subglottic stenosis, <sup>‡</sup>malrotation, preduodenal portal vein, duodenal web.

**Table 3.** Symptoms and Signs Leading to Fundoplication

Symptom	Number (%)
Gastrointestinal	
Vomiting	9 (81.8)
Feeding intolerance	6 (54.5)
Failure to thrive	3 (20.0)
Respiratory	
Apnea/desaturation episode	6 (54.5)
Cough	2 (18.2)
Choking	1 (9.1)
Aspiration pneumonia	1 (9.1)
Dyspnea	1 (9.1)

been published. One report documented that laparoscopic Nissen fundoplication can be performed safely and effectively in small children (weight, < 5 kg) with similar outcomes and rates of complications as those reported in older children [18]. In another study, fundoplication [19] increased the growth potential of infants aged 2 weeks to 6 months (weight, 1.02-6.95 kg), and no complications or feeding problems were noted. Kimber et al. [20] reported that fundoplication is an effective method of management when used early in the treatment of chronic GERD in preterm infants. Another study reported that only anti-reflux surgery can prevent recurrent infant apneic episodes [10]. In our study, the patients were relatively small and young because the median age and body weight of patients at the time of operation was approximately 50 days and 2,800 g, respectively. The time interval between the first visit and operation was relatively long (20 days), compared with that between symptom onset and first visit (15 days). This duration may be needed to differentiate pathologic reflux from physiologic reflux and verify the effect of medical treatment on reflux. The appropriateness of this term is debatable.

On the contrary, several studies in young infants have demonstrated poor outcomes of fundoplication with high failure rates [7,8]. In these studies, fundoplication was performed in infants with associated abnormalities such as post-esophageal atresia repair or neurological syndromes [7,9]. Wheatley et al. [13] have reported a 33% recurrence rate of GERD in patients who underwent Nissen fundoplication after esophageal atresia repair [13]. In our study, symptoms persisted in one patient after fundoplication. Loose Nissen was the suspected cause of recurrence, and the patient underwent reoperation. The outcomes of fundoplication in our patients were favorable because symptoms disappeared completely and full enteral feeding was feasible after surgery in all patients, except one who died of underlying heart disease.

Postoperative complications after fundoplication included wound infection, pneumonia, perforation, intra-abdominal abscess, tight wrap, adhesive bowel

obstruction, and dumping syndrome [7]. No complications related to fundoplication were noted in our study.

The 24-h reflux index is acknowledged by both the European and North American working parties as the most specific and sensitive predictor of GERD in infants, although is limited by the inability to detect non-acid reflux [21,22]. Single probe conventional pH monitoring may severely underestimate the incidence of GERD in infants [23,24], and a dual channel probe approach significantly increases the diagnosis rate [24]. Recently, multichannel intraluminal impedance enables assessment of the velocity and direction of liquid and gas flow through the esophagus. However, the reference value of the 24-h reflux index and data on non-acid reflux in Korean infants are not available. In this study, GERD was diagnosed using a combination of clinical symptoms and the results of barium swallow esophagography and endoscopy.

Symptoms may resolve as infants mature, and medical treatment may be effective. However, fundoplication seems to be effective in controlling symptoms of GERD. The results of this study indicate that fundoplication is effective and safe, and can be recommended for infants with severe GERD when medical management fails. We believe that fundoplication performed at the appropriate time can facilitate prevention of morbidity in infants with GERD. However, this study has several limitations. This was a single-center retrospective study and the number of patients was small. Long-term complications of the surgical treatment of GERD in early infancy were not evaluated. Further larger-scale studies may be needed.

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