SYMPOSIUM 329

# Nutritional support in children with neurodevelopmental disabilities

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#### **Abstract**

Feeding difficulties, mainly determined by oral motor problems, are common in patients with severe neurodevelopmental disabilities (NDD). These problems have a negative impact on health and developmental outcome as a consequence of insufficient intake.

Research data show that insufficient intake, and not enhanced caloric needs, is the major cause of malnutrition. However, no direct relation between intake and nutritional state has been shown, illustrating the wide variety in caloric needs in this population. Individual caloric needs in patients with NDD show a wide variety, but are generally lower than in normal children.

Treatment of these patients is complex as data on adequate daily allowances for this population are not available and standard anthropometric cut-off points to define malnutrition need adaptation.

In order to prevent and treat malnutrition in patients with neurodevelopmental problems, careful multidisciplinary follow-up is indicated, aimed at early detection of feeding problems, nutritional deficiencies and growth failure. Oral food intake can be enhanced using adapted food texture and special feeding devices, giving positional support combined with specialized dietary advice on nutrient- and caloric-dense food. When oral feeding is unsafe or inefficient, partial or total enteral nutrition is started through a gastrostomy, with or without concomitant fundoplication. Evidence based criteria guiding this decision are lacking. (Acta gastroenterol. belg., 2013, 76, 329-334).

**Key words**: nutritional support, gastrostomy, neurodevelopmental disabilities, gastro-oesophageal reflux, fundoplication.

#### Introduction

The prevalence of feeding problems in children with neurodevelopmental disabilities (NDD) is high (30 -80%). The more severe the disability, the higher the prevalence of feeding difficulties (1,2,3,4). These feeding problems can cause malnutrition which has a negative impact on health and developmental outcome (5). Hence, proper care for patients with NDD implies screening and prevention of malnutrition involving a multidisciplinary team of physicians, nurses, dietitians, speech therapists and psychologists (6). This paper gives an overview of the causes of malnutrition, the use of anthropometric measures for screening and diagnosis and describes possibilities and indications of nutritional support in children with NDD.

## Causes and consequences of feeding difficulties

Feeding difficulties are mainly determined by oral motor problems, or dysphagia, associated with the underlying neurological impairment. Children with spastic quadriplegia need up to 15 times more time to eat the same food quantity than their normal weight-equivalent peers (7). The prevalence of feeding difficulties and malnutrition is highest in patients with more severe neurological impairment, however, less severe impairment does not preclude feeding problems (8).

The inability to self-feed, to maintain a stable position while eating, and to communicate hunger and/or satiety contribute to the feeding problems. These feeding problems, apart from causing distress for patients and caregivers, often result in insufficient intake and malnutrition. Indeed, research data show that insufficient intake, and not enhanced caloric needs, is the major cause of malnutrition (9). However, there is no direct relation between intake and nutritional state, illustrating the wide variety in caloric needs in this population (10). Individual caloric needs in patients with NDD show a wide variety, but are generally lower than in normal children (11). There are no data on daily allowances for population.

Often, gastrointestinal problems as well as behavioral and parent-child interaction problems will negatively influence intake (12). Gastro-esophageal reflux disease (GERD) is present in up to 57% of these patients (13). It is influenced by severity of the underlying disease and the presence of chronic obstructive pulmonary disease (14). GERD will negatively influence the intake and subsequently the risk for malnutrition, however, malnutrition has also been suggested to have a deleterious effect on GERD (15).

### Practical clinical approach (Fig. 1)

The questions guiding the clinical approach concerning nutritional support in children with NDD, are simple. Are feeding problems present? Is oral feeding safe? Is feeding efficient? Is the child malnourished or at risk for malnutrition? Is it possible to enhance and optimize oral intake? Are these measures efficient? Is tube feeding indicated?

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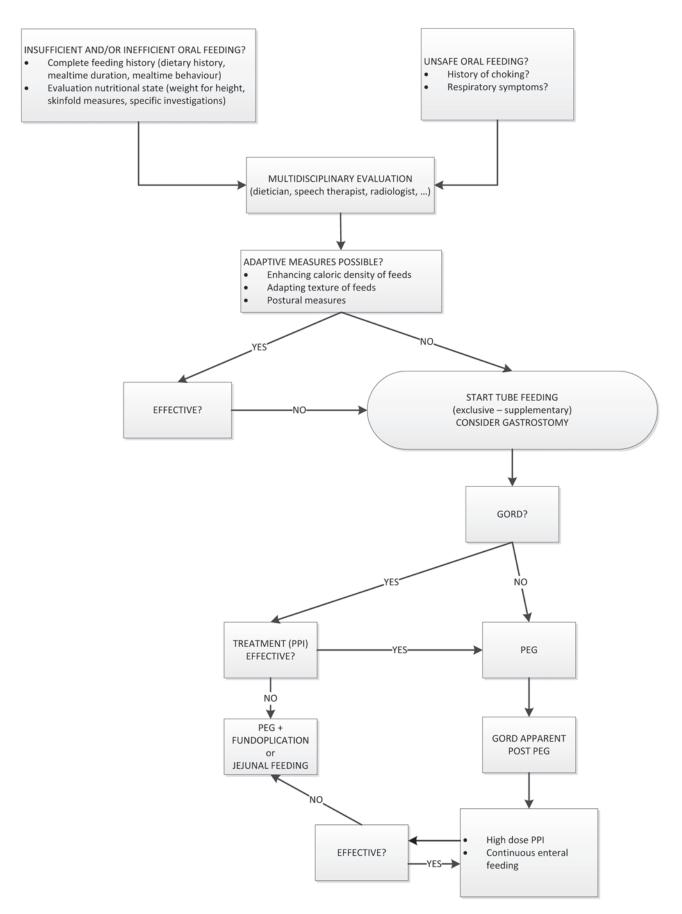


Fig. 1. — Flow-chart: nutritional support in patients with neurodevelopmental disabilities

Whereas these questions seem simple, the answers seldom are clear-cut.

### Are feeding problems present?

A feeding history includes detailed information on what and how much a child is eating, on the duration of mealtimes, whether feeding skills are age-adapted, what textures are preferred, whether adapted feeding gear is used, whether the child is able to self-feed, in which position feeding is taking place and whether adaptation strategies have been developed by patient and/or carers (16). Preferably this information is gathered by a dietitian and a speech therapist, skilled in the evaluation of oral motor function. Structured questionnaires to guide meal-time observation have been developed in order to monitor feeding behavior (17). Meal-time observation is a valuable additional tool for diagnosing feeding problems, not always apparent from the feeding history (17).

## Is oral feeding safe?

Aspiration of food, liquid or secretions but also of refluxate from the stomach, is a frequent problem in patients with oral motor dysfunction which is a major cause of recurrent pulmonary infections and lung damage, with concomitant morbidity and mortality (18). Clinical signs of aspiration, although not always present, include repeated chest infections, coughing and/or choking during/after feeds, and change in breathing rhythm or apnoe during feeds. Videofluoroscopy is a valuable additional tool, enabling to visualize "silent aspiration" (19). Whereas videofluoroscopy can be a very informative investigation, interpretation needs to be done carefully, taking into account the conditions at the time of the examination (position, adapted gear, familiar person, adaptation time) and incorporating the result in the global evaluation.

## Is the child malnourished or at risk of malnutrition?

Monitoring for malnutrition includes the use of weight and height curves. Undernutrition is defined as weight for height below 80% of median weight for height or as a body mass index below -2SD (20). In patients with severe NDD, however, growth is impaired not only as the consequence of malnutrition, but also by neuro-endocrine factors and muscle impairment. It is well known that, in patients with hemiplegia, the hemiplegic bodyside is smaller and leaner. The older the child, the more pronounced the difference becomes (21). Hence, standard anthropometric cut-off points to define malnutrition, need adaptation. At this moment, it is not clear how to define the goal of nutritional support in children with NDD, in terms of "ideal weight for height". Growth charts according to the severity of the neurological impairment (based upon the General Motor Function Classification System classes) have been developed based on observational data in a large cohort of patients with NDD (www.lifeexpectancy.org/articles/growthcharts). The charts can't be considered as normative as they did not take into account whether their nutritional state was optimal. Another problem is the inability to precisely measure height, especially when they are having contractures. This problem can be addressed by using segmental measures such as upper arm length or lower leg length/tibial length (22,23).

Skinfold measures (triceps, sugscapular, biceps, iliacal) give an indication of fat mass, and are easily available. Again, it remains to be shown whether normal reference values are applicable in NDD patients as some data indicate a different fat distribution in this population

Other methods to measure body composition show promising possibilities in giving more precise information on body composition. A study comparing the results of bio-electrical impedance (BIA) and equations using the sum of 4 skinfold thicknesses with isotope dilution (golden standard for measuring lean and fat body mass) has shown BIA to be more concordant with the reference than the skinfold equation (R<sup>2</sup>: 0,92 versus 0,44) (11). Further research is needed before BIA can be advised as a routine screening tool in this population.

Longitudinal data on weight, height and skinfold evolution are the most informative in guiding decisions on the indication of artificial nutritional support on an individual basis.

Apart from the risk of malnutrition, attention needs to be given to prevent deficiencies of micro-nutrients. Iron deficiency is common as result of gastrointestinal losses caused by GER related esophagitis. Also, vitamin D deficiency is highly prevalent, related to insufficient sunlight exposure and/or increased needs associated with the use of anti-epileptics (24).

## Management of feeding problems

Guidelines are available advocating a step-wise approach, aimed at optimizing oral intake, and indicating the placement of a gastrostomy for nutritional support by tube feeding in case of insufficient/unsafe oral intake (6,25,26).

The aim of treatment is attaining acceptable weight gain (avoiding overnutrition) with acceptable feeding times. Patient comfort and well-being take central place in the decision-making.

Although evidence is scarce regarding the effect on food intake of sensorimotor oral stimulation, using adapted food texture or special feeding devices and giving positional support during feeding, together with specialized dietary advice on nutrient- and caloric-dense food, are used (27).

When oral feeding is unsafe or when malnutrition develops despite the above mentioned advice, partial or total enteral nutrition is started. Patients with NDD will need long term tube feeding when indicated, therefore the placement of a gastrostomy offers advantages over the use of nasogastric tube feeding (28). These patients

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represent 30 to 40% of all the indications of PEG (13).

Longstanding malnutrition may reveal to be irreversible due to limited feeding tolerance because of severe gastrointestinal motor dysfunction. Nutritional outcome is better in children in whom the gastrostomy was placed before the age of 18 months, compared to those in whom it was placed later (29).

Although the decision to insert a gastrostomy can be very difficult for care-givers, as it is perceived as yet another loss of normality, several reports indicate that most care-givers are satisfied with the procedure afterwards, and recognize that they would have accepted an earlier placement of the gastrostomy had they anticipated the outcome (29,30). Gastrostomy tube feeding leads to improved weight gain, shorter feeding time and improved quality of life for carers (31).

In practice, the amount of tube feeding is tailored to the caloric intake before the placement of the gastrostomy, augmenting it gradually according to tolerance and needs. In order to provide enough micronutrients and fluid without excess calories, new low-energy, micronutrient complete enteral formulas providing 0,75 kcal/ml instead of 1 kcal/ml, have been developed and are preferred to diluting standard formula in case less than standard intake is needed (32).

Administration schedules (bolus feeding / intermittent slow administration / continuous feeding) are adapted according to gastrointestinal tolerance and daily activities. When gastric feeding is not well tolerated, jejunal continuous tube feeding can be proposed (28).

Is it necessary to perform a fundoplication systematically when placing a PEG tube?

Up to 57% of NDD patients have GERD. Despite increasing experience, the relationship between PEG and GERD is still a matter of debate. Can PEG placement lead to the development or worsening of GERD? Do we have to perform a systematic fundoplication at the time of gastrostomy in neurologically impaired children (33)?

Several factors may contribute to the occurrence or worsening of GERD after gastrostomy placement: severity of the underlying disease, presence of chronic obstructive pulmonary disease, type and location of the gastrostomy tube (14) and type of feeding (bolus versus continuous) (14,34). In adults, using scintigraphic and manometry techniques, it has been shown that rapid intragastric bolus infusion leads to a reduction of the lower esophageal sphincter (LES) pressure and increased gastroesophageal reflux whereas continuous gastrostomy feedings did not (34).

Malnutrition is also suggested to have a deleterious effect on GERD. In some children, nutritional restitution is associated with the complete cessation of vomiting attributed to GER. Nutritional restitution in children with PEG tube is associated with significant decreases in the number of episodes of GERD, as well as the frequency of esophagitis (15).

Contradictory data exist in the literature on the relationship between PEG and GER. Most studies show that GER does not worsen after PEG (35-38), but these studies conflict with others (39-40). The published studies, up to now, include children with a very wide age range and different underlying diseases. Some include all children requiring PEG, whereas others include only children with signs of GER. Methods for diagnosing GER were also different among the studies: only clinical symptoms, pH-metry (36), manometry or endoscopy. Two recent papers using repeated pH-impedancemetry in small cohorts of NDD children have completely opposite conclusions (41-42).

The presence of GERD before PEG and/or aggravation of GERD after PEG in some NDD children has led some teams to perform systematic antireflux surgery at the time of gastrostomy. However, such surgery is frequently complicated with a high rate of perioperative and late complications and recurrence of complaints, resulting in an operative failure rate of 25%, in whom a reoperation rate of 50% is described (43-44).

In Lille (France) the outcome of 368 patients who received a PEG-tube between 1990 and 2003 is reviewed. GERD is diagnosed in 237 patients (75%) at the time of PEG placement. Subsequently, GERD disappears spontaneously in 32 patients (41%) or aggravates in 82 patients (38%). Fifty-five patients (17%) need antireflux surgery after PEG placement. In 22 of these patients, the surgery is performed within the first year following PEG placement, whereas for the remaining 33 patients, GERD surgery is performed after 1 to 7 years of follow-up. The only factor associated with GERD worsening and requiring antireflux surgery after PEG placement is the presence of a neuromuscular disease. Neurologically impaired patients present more often with aggravation of the GERD (49% vs 26%, p < 0.05) and require more antireflux surgery (22% vs 10%, p < 0.05) compared with the other children. Thus, 71% of all operations for a GERD are done in NDD patients, but conversely only 22% of NDD patients need antireflux surgery after PEG placement.

In practice several parameters should be taken into account needing a multidisciplinary approach: nutritional status, aetiology and prognosis of underlying disease, and respiratory status must all be considered. The concept of systematic prophylactic fundoplication associated with PEG placement should obviously be ruled out (35). In all cases, patients should be evaluated at least clinically to determine the presence of GERD and its importance before PEG placement. Esophagoscopy concomitant to PEG may also help to assess the presence of esophagitis, which indirectly proves the pre-existence of GERD before PEG.

If GERD is absent or controlled by early medical treatment including proton pump inhibitors, PEG should be performed. Careful follow-up is therefore needed to diagnose GERD and/or complications related to GER such as lung aspiration. If GERD occurs or worsens after

PEG, medical treatment (medication, feeding mode) should first be adapted. Fundoplication or gastro-jejunostomy should be proposed in case of failure. If a severe GERD associated with impaired pulmonary function is present before PEG feeding is decided, or when GERD is not controlled by medical treatment, Nissen fundoplication associated with gastrostomy should be performed. Figure 1 proposes an algorithm for managing GERD in NDD children with PEG tube feeding.

#### Conclusion

Patients with NDD are at risk of malnutrition, a serious cause of co-morbidity. Prevention and treatment of malnutrition is a central issue in their care, preferably in an experienced multidisciplinary setting. They are a heterogeneous group so that a "one size fits all" approach is inappropriate. Individually tailored enhancement of safe oral intake, but not delaying gastrostomy tube feeding when needed, is important in order to improve general health and quality of life of both patient and care-giver. Further research however, is needed in order to define "optimal nutritional state" in this complex group of patients.

#### References

- KRICK J., MURPHY-MILLER P., ZEGER S., WRIGHT E. Pattern of growth in children with cerebral palsy. J. Am. Diet Assoc., 1996, 96: 680-685.
- STALLINGS V.A., CRONK C.E., ZEMEL B.S., CHARNEY E.B. Body composition in children with spastic quadriplegic cerebral palsy. *J. Pediatr.*, 1995, 126: 833-839.
- STALLINGS V.A., CHARNEY E.B., DAVIES J.C., CRONK C.E. Nutrition-related growth failure of children with quadriplegic cerebral palsy. *Dev. Med. Child. Neurol.*, 1993, 35: 126-138.
- HENDERSON R.C., GROSSBERG R.I., MATUSZEWSKI J., MENON N., JOHNSON J., KECSKEMETHY H.H. et al. Growth and nutritional status in residential center versus home-living children and adolescents with quadriplegic cerebral palsy. J. Pediatr., 2007, 151: 161-166.
- SAMSON-FANG L., FUNG E., STALLINGS VA., CONAWAY M., WOL-REY G., ROSENBAUM P. et al. Relationship of nutritional status to health and societal participation in children with cerebral palsy. J. Pediatr., 2002, 141: 637-643.
- MARCHAND V.; CANADIAN PAEDIATRIC SOCIETY, NUTRITION AND GASTROENTEROLOGY COMMITTEE. Nutrition in neurologically impaired children. *Paediatr. Child Health*, 2009, 14: 395-401.
- GISEL E.G., PATRICK J. Identification of children with cerebral palsy unable to maintain a normal nutritional state. *Lancet*, 1988, I (8580): 283-286.
- SHEVELL M., DAGENAIS L., HALL N. Comorbidities in cerebral palsy and their relationship to neurologic subtype and GMFCS level. *Neurology*, 2009, 2090-2096.
- FUNG E., SAMSON-FANG L., STALLINGS V., CONAWAY M., LIPTAK G., HENDERSON R. et al. Feeding dysfunction is associated with poor growth and health status in children with cerebral palsy. J. Am. Diet Assoc., 2002, 102: 361-373.
- CALAIS E., VEUGELERS R., RIEKEN R., TIBBOEL D., EVENHUIS H., PENNING C. Energy intake does not correlate with nutritional state in children with severe generalized cerebral palsy and intellectual disability. Clin. Nutr., 2010, 29: 617-621.
- RIEKEN R., VAN GOUDOEVER J., SCHIERBEEK H., WILLEMSEN S., CALIS E., TIBBOEL D. et al. Measuring body composition and energy expenditure in children with severe neurologic impairment and intellectual disability. Am. J. Clin. Nutr., 2011, 94: 759-766.
- SULLIVAN P., LAMBERT B., ROSE M., FORD-ADAMS M., HOHNSON A., GRIFFITHS P. Prevalence and severity of feeding and nutritional problems in children with neurological impairment: Oxford Feeding Study. Dev. Med. Child Neurol., 2000, 42: 674-680.

- DAVELUY W., GUIMBER D., MENTION K., LESCUT D., MICHAUD L., TURCK D. et al. Home enteral nutrition in children: an 11-year experience with 416 patients. Clin. Nutr., 2005, 24: 48-54.
- RAZEGHI S., LANG T., BEHRENS R. Influence of percutaneous endoscopic gastrostomy on gastroesophageal reflux: a prospective study in 68 children. J. Pediatr. Gastroenterol. Nutr., 2002, 35: 27-30.
- LEWIS D., KHOSHOO V., PENCHARZ P.B., GOLLADAY E.S. Impact of nutritional rehabilitation on gastroesophageal reflux in neurologically impaired children. J. Pediatr. Surg., 1994, 29: 167-169.
- REILLY JJ., HASSAN T.M., BRAEKKEN A., JOLLY J., DAY R.E. Growth retardation and undernutrition in children with spastic cerebral palsy. J. Hum. Nutr. and Diet, 1996, 9: 429-435.
- CALIS E., VEUGELERS R., SHEPPARD J., TIBBOEL D., EVENHUIS H., PENNING C. Dysphagia in children with severe generalized cerebral palsy and intellectual disability. *Dev. Med. Child Neurol.*, 2008, 50: 625-630.
- CASS H., WALLIS C., RYAN M., REILLY S., MC HUGH K. Assessing pulmonary consequences of dysphagia in children with neurological disabilities: when to intervene? *Dev. Med. Child Neurol.*, 2005, 47: 320-329.
- DEMATTEO C., MATOVICH D., HJARTARSON A. Comparison of clinical and videofluoroscopic evaluation of children with feeding and swallowing difficulties. *Dev. Med. Child Neurol.*, 2005, 47: 149-157.
- JOOSTEN K., HULST J. Malnutrition in pediatric hospitals: current issues. Nutrition, 2011, 27: 133-137.
- KUPERMINC M., STEVENSON R. Growth and nutrition disorders in children with cerebral palsy. Dev. Disabil. Res. Rev., 2008, 14: 137-146.
- STEVENSON R. Use of segmental measures to estimate stature in children with cerebral palsy. Arch. Pediatr. Adolesc. Med., 1995, 149: 658-662.
- BELL K., DAVIES P. Prediction of height from knee height in children with cerebral palsy and non-disabled children. Ann. Hum. Biol., 2006, 33: 493-499.
- HILLESUND E., SKRANES J., TRYGG K., BOHMER T. Micronutrient status in children with cerebral palsy. Acta Paediatr., 2007, 96: 2295-2298.
- MARCHAND V., MOTIL K. AND THE NASPGHAN COMMITTEE ON NUTRITION. Nutrition Support for neurologically impaired children: a clinical report of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J. Pediatr. Gastroenterol. Nutr., 2006, 43: 123-135.
- POSITION OF THE AMERICAN DIETETIC ASSOCIATION: Providing nutrition services for people with developmental disabilities and special health care needs. J. Am. Diet Assoc., 2010, 110: 296-307.
- SNIDER L., MAJNEMER A., DARSAKLIS V. Feeding interventions for children with cerebral palsy: a review of the evidence. *Phys. Occup. Ther. Pediatr.*, 2011, 31: 58-77.
- LÖSER C., ASCHL G., HÉBUTERNE X., MATHUS-VLIEGEN E., MUSCARITOLI M., NIV Y. et al. ESPEN guidelinen on enteral nutritionpercutaneous endoscopic gastrostomy (PEG). Clin. Nutr., 2005, 24: 848-861.
- MARTINEZ-COSTA C., BORRAZ S., BENLLOCH C., LOPEZ-SAIZ A., SANCHIZ V., BRINES J. Early decision of gastrostomy tube insertion in children with severe developmental disability: a current dilemma. *J. Hum. Nutr. Diet*, 2011, 24: 115-121.
- SULLIVAN P., JUSZCZAK E., BACHLET A., LAMBERT B., VERNON-ROBERTS A., GRANT H. et al. Gastrostomy tube feeding in children with cerebral palsy: a prospective, longitudinal study. Dev. Med. Child Neurol., 2005, 47: 77-85.
- SAMSON-FANG L., BUTLER C., O'DONNELL M. Effects of gastrostomy feeding in children with cerebral palsy: an AACPDM evidence report. *Dev. Med. Child Neurol.*, 2003, 45: 415-426.
- VERNON-ROBERTS A., WELLS J., GRANT H., ALDER N., VADAMALAYAN B., ELTUMI M., SULLIVAN P. Gastrostomy feeding in cerebral palsy: enough and no more. *Dev. Med. Child Neurol.*, 2010, 52: 1099-1105.
- GOTTRAND F., MICHAUD L. Percutaneous endoscopic gastrostomy and gastro-esophageal reflux: are we correctly addressing the question? J. Pediatr. Gastroenterol. Nutr., 2002, 35: 22-24.
- COBEN R.M., WEINTRAUB A., DIMARINO A.J., J.R., COHEN S. Gastroesophageal reflux during gastrostomy feeding. *Gastroenterology*, 1994, 106: 13-18.
- KAWAHARA H., MITANI Y., NOSE K., NAKAI H., YONEDA A., KUBOTA A. et al. Should fundoplication be added at the time of gastrostomy placement in patients who are neurologically impaired? J. Pediatr. Surg., 2010, 45: 2373-2376.
- 36. LAUNAY V., GOTTRAND F., TURCK D., MICHAUD L., ATEGBO S., FARRIAUX J.P. Percutaneous endoscopic gastrostomy in children: influence on gastroesophageal reflux. *Pediatrics*, 1996, **97**: 726-728.
- PLANTIN I., ARNBJORNSSON E., LARSSON L.T. No increase in gastroesophageal reflux after laparoscopic gastrostomy in children. *Pediatr. Surg. Int.*, 2006. 22: 581-584.

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38. ISCH J.A., RESCORLA F.J., SCHERER L.R. 3RD., WEST K.W., GROSFELD J.L. The development of gastroesophageal reflux after percutaneous endoscopic gastrostomy. J. Pediatr. Surg., 1997, 32: 321-322.

- SULAEMAN E., UDALL J.N. JR., BROWN R.F., MANNICK E.E., LOE W.A., HILL C.B. et al. Gastroesophageal reflux and Nissen fundoplication following percutaneous endoscopic gastrostomy in children. J. Pediatr. Gastroenterol. Nutr., 1998, 26: 269-273.
- HEINE R.G., REDDIHOUGH D.S., CATTO-SMITH A.G. Gastrooesophageal reflux and feeding problems after gastrostomy in children with severe neurological impairment. *Dev. Med. Child Neurol.*, 1995, 37: 320-329.
- 41. TOPOROWSKA-KOWALSKA E., GEBORA-KOWALSKA B., JABLONSKI J., FENDLER W., WASOWSKA-KROLIKOWSKA K.
- Influence of percutaneous endoscopic gastrostomy on gastro-oesophageal reflux evaluated by multiple intraluminal impedance in children with neurological impairment. *Dev. Med. Child Neurol.*, 2011, **53**: 938-943.
- THOMSON M., RAO P., RAWAT D., WENZL T.G. Percutaneous endoscopic gastrostomy and gastro-oesophageal reflux in neurologically impaired children. World J. Gastroenterol., 2011, 17: 191-196.
- 43. WOCKENFORTH R., GILLESPIE C.S., JAFFRAY B. Survival of children following Nissen fundoplication. *Br. J. Surg.*, 2011, **98**: 680-685.
- 44. ESPOSITO C., VAN DER ZEE D.C., SETTIMI A., DOLDO P., STAIANO A., BAX N.M. Risks and benefits of surgical management of gastroesophageal reflux in neurologically impaired children. Surg. Endosc., 2003, 17: 708-710.