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Original article

The effect of protein composition in liquid meals on gastric emptying rate in children with cerebral palsy[☆,☆☆]

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S U M M A R Y

Background & aim: Dysmotility, nausea and vomiting are common among children with cerebral palsy. This study aimed to evaluate influence of protein composition on rate of gastric emptying and study the relation between gastric emptying and postprandial gastrointestinal symptoms.
Methods: 15 children with cerebral palsy, using gastrostomy, received four liquid test meals on separate days in random order. The meals contained a standard carbohydrate and fat base plus one of four protein modules (100% casein (A), hydrolysed whey (B), amino acids (C) and 40% casein/60% whey (D)) with a total energy of 1 kcal/ml. The ^{13}C octanoic acid breath test was applied to assess gastric emptying.
Results: When comparing half emptying time ($T_{1/2}$) of the fast emptying meals (meal B, C and D) with the slowest emptying meal (meal A), more rapid emptying was demonstrated for meal D ($p < 0.001$). For meal D, emptying was significantly faster in children with postprandial symptoms than in those without ($p < 0.01$).
Conclusion: In children with cerebral palsy using gastrostomy, gastric emptying is influenced by type of protein in the meal. The present results also suggest that there is a relation between rapid gastric emptying and postprandial gastrointestinal symptoms.
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1. Introduction

The prevalence of cerebral palsy (CP) in Norway is 2.1/1000 live births.[1] This is similar to other populations in Europe.[2] Children most at risk for feeding problems are those with severe total body involvement of CP (spastic quadriplegic and dystonic type).[3,4] They account for one third of all cases of CP in developed countries[5] and are often growth restricted with median centiles more than 20% below the general population at age 2 years, and the gap increases with age.[6] Malnutrition is common in children with neurodevelopmental disabilities, and may be related to dysphagia, vomiting, symptoms of pulmonary aspiration, gastrooesophageal reflux and constipation.[7] Moreover, children with disorders of the central nervous system and GI symptoms may have delayed gastric emptying (GE) and symptoms possibly related to gastric dysmotility.[8]

Gastrostomy tube feeding is increasingly used for nutritional support in children with neurodevelopmental disabilities and is associated with improved height and weight in the most disabled patients with CP.[6] Persisting feeding difficulties among disabled children with gastrostomy is, however, a common and well known problem in paediatric medicine.[4,9,10] The relevance of dysmotility for GI symptoms and need for nutritional support in these patients is at present unclear. However, changes in formula composition of the enteral feed administered through the gastrostomy may, according to clinical observations, result in relief of GI symptoms. This might be related to an altered rate of GE, since meal volume, fat content, caloric content, and meal viscosity all may influence GE.[11] At present, there are no available studies addressing the influence on rate of GE by changing only the protein composition of a meal.

If an influence on rate of GE by protein composition in meals and a relation to postprandial symptoms can be demonstrated, then

Abbrevations: CP, cerebral palsy; GI, gastrointestinal; GE, gastric emptying; GEC, gastric emptying coefficient; GORD, gastrooesophageal reflux disease; NF, Nissen fundoplication.

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meal composition could have consequences for nutritional status. The aim of the present study was thus to examine the influence of protein composition in liquid meals on rate of GE in children with CP and gastrostomy. In addition, the relation between GE and postprandial GI symptoms was studied.

2. Materials and methods

2.1. Patients

Fifteen children with CP (7 girls), using gastrostomy as their main route of feeding, were examined. Mean age was 10.7 years (range 4–15 years) (Table 1). Five of the children had undergone a Nissen fundoplication (NF). The children were selected from four different hospitals in the southern part of Norway (Oslo University Hospital, Ullevål, Akershus University Hospital, Ostfold Hospital Trust, Fredrikstad, and Hospital Innlandet, Elverum). Children with CP with age below 16 years and gastrostomy for at least one year were identified in the patient registers. The diagnosis of CP was verified by review of the medical record of the patient. Patients with information in the records indicating problems with breath test sampling (confer below), known or suspected immunological reactions against dietary proteins, in need for continuous treatment with prokinetic medication or use of valproic acid (interferes with breath test for GE[12]) were not eligible for inclusion. Families of eligible patients were contacted by telephone for information and asked to participate in the study. If willing to participate, the parents/legal guardian received written information by mail and informed consent was signed before inclusion in the study.

2.2. Test meals

In all patients, four different meal formulas were used. The main criterion for the selection of proteins was that formulas with fast or slow proteins should be applied and the selected formulas should be commercially available. The meal formulas were made up of a standardised carbohydrate and fat base (Energivit (SHS), Liverpool, United Kingdom), which was added one of four protein sources (confer below) resulting in a meal formula containing a total energy of 1 kcal/ml with protein equivalent 2.8 g/100 ml, carbohydrate 12.0 g/100 ml and fat 4.5 g/100 ml. The protein sources were (A) 100% casein, (B) hydrolysed whey, (C) amino acids and (D) 40% casein/60% whey. The protein fractions were packed by a pharmacist and were blinded for the investigator and patients. ^{13}C octanoic acid was added to the meal formula prior to administration.

2.3. Gastric emptying (GE) – ^{13}C breath test

The test meals were labelled with 91 mg ^{13}C octanoic acid (EUROISO-TOP, Saint-Aubin, Cedex, France) as marker to measure GE. The fraction of $^{13}CO_2$ content in exhaled CO_2 was determined by gas chromatographic purification isotope ratio mass spectrometry (Analytical Precision, Cheshire, UK). This technique is based on that GE is the rate-limiting step for the appearance of ^{13}C in exhaled CO_2.[13] Three variables of GE were calculated; the half-time of GE ($T_{1/2}$), the GE coefficient (GEC) and time until maximum excretion of ^{13}C (T_{max}).[14]

2.4. Experimental protocol

All patients were studied in the morning after an overnight fast on four consecutive days. The tests were performed at the outpatient/daycare ward, with a parent, legal guardian or other adult caretaker present.

Prior to administration of the first test meal, age, sex, height, weight, current feeding regimen and medications were recorded. Furthermore, history of symptoms of gastrooesophageal reflux disease (GORD), constipation and other GI symptoms were obtained and a history of previous abdominal surgery was recorded. The frequency of general GI symptoms were assessed by using a standardised questionnaire.

Meals were administered with a feeding pump, randomised and double blinded, and administered at a rate of 600 ml/h for 20 min (total 200 ml). Prior to meal administration, a baseline breath sample was collected. Thereafter, breath samples were collected at 5 min intervals during the first 30 min after start of meal administration followed by sampling at 15 min intervals for 4 h. Most of the children had difficulties with breath sampling due to their handicap. In most cases samples had to be collected through a face mask into a breath sampling bag (Quintron, Milwaukee, WI 53215, USA). The sampling bag had a valve to avoid leaks.

After receiving the test meal, the children were allowed to perform their usual physical activity. No other meals were allowed during the test period with breath sampling. The children received their ordinary meal formulas in the periods between the test meals.

GI symptoms occurring in the test period (4.5 h after meal administration) were recorded by the physician conducting the study (ACB).

2.5. Statistics

Summary data are given as median with 25 and 75 percentiles in brackets, unless otherwise stated. Wilcoxon test, Mann Whitney test, Fisher exact test, and Friedman test were applied. Level of statistical significance was set at 5%.

The sample size was calculated by using a standard deviation of 18.6 min of $T_{1/2}$ based on data from preterm infants[15] and adult volunteers.[16] With a significance level of 0.05 (α), power of 80% (β) and 15 min regarded as clinically important differences in $T_{1/2}$, at least 12 patients should be included.

2.6. Ethics

Written, informed consents were obtained from the parents of all patients.

The protocol was approved by the Regional Medical Ethics Committee and the Local data protection supervisor. The methods used are well known and do not imply risk or discomfort for the children.

3. Results

3.1. Rate of gastric emptying (GE) and protein source

The rate of GE differed significantly between the four meals for all GE variables (Table 1). When comparing $T_{1/2}$ of the fast emptying

Table 1
Variables of gastric emptying in relation to type of meal.

	Meal A 100% casein	Meal B Hydrolysed whey	Meal C Amino acids	Meal D 40% casein/ 60% whey	p-value*
$T_{1/2}$ (min)	153.9 (76.4–230.6)	82.0 (27.1–169.9)	74.4 (34.3–107.3)	63.3 (41.9–99.5)	0.02
Gastric emptying coefficient	1.9 (1.8–2.1)	2.4 (2.2–2.6)	2.5 (2.3–2.7)	2.4 (1.9–2.7)	0.003
T_{max} (min)	135 (30–195)	60 (45–135)	60 (45–120)	60 (30–105)	0.04

Results are median with 25 and 75 percentiles in brackets. *Friedman test.