Rapid Orocecal Transit Time in Obese Children Measured by Hydrogen Breath Test

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Background: *Gastrointestinal motility may correlate with an unusual nutritional status, such as obesity. The orocecal transit time (OCTT) is one parameter of GI motility.*

Objective: *The primary objective of the present study was to compare OCTT in obese and non-obese children; secondary objectives were to assess the correlation between OCTT and body mass index (BMI) or appetite score.*

Material and Method: *A cross-sectional study was conducted in 44 children. Twenty-one obese and 18 non-obese children were included in the final analysis. Demographic data and anthropometric parameters were collected. The breath hydrogen test (BHT) using lactulose was performed to determine OCTT. Appetite score using visual analog scale was measured at the beginning and end of the present study. The difference between these scores was attributed as an increase of appetite. Student t-test and Chi-square test were employed to compare the differences between groups. Pearson's correlation was used to measure the correlation between parameters.*

Results: *Mean OCTT in obese children was significantly faster than in non-obese children (70.0 versus 81.1 min, respectively; p-value = 0.005). The increases of appetite score during study were not significantly different between obese and non-obese children (4.3 vs. 2.9; p-value = 0.19). OCTT was significantly associated with BMI in the inverse manner (r = -0.51; p-value = 0.001), but was not significantly correlated with the appetite score (r = -0.24; p-value = 0.15).*

Conclusion: *OCTT in obese children was faster than in non-obese children. OCTT was moderately inversely correlated with the BMI, and had a trend to negative correlation with the appetite score, though without reaching a significant value.*

Keywords*: Breath test, Gastrointestinal transit, Hydrogen, Obesity, Lactulose*

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Obesity is one of the most prevalent morbidities and is world-wide[1]. It is caused by an excess of body fat due to excessive caloric intake and/or limited energy expenditure, it is a proven risk factor for many diseases, such as cardiovascular diseases, metabolic disorders, type II diabetes, degenerative arthritis and cancer[2]. Even though important efforts are undertaken by public and private healthcare institutions to control this condition[3], few therapies are currently available to manage obesity and improve patient's quality of life, which is significantly compromised by the disease. A novel class of drug, regulating gastrointestinal motility, is under evaluation in current clinical studies since some aspects of gastrointestinal motility are altered in obesity[4,5]. Gastrointestinal motility is a segmented process that regulates gastric, intestinal and colon motility, controls food consumption, digestion, and nutrient absorption[6]. Obese patients tend to have an augmented gastric capacity, but normal fasting gastric volume, gastric accommodation and perception of gastric distension[7]. In studies of gastric physiology in obese patients, it has been found that gastric emptying of liquid seems to be well regulated, while solid gastric emptying seems to be accelerated, thus reducing the negative feedback satiety signal generated by the presence of food in the stomach[8]. Moreover, it has been demonstrated that a delay in intestinal transit increases nutrient absorption and results in weight gain[9]. Conversely, another study of orocecal transit time (OCTT) in malnourished children has shown a delayed OCTT even if without reaching a statistically significant value in those subjects[10]. From these controversial results it may be difficult to associate

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the OCTT delay with an increase in nutrient absorption. OCTT can be evaluated by the lactulose hydrogen breath test[11]. This test quantifies the hydrogen exhaled in the breath by gas chromatography. When ingested lactulose is fermented in the colon, hydrogen is absorbed through the wall of the intestine, it reaches the lungs and is released in the breath, thus allowing an estimate of the orocecal transit time[11]. Not many studies are reported in the literature regarding the orocecal transit time in obese patients as measured by the hydrogen breath test and the results are controversial[9,10].

The present study seeks to compare the OCTT in obese and non-obese children and as a secondary goal, to identify whether there is a correlation between the OCTT and appetite or body mass index.

Material and Method

A cross-sectional study was conducted in 44 child volunteers aged between 6 and 15 years.

Written informed consents and assents were obtained from parents and children, respectively, before data collection. The present study was approved by the Ethics Committee of the Faculty of Medicine, Srinakharinwirot University.

Twenty-two normal weight and twenty-two obese children were invited to participate in the present study. All were non-smokers. Children who had a history of chronic diarrhea or had taken antibiotics within 2 weeks prior to the present study were excluded. Children who could not refrain from oral intake, as required in the study protocol, were also excluded.

Study protocol

Children were divided according to their body mass index into 2 groups, obese and non-obese. After obtaining written informed consents and assents, anthropometric data were collected by a trained staff. Weight was measured to the nearest 0.1 kg and per cent of total body fat was measured using an electronic scale, the Tanita Body Composition Analyzer (Model No. BF-680W, Tokyo, Japan). Height was measured to the nearest 0.1 cm. The body mass index (BMI) was calculated as the ratio of weight/(height)^2 (kg/m^2). Waist circumference was measured to the nearest 0.1 cm at the midpoint between the lower costal margin and the top of the iliac crest using a non-elastic flexible tape when the subject was standing. Hip circumference was measured to the nearest 0.1 cm in the standing position at the maximum circumference over the buttocks. According to WHO criteria, children who had BMI less than 1 SD for the sex and age were defined as non-obese children, whereas children who had BMI more than 2 SD were defined as obese children[12].

Appetite score measurement

Appetite sensations were subjectively measured by each child at the beginning and end of the study using a visual analog scale (VAS). Children were asked to rate their appetite sensation on 10 cm VAS with words anchored at each end (0 equals I am not hungry at all to 10 equals I am extremely hungry). Difference between 2 rating scores was representative for the change of appetite score during the study.

Orocecal transit time (OCTT) measurement

After overnight fasting, children were asked to brush their teeth and rinse their mouth before the breath sample was collected. Baseline breath hydrogen test was performed using the Micro H_2 meter (Micro medical Ltd., UK). Children were instructed to take a deep inspiration and exhale slowly and fully through the mouthpiece connected with the machine for as long a period as possible. Breath hydrogen concentration was read on the machine screen and represented as parts per million (ppm). The children then orally consumed 10 g of lactulose (Duphalac) in 100 ml solution within 5 minutes. Breath hydrogen tests were measured every 10 minutes for a total time of 150 minutes by the same technique. Orocecal transit time was defined as the interval from the baseline time to the first sustained increase in breath hydrogen concentration by at least 3 ppm. Children with a breath hydrogen concentration less than 10 ppm above the baseline values in 90 minutes sample or in any later samples were defined as hydrogen non-producers[10].

Sample size calculation

To detect the anticipated difference in mean of OCTT of 20 ppm between groups and the anticipated standard deviation of 20 ppm with 80% power and 2-tailed alpha error of 0.05, a sample size of 17 elements per group was required. Accounting for hydrogen non-producers, the authors decided to enroll 22 children in each group.

Statistical analysis

Continuous variables were tested for their normal distributions by the Kolmogorov-Sminov test and all were distributed normally. Continuous variables were descriptively presented as means and standard deviations. Categorical variables were presented as number and percent. Student's t-test and Chi-square test were employed to compare the continuous and categorical variables between 2 groups, respectively. Paired t-test was used to test the difference of appetite score between at the beginning and at the end of study of each child. Correlations between OCTT with the changing of appetite score and BMI were tested using Pearson correlation test. Statistical analysis was performed using SPSS 11.0 software package (SPSS Inc., Chicago, IL, USA). A p-value < 0.05 was considered as statistically significant.

Results

Five children (11%) were hydrogen non-producers and were excluded from the present study. Thus, twenty one obese children and eighteen non-obese children were included for further analysis. Demographic characteristics of both groups were summarized in Table 1. Obese children were younger than non-obese children (11.7 vs. 12.9 years; p-value = 0.01), while all anthropometric parameters, except for height, of obese children were significantly higher than non-obese children. In particular, the body mass indices were 18.1 and 27.8 in non-obese and obese children, respectively (p-value < 0.001). Mean OCTT in obese children was significantly faster than in non-obese children (70.0 vs. 81.1 min, respectively; p-value = 0.005). In the non-obese group, children rated their appetite score by 5.4 at the beginning to 8.3 at the end of the study (p-value < 0.001) with the mean change of 2.9 (95% CI 1.6, 4.3). In the obese group, children rated the appetite score by 3.3 at the beginning of the study to 7.6 at the end (p-value = 0.001) with the mean change of 4.3 (95% CI 2.6, 6.0). OCTT was significantly inversely correlated with BMI (r = -0.51; p-value = 0.001), but the results were not significantly correlated with the appetite score (r = -0.24; p-value = 0.15).

Discussion

This work has evaluated the orocecal transit time in obese and normal weight children using the lactulose breath hydrogen test. Hydrogen breath test (HBT) is a non-invasive and safe diagnostic strategy to assess *in vivo* a variety of physiological and pathological processes. For safety reasons, this test is evaluable in children and during pregnancy[13]. The hydrogen breath test is used widely in clinical practice to explore gastrointestinal disorders, for the diagnosis of carbohydrate malabsorption, small intestinal bacterial overgrowth and for measuring the orocecal transit time. Depending on the choice of the substrate, it allows assessment of gastric emptying, liver and pancreatic function and measurement of many other enzyme activities and processes[13]. Lactulose is the substrate of choice for the measurement of orocecal transit time[11] and the hydrogen breath test using lactulose as a substrate has been compared with other methodologies to validate the orocecal transit time resulted. Radiological methods with barium meal study, has shown the appearance of barium in the cecum corresponded with the increase of expiratory hydrogen[14], demonstrating HBT correlates well with

Table 1. Demographic characteristics, orocecal transit time and appetite score of the study groups

	Non obese (n = 18)	Obese (n = 21)	p-value
Age (year)	12.9 (0.6)	11.7 (2.0)	0.01
Male; n (%)	10 (55.6)	10 (47.6)	0.75
Weight (kg)	42.4 (6.8)	66.7 (16.1)	< 0.001
Height (cm)	152.6 (6.2)	154.0 (10.4)	0.62
Body mass index (kg/m^2)	18.1 (1.8)	27.8 (4.4)	< 0.001
Waist (cm)	59.4 (8.2)	90.2 (12.0)	< 0.001
Hip (cm)	78.0 (7.4)	99.8 (9.4)	< 0.001
Waist/ hip ratio	0.76 (0.06)	0.91 (0.09)	< 0.001
% fat mass	13.2 (6.5)	32.0 (7.4)	< 0.001
Orocecal transit time (min)	81.1 (10.2)	70.0 (12.6)	0.005
Appetite score			
At the beginning	5.4 (2.4)	3.3 (2.9)	0.02
At the end of study	8.3 (2.1)	7.6 (2.1)	0.34
Changing of appetite score[1]	2.9 (1.6, 4.3)	4.3 (2.6, 6.0)	0.19

[1] Presented as mean (95% CI)

radiological methods currently accepted as the gold standard test. HBT has been correlated also with scintigraphy methods, also considered as a gold standard[15]. The main difference between barium meal, scintigraphy and HBT is that the former two are real time methods in which it is possible to analyze the meal when it passes through the large bowel. In contrast, HBT is not a real time test, but it requires neither radiation exposure nor radioisotope, thus making it more feasible and acceptable for patients and healthy volunteers.

The present study has demonstrated that the orocecal transit time is faster in obese children than in non-obese children and is inversely correlated to the body mass index. This result is in contrast with other evidences in which a delay of orocecal transit time has been shown in adult obese patients with lactulose breath test[9]. This discrepancy may be explained by considering that the two studies analyze different populations in terms of age and dietary habits. Indeed, dietary habits seem to be important in modifying the orocecal transit time[16]. For instance, migration has some effect in the orocecal transit time and it has been suggested to validate the breath test in each population studied in order to establish the diagnostic value[16]. OCTT study in Myanmar children has demonstrated that the orocecal transit time in Myanmar is delayed in respect to that of children from developed countries where the diet is different, but this difference is not statistically significant and no correlation has been reported with the nutritional status of malnutrition[10]. The present study concerned with obesity, the opposite nutritional status, has found a speeding of OCTT. The authors might hypothesize that both studies go in the same direction and support each other. However, the exact mechanism underlying this opposite change of OCTT is not totally understood and further studies are needed. One factor that may interfere with the results is the presence of hydrogen non-producer patients in the present study groups. Non-producer subjects may lack organisms in their large bowel for digestion of lactulose to hydrogen, or they may have been treated with antibiotics that kill bacteria able to produce hydrogen[17]. In present study, the number of hydrogen non-producer patients (11%) is comparable to those reported in literature which ranged from 10% to 16%[10,17].

As a secondary endpoint, a possible correlation between the orocecal transit time and the appetite score has been investigated. The authors' data indicate that OCTT has a negative, but not statistically significant, correlation with the appetite score. Further studies with the primary objective to evaluate this correlation and that would examine a correct sample size to explore the problem are needed. Appetite scores are largely used to determine the role of appetite in human diseases[18], but these methodologies are often poorly reproducible because of day to day variation in the subjective appetite sensation[19]. Thus, further improvement of these methodologies is required in order to apply appetite score to other clinical analyses. In conclusion: childhood obesity determines a faster OCTT than non-obese children and OCTT is significantly correlated with BMI in a negative manner. OCTT also negatively correlates with the appetite sensation, however, this correlation did not reach significant levels. Further study to investigate the abnormality of transit time in obesity is needed and may lead to new insights for treatment.

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Potential conflicts of interest

None.

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การผ่านของอาหารจากปากถึงส่วนต้นของลำไส้ใหญ่อย่างรวดเร็วในเด็กอ้วนตรวจวัดโดยปริมาณก๊าซไฮโดรเจนในลมหายใจ

สงวนศักดิ์ ฤกษ์ศุภผล, ลัคนา ฤกษ์ศุภผล

ภูมิหลัง: *การเคลื่อนไหวของระบบทางเดินอาหารมีความสัมพันธ์กับภาวะผิดปกติทางโภชนาการรวมถึงโรคอ้วน การตรวจวัดความเร็วของการผ่านของอาหารจากปาก จนถึงส่วนต้นของลำไส้ใหญ่เป็นวิธีหนึ่งที่ใช้ประเมินการเคลื่อนไหวของทางเดินอาหาร*

วัตถุประสงค์: *การศึกษานี้มีวัตถุประสงค์หลักเพื่อที่จะเปรียบเทียบระยะเวลาการผ่านของอาหารจากปากจนถึงส่วนต้นของลำไส้ใหญ่ในเด็กอ้วนและเด็กไม่อ้วน และวัตถุประสงค์รองเพื่อศึกษาความสัมพันธ์ระหว่างระยะเวลากับดัชนีมวลกายและความรู้สึกหิว*

วัสดุและวิธีการ: *การศึกษาแบบตัดขวางในเด็ก 44 คน โดยข้อมูลของเด็กอ้วนจำนวน 21 คน และเด็กไม่อ้วนจำนวน 18 คน ถูกนำมาวิเคราะห์ขั้นสุดท้าย เด็กทุกคนได้รับการเก็บข้อมูลประชากรและการวัดขนาดร่างกาย ระยะเวลาการผ่านของอาหารจากปากถึงส่วนต้นของลำไส้ใหญ่ ประเมินโดยการตรวจปริมาณก๊าซไฮโดรเจนในลมหายใจโดยใช้แลคตูโลส ความรู้สึกหิวเมื่อเริ่มและสิ้นสุดการศึกษาประเมินโดย Visual analog scale ความแตกต่างของความรู้สึกหิวจากทั้ง 2 เวลา หมายถึงความหิวที่เพิ่มขึ้น การวิเคราะห์สถิติโดย Student t-test, Chi-square และ Pearson's correlation*

ผลการศึกษา: *ความเร็วของการผ่านของอาหารจากปากถึงส่วนต้นของลำไส้ใหญ่ในเด็กอ้วนเร็วกว่าเด็กไม่อ้วน (70.0 และ 81.1 นาที ตามลำดับ; p-value = 0.005) ความหิวที่เพิ่มขึ้นระหว่างการศึกษาไม่แตกต่างระหว่างกลุ่ม (4.3 ในเด็กอ้วน และ 2.9 ในเด็กไม่อ้วน; p-value 0.19) ระยะเวลาการผ่านของอาหารมีความสัมพันธ์แบบผกผันกับดัชนีมวลกาย (r = -0.51; p-value = 0.001) แต่ไม่มีความสัมพันธ์อย่างมีนัยสำคัญกับความหิวที่เพิ่มขึ้น (r = -0.24, p-value = 0.15)*

สรุป: *เด็กอ้วนมีความเร็วของการผ่านของอาหารจากปากถึงส่วนต้นของลำไส้ใหญ่เร็วกว่าเด็กไม่อ้วน ความเร็วของการผ่านนี้สัมพันธ์แบบผกผันกับดัชนีมวลกายอย่างมีนัยสำคัญทางสถิติ และมีแนวโน้มสัมพันธ์แบบผกผันกับความหิวแต่ไม่ถึงระดับนัยสำคัญ*