Indian Journal of Gastroenterology (September 2018) 37(5):410–415
https://doi.org/10.1007/s12664-018-0902-5

ORIGINAL ARTICLE

Assessment of stool frequency and colonic transit time in Indian children with functional constipation and healthy controls

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Received: 13 June 2018 / Accepted: 22 September 2018 / Published online: 17 October 2018

Abstract

Introduction Indian adults have higher stool frequency and shorter colonic transit time compared to the Western population. Colonic transit time has not been studied well in Indian children. We aimed to compare colonic transit time in normal and constipated children.

Methods In this prospective study, stool characteristics and colonic transit time by radio-opaque markers were studied in healthy children (group A, $n = 39$) and functional constipation patients (group B, $n = 61$). Twenty radio-opaque markers were ingested per orally at 0, 12, and 24 h followed by a single abdominal X-ray at 36 h. Total and segmental colonic transit times were calculated using the standard formula.

Results Stool frequency per week and consistency were significantly different between group A (9 [2.5–17] years) vs. group B (4.5 [2–14] years), 7 (7–14) vs.1 (1–2), and Bristol type 4 (3–5) vs. type 2 (1–3). Total colonic transit time of groups A and B was 16.2 (0.6–36) vs. 22.8 (1.8–35.4) hours; $p = 0.003$. Ninety-fifth percentile (upper limit of normal) cutoff derived from group A was 31.8 h. Ninety-two percent of group B had colonic transit < 95th percentile of normal healthy children. Despite 8% with colonic transit > 95th percentile, all group B patients responded well to standard therapy with laxatives.

Conclusion Indian children have significantly higher stool frequency and shorter colonic transit time, which are different compared to the reported figures from the West. Most of the Indian children with functional constipation had normal colonic transit time.

Keywords Constipation · Functional gastrointestinal disorder · Gut transit · Rome criteria

Introduction

Functional constipation (FC) is a common problem in children of both developed and developing countries [1, 2]. It has been observed that Indian adults have faster total colonic transit time (CTT) and higher stool frequency as compared to the Western population [3, 4]. Assessment of total and segmental CTT sub-classifies abnormal colonic motility into right-sided colonic inertia, hindgut dysfunction, and outlet obstruction, guiding the appropriate management [5]. To our knowledge, there is no study in children that addressed the CTT from the developing countries. There are three major unanswered issues in literature that our study aimed to address in a sequential manner: (a) the normal stool frequency, consistency and CTT in healthy Indian children; (b) in comparison to healthy children, what is the CTT in patients with FC?; (c) if CTT is different from the West, do Indian children require a different Rome definition with respect to stool frequency? So far, for clinical practice in Indian children, physicians have relied more on stool consistency and other parameters than stool frequency for the Rome criteria of FC.

Methods

This was a prospective study from July 2014 to January 2016 conducted in the Department of Pediatric Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India. Institutional Ethics Committee clearance (IEC code no. 2014-109-IMP-78, dated 01-07-2014) was obtained prior to the start of the study and all patients were recruited with informed written consent from their guardians.

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Healthy children (group A) Information about the study was circulated among the families of the local residential colonies. Healthy children aged 2–18 years were invited to participate. Normal healthy children fulfilled all the criteria in the last 2 months: (a) passage of daily soft well-formed stools, (b) clinical history not suggestive of any organic or functional gastrointestinal (GI) symptoms [6], (c) no chronic systemic illness or recent drug therapy affecting GI motility, (d) on a normal balanced diet (3-day recall), and (e) normal growth parameters [7] and physical examination.

Patients with FC (group B) All consecutive patients aged between 2 and 18 years seen in our out-patient department with FC based on ROME III criteria [8] were enrolled after detailed history and clinical examination. In newly diagnosed FC patients (group B_1) with fecal impaction, CTT was done after 1 week of disimpaction (polyethylene glycol). Similarly, CTT was done after 1 week of stopping maintenance laxatives (lactulose or polyethylene glycol) in FC patients on regular follow up (group B_2) who were on a compliant maintenance laxative therapy and having normal stool pattern.

Assessment of colonic transit time using radio-opaque markers

Radio-opaque markers

Sterile, non-allergic, non-biodegradable medically approved indigenous radio-opaque markers were used. These were approved by the institute's ethics committee. In children aged > 6 years, markers were ingested as capsules each containing 5 radio-opaque markers. Those aged < 6 years, markers (either full or half sized) were given mixed with food like jam or curd.

Standardization of protocol

Since the CTT in normal and constipated children was unknown in the Indian population, the methodology was extrapolated from Indian adult experience [9]. In the initial standardization of protocol, 20 radio-opaque markers each were given per orally at 0, 12, and 24 h. Single digital abdominal radiograph (AR) was taken at 60 h from the first ingested markers. In the pilot phase, 12 of 15 normal children excreted all the markers by 60 h, which did not allow us to calculate CTT. So, the time point for AR was changed to 36 h from the first dose of markers (Fig. 1a). This protocol was followed in both groups of children.

Calculation of CTT [5]

CTT = (total number of retained markers in the abdomen at 36 h divided by number of markers at each dose) × (interval between each dose) = $(n/20) \times (12) = n \times 0.6$. Segmental CTT was calculated by counting the markers in respective segments and using the formula mentioned above, taking "n" as markers in that particular segment. The AR was divided into right, left, and recto-sigmoid segments using three lines. The first line was drawn over spinous process from sacral promontory. The second line was from sacral promontory to left anterior superior iliac spine and the third line was from sacral promontory to midpoint of pelvic brim on right side.

Percentiles of CTT in normal healthy children were calculated. Ninety-fifth percentile was the upper limit of normal (ULN) of CTT.

Statistical analysis

Data were expressed as median and range. Data between the groups were compared by Mann-Whitney U or Chi-square/Fisher's exact and Spearman's correlation test. P-value of < 0.05 was taken as significant. All calculations were performed using the SPSS statistical package (SPSS Inc., Chicago, USA) version 22.

Results

Thirty-nine healthy children (group A 25 boys, median age 9 [2.5–17] years) and 61 children with FC (group B 34 boys, median age 4.5 [2–14] years) were studied for CTT. Of 61 FC patients, 23 (group B_1) were newly diagnosed and 38 (group B_2) were follow up cases.

Group A ($n = 39$)

The median weight, height, and BMI z-scores of healthy children were −0.60 (−1.34 to +1.04), −0.90 (−1.93 to +1.73), and −0.26 (−1.11 to +1.93), respectively. Median stool frequency per week was 7 (7–14). Fifty-six percent passed 7 stool/week (daily) and 44% passed 8–14 stools/week. Median Bristol stool consistency was type 4 (3–5); types 3, 4, and 5 were 3%, 82%, and 15%, respectively.

The median (range) of total, right segmental, left segmental, and rectosigmoid segmental CTT in healthy children were 16.2 (0.6–36) h, 2.4 (0–13.8) h, 5.4 (0–19.2) h, and 1.2 (0–21.6) h, respectively. Normal centiles of total and segmental CTT are given in the legend of Fig. 1a. No significant

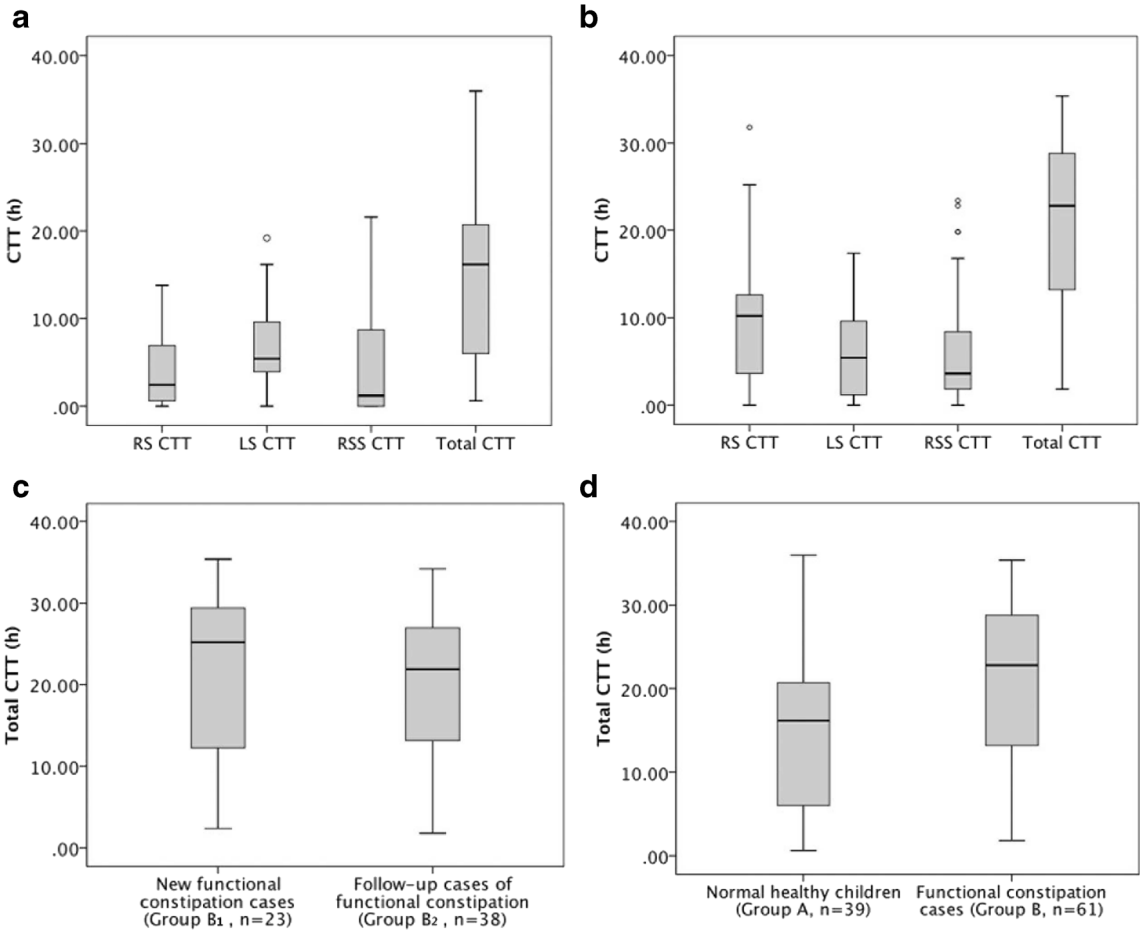

Fig. 1 Box-plot graph comparing total and segmental CTT. **a** 95th and 50th CTT percentiles ($n = 39$ healthy children): Total (31.8,16.2h); right segmental (10.8,2.4 h); left segmental (16.2,5.4 h); rectosigmoid (15.6,1.2h). **b** Total and segmental CTT in group B (children with functional constipation, $n = 61$). **c** Comparison of total CTT between B_1 (new FC cases) and B_2 (follow up FC cases). **d** Comparison of total CTT between group A (normal healthy children) and group B (FC patients). *RS* right segment, *LS* left segment, *RSS* recto-sigmoid segment, *CTT* colon transit time, *FC* functional constipation

difference was found between boys and girls in total CTT (15.6 h vs. 20.1 h, $p = 0.16$). No significant correlation of total CTT with age ($r = 0.26$, $p = 0.10$) or anthropometric parameters (weight z-score [$r = 0.01$, $p = 0.10$], height z-score [$r = 0.16$, $p = 0.33$], and BMI z-score [$r = 0.06$, $p = 0.73$]) was found.

Group B ($n = 61$)

Clinical parameters are shown in Table 1. Except for retentive posturing, there were no significant differences between new (B_1) and follow up (B_2) cases in their clinical parameters. The median (range) total CTT, right segmental, left segmental, and rectosigmoid CTT in 61 children with FC were 22.8 (1.8–35.4) h, 10.2 (0–31.8) h, 5.4 (0–17.4) h, and 3.6 (0–23.4) h, respectively as shown in Fig. 1b. No significant difference in total CTT was found between group B_1 (25.2 [2.4–35.4] h) and B_2 (21.9 [1.8–34.2] h), $p = 0.48$ (Fig. 1c).

Comparison of groups A and B

There were no significant differences in anthropometric parameters between healthy controls and patients with FC (weight z-score, $p = 0.98$; height z-score, $p = 0.33$; BMI z-scores, $p = 0.977$). The median stool frequency/week and Bristol stool consistency were significantly different between groups A and B (7 [7–14] vs. 1 [1, 2], $p < 0.001$, and 4 [3–5] vs. 2 [1–3], $p < 0.001$). The median total CTT between group A and group B was significantly different (16.2 h vs. 22.8 h, $p = 0.003$) indicating that FC had prolonged CTT in comparison to healthy controls (Fig. 1d). Sub-analysis in group B showed that 92% (56/61) of this group had their total CTT (21.9 [1.8–31.8] h) within normal range, i.e. < 95th percentile of healthy children. Eight percent (5/61) of FC patients had median total CTT (34.2 [33.6–35.4] h) more than the 95th percentile (i.e. > 31.8 h) of healthy children. Of these five patients, two were of group B_1 and three of group B_2. CTT was prolonged in both

Table 1 Clinical characteristic of patients with functional constipation at presentation

Clinical parameters	Total FC case group B ($n = 61$)	New FC cases group B_1 ($n = 23$)	Follow up FC cases† group B_2 ($n = 38$)	p-value*
Media age of onset (months)	24 (12–164)	24 (12–164)	24 (12–84)	0.321
Median duration of symptoms (months)	16 (2–71)	11 (2–71)	18 (4–60)	0.156
Median of presentation (months)	42 (22–167)	53 (23–167)	42 (22–105)	0.208
Stool frequency per week	1 (1–2)	2 (1–2)	1 (1–2)	0.337
Hard stools	59 (97%)	22 (96%)	37 (97%)	0.718
Large diameter stools	56 (92%)	21 (91%)	35 (92%)	0.913
Retentive posturing	49 (80%)	15 (65%)	34 (90%)	0.022
Encopresis	41 (67%)	15 (65%)	26 (68%)	0.798
Painful bowel movements	22 (36%)	10 (44%)	12 (32%)	0.352
Median weight z-score	− 0.5 (− 1.95 to + 3.14)	− 0.03 (− 1.81 to + 1.80)	− 0.79 (− 1.95 to + 3.14)	0.106
Median height z-score	− 0.72 (− 1.85 to + 2.72)	− 0.65 (− 1.85 to + 1.61)	− 0.73 (− 1.85 to + 1.61)	0.368
Median BMI z-score	0.12 (− 1.93 to + 3.10)	0.03 (1.61 to + 3.10)	− 0.3 (− 1.93 to + 3.10)	0.188

*p-value is between new cases (B_1) and follow up cases (B_2)

† Clinical characteristics were at time of disimpaction and starting of maintenance therapy

BMI body mass index, *FC* functional constipation

right and left segments in three out of five children of FC, and in the other two, there was prolongation in right segmental CTT. No significant differences in the clinical presentation and response to treatment were noted between FC patients with normal CTT (92%) and FC patients with prolonged CTT (8%). Median follow up of five patients with prolonged CTT was 6 (1–18) months. All the patients with FC including patients with prolonged total CTT responded well to standard therapy of FC, thereby showing that children with prolonged CTT did not come under ambit of refractory constipation [10].

Discussion

Large epidemiological and population-based adult studies from India showed that average stool frequency to be 12 ± 4.7/week with most of the normal adults defecating once/day (56%) or twice/day (34%) [3, 11]. Similarly, questionnaire-based studies from Iran and China in adolescent and adults reported mean stool frequency of 13.2 ± 7.7 and 7.1 stools/week, respectively, 84% having daily passage [12, 13]. Defecation frequency in 300 healthy children from Myanmar aged between 1 and 4 years has been reported to be 6.98 ± 2.1/week [14]. We concur with the above studies as our healthy children (aged 2.5–17 years) had a stool frequency of 7–14/week, 50% once/day and 44% more than once/day. Hence, keeping all the above studies into consideration, normal stool frequency of at least 7/week is seen in children or adults from developing countries. Normal stool frequency in the West is 3–21/week [15]. Normal stool consistency (Bristol type 4) does not differ in Western or Indian children as was observed in the present study.

In the first part of our study, median CTT in healthy children was 16.2 (0.6–36) h, similar to CTT in Indian (15.8 [4.2–27.5] h) and Chinese (mean 24.5 ± 18.8 SD h) healthy adults [4, 16]. A review of the radio-opaque marker-based CTT studies with near similar designs as ours in healthy age-matched children is shown in Table 2 [17–20]. Western children have higher CTT than Indians presumably due to lower content of dietary fiber. Ninety-fifth percentile of total CTT in our children (31.8 h) was almost less than half of that reported (81.8 h) in healthy Belgian children [20]. The first part of our study has an important observation that healthy Indian children have higher stool frequency and faster CTT than Western children.

In the second part of our study, we compared the CTT of healthy children vs. those with FC. The median time of movement of the markers through the colon (total CTT) was significantly delayed in FC as compared to healthy group (22.8 h vs. 16.2 h, $p = 0.003$). However, the maximum total CTT value indicating the slowest movement in the colon was within normal range of healthy controls in 92% of our FC patients (i.e. 31.8 h). The other five cases with total CTT > 31.8 h (> 95th percentile of normal healthy children) ultimately did well on follow up on laxative therapy. This observation implies three messages: (a) our FC group (new or follow up) patients largely had normal transit, (b) we can assume that Indian children whether normal or FC take the same amount of maximum time in expelling colonic markers, (c) it emphasizes the basis for the need for change of Rome foundation guidelines on FC with regard to Indian children. Stool frequency of ≤ 2/week

Table 2 Comparison of studies on normative values of colonic transit time in healthy children by radio-opaque marker study

	Arhan et al. [17] 1981 France	Gutierrez et al. [18] 2002 Spain	Wagener et al. [19] 2004 England	Velde et al. [20] 2013 Belgium	Current study India
No. of subjects	23	30	22	54	*39*
Age (years)	< 15	2–14	4–15	3–18	*2.5–17*
Total CTT (h)					
Mean	29	29.1	39.6	38.8	*15.1*
Median	–	–	–	36	*16.2*
ULN	62*	45.7*	84#	79.2#	*31.8#*
Right CTT (h)			(AC) (TC)		
Mean	7.7	7.5	5.5, 10.9	7.0	*4.0*
Median	–	–	–	4.8	*2.4*
ULN	18*	19.0*	–	19.8#	*10.8#*
Left CTT (h)			(DC)		
Mean	8.7	6.6	6.1	7.0	*6.6*
Median	–	–	–	2.4	*5.4*
ULN	20*	19.0*	20.6#	26.4#	*16.2#*
Rectosigmoid CTT (h)					
Mean	12.4	14.9	18.2	24.7	*4.5*
Median	–	–	–	24	*1.2*
ULN	34*	32.4*	40.8#	63.0#	*15.6#*

AC ascending colon, *TC* transverse colon, *DC* descending colon, *CTT* colonic transit time, *ULN* upper limit of normal

*Mean + 2SD, # 95th percentile

(Rome III or IV criteria) as the criterion for stool frequency cutoff may be suited for definition of FC in the Western population [8, 21]. Taking the stool frequency and CTT into consideration, the cutoff of ≤2 stools/week might not be applicable to the Indian population. Further studies with comparisons with larger population of healthy pediatric controls would be required to validate our findings. If future studies are agreeable, then Rome foundation could consider modifying the stool frequency criterion to suit the definition at a global level. However, the stool consistency inclusive of other 4 points of Rome criteria should remain unchanged.

The issue of CTT values in healthy and constipated children arises in the context of slow transit constipation. In the earlier two prospective European studies, arbitrary cutoffs of 63 h and 100 h were taken to define delayed and slow-transit constipation, respectively [22, 23]. We suggest a CTT value of 31.8 h (95th percentile) as upper limit of normal for Indian children. We agree with European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) recommendation that CTT as a routine initial investigation is not required in FC [10].

The strengths of our prospective radio-opaque marker-based study are (1) for the first time, we established normal stool frequency corroborated by CTT values in healthy Indian children; (2) having established normative data, we confirmed the postulation that Indian children with FC mostly have normal transit constipation, (3) we could derive CTT cutoff levels for defining delayed or slow-transit constipation in Indian population, (4) the protocol of study, which we standardized for our children can be used for future studies in Indian children allowing minimal radiation exposure. Future studies may confirm the findings of radiographic CTT with wireless motility capsules once standardized in younger children. Our limitation is that the study is neither community-based nor socioeconomic strata-based to recruit large numbers of healthy children for stool characteristics and CTT. Prospective head-to-head comparison of CTT with Western healthy or constipated children was beyond the scope of this study.

This is the first study on CTT in children from developing countries providing normal total and segmental CTT values. By this study, we have standardized the protocol for assessment of CTT in Indian children using radio-opaque markers. Stool frequency is higher (7/week) and CTT (16.2 h) is faster in Indian healthy children with 95th percentile being 31.8 h. Though the children with FC have prolonged median CTT (22.8 h), 92% have CTT within normal range as compared to healthy children.

Acknowledgments We thank all the children who helped us conduct this study by volunteering to participate in the study.

Funding information The study received an intramural financial grant from our institute.

Compliance with ethical standards

Conflict of interest US, SKY, AS, UP, and MSS declare that they have no conflict of interest.

Ethical statement The authors declare that the study was performed in a manner conforming to the Helsinki declaration of 1975, as revised in 2000 and 2008 concerning human and animal rights, and the authors followed the policy concerning informed consent as shown on Springer.com.

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