Investigation of Colonic Transit in Constipated Adults Using 99mTc–DTPA –Carbo Medicinalis Labeled Meal

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Article

Investigation of Colonic Transit in Constipated Adults Using 99mTc—DTPA—Carbo Medicinalis Labeled Meal

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Abstract

Background and Objectives: Constipation is a common problem in the general population. About 15% of the population suffers from one of the defecation disorders caused by various etiological factors. The goal of this work was the implementation of scintigraphic evaluation of colonic transit in patients with constipation. *Materials and Methods*: A total of 117 patients were examined (68 (58%) women and 49 (42%) men, in whom the existence of constipation was determined in the previous period by self-evaluation and using the ROMA IV criteria. All patients were given an oral test meal containing 99mTc-labeled charcoal in a dose of 370 MBq. Targeted static scintigrams were performed 8, 24, and 48 hours after the application of the test meal in the anterior projection over the abdomen. All scintigrams were qualitatively examined, and after the qualitative assessment, the geometric center (GC) of the radiopharmaceutical distribution was calculated. *Results*: Generalized slowing of colonic transit was detected in 85% of women while 15% of female subjects showed both qualitatively and GC-estimated normal colonic transit. In men, slowed colonic transit was detected in 78% of examined patients, while 22% of patients had qualitatively normal colonic transit and GC that fell within normal values. Idiopathic constipation was detected in 85% of women and 88% of men. A smaller number of patients showed the existence of etiological factors for slowed colonic transit. *Conclusions*: Scintigraphic evaluation of colonic transit using 99mTc-DTPA-labeled medical charcoal has proven to be an easy-to-perform, non-invasive method by which it is possible to detect the presence of slowing of colonic transit. In addition to the qualitative assessment of the obtained scintigrams, quantification by calculating the geometric center enables an even more precise insight into the assessment of the segment of the large intestine in which the slowing of colonic transit occurred.

Keywords: constipation; scintigraphy; colonic transit; geometric center of distribution

1. Introduction

Constipation is a common problem in the general population. According to the ROMA IV criteria, about 15% of the population suffers from one of the defecation disorders caused by various etiological factors [1]. According to the ROMA IV criteria, chronic constipation can be divided into (a) functional constipation (FC), (b) irritable bowel syndrome with constipation (IBS), (c) opioid-induced constipation (OIC), and (d) functional defecation disorders (FCD) [2]. The Rome IV criteria for bowel disorders. According to the ROMA IV criteria, patients with FC are considered to have two or more of the following characteristics: (a) Straining more than 25% of defecation. (b) Lumpy or hard stools (BSFS type 1 or 2) more than 25% of defecation. (c) Sensation of incomplete evacuation more than one-fourth (25%) of defecation. (d) Sensation of anorectal obstruction/blockage more than one-fourth (25%) of defecation. (e) Manual maneuvers to facilitate more than one fourth (25%) of defecation. (f) Fewer than three spontaneous bowel movements per week.

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Recognizing the existence of FC can greatly help clinicians in the further treatment of this disorder, i.e., contribute to the correction of the hygienic diet regime and/or the application of appropriate therapy. The diagnostic approach to examining FC involves a detailed history, clinical examination, the use of various laboratory tests, most of which have limited diagnostic utility, colonoscopy, balloon expulsion test, anorectal manometry, and the use of colonic transit assessment studies [3]. Among the studies for the evaluation of colonic transit, we find a scintigraphic approach that involves the non-invasive application of radioisotopes and/or radioisotope-labeled solid meals and the monitoring of radioactivity in the colon at different intervals, with the possibility of applying semiquantification, which facilitates the establishment of a diagnosis [4].

2. Materials and Methods

In this work, a total of 117 patients were examined, (68 (58%) women and 49 (42%) men, in whom the existence of constipation was determined in the previous period by self-evaluation and using the ROMA IV criteria. The average age of the patients was 39 years (21-57) in women, and 45 (24-61) in men. All patients were referred by an abdominal surgeon after a detailed clinical examination and the existence of a clinical picture that corresponds to chronic Constipation. Two days before the scintigraphic method, all patients were excluded from lactose intolerance. On the day of the test, all patients were given an oral test meal containing 99mTc-labeled charcoal in a dose of 370 MBq. The labeling of DTPA was done according to the manufacturer's specification carried out is 15 minutes long. The radiopharmaceutical was then dissolved in 300 ml of water. The application of the radiopharmaceutical prepared in this way was followed by taking a solid meal not labeled with the radioisotope. An unlabeled solid meal included: 120g of scrambled egg white, two slices of white bread, 30 grams of strawberry jam, 150 ml of water. Immediately before the application of the test meal, the number of pulses in the prepared radiopharmaceutical was measured on a gamma camera. This preparation of the test meal was done according to the EANM protocol for evaluating the motility of the intestinal tract. Maurer AH, Camilleri M, Donohoe K, et al. The SNMMI and EANM practice guideline for small bowel and colon transit 1.0. J Nucl Med 2013; 54:2004–2013 [Erratum in J Nucl Med 2014; 55:521]. After oral administration, the residual activity in the serving vessel was measured for the application in order to accurately calculate the applied radiopharmaceutical activity in the test meal. Targeted static scintigrams were performed 8, 24 and 48 hours after the application of the test meal in the anterior projection over the abdomen. The studies were performed on Siemens – double headed eCam in anterior and posterior projections with the duration of acquisition of 10 minutes. All scintigrams were qualitatively examined with an assessment of the localization of possible retention of radiopharmaceuticals. After the qualitative assessment, the geometric center (GC) of the radiopharmaceutical distribution was calculated. The colon is divided on the obtained scintigrams into four regions: 1 Ascending colon (AC), 2 Transverse colon (TC), 3 Descending colon (DC), 4 Rectosigmoidal region (RR). The geometric center of distribution of radiopharmaceuticals is calculated according to the formula:

$$GC= [(\%AC \times 1) + (\%TC \times 2) + (\%DC \times 3) + (\%RR \times 4)] / 100].$$

For each of the performed scintigrams, during the acquisition of the number of pulses from each of the regions, a correction was made for the decay of 99mTc according to the formula:

$$N(t) = N_0 * e^{(-\lambda t)}$$

where N(t) is the activity at time t, N_0 is the initial activity, λ is the decay constant (related to the half-life), and t is time.

Normal values for scintigraphic colon transit were considered with geometric center at four hours less than or equal to 1.4, geometric center at 24 hours between 1.7 and 4.0, and geometric center at 48 hours between 3.0 and 4.8 (87,91-93). Patients with geometric centers less than the above values are considered to have slow transit, and those with greater values are classified as accelerated transit [5]. The studies were performed in outpatient settings because there was no need to hospitalize the

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patients, and the patients were instructed to come to the facility 15-20 minutes before the scintigraphy time.

All patients signed an informed consent before conducting the study, and all studies were conducted in accordance with the World Medical Association (WMA) Declaration of Helsinki.

The study was approved by the Ethics Committee of the University Clinical Center in Niš, in whose part - the Center for Nuclear Medicine - the colonic transit test was performed.

3. Results

The qualitative assessment yielded the following results: The majority of examined patients with symptomatology I after self-evaluation indicating constipation showed a generalized slowed transit time through the large intestine. By general analysis between genders, it was observed that generalized slowing of colonic transit was detected more often in women compared to the male part of the examined patients. In 85% of women, a significant slowing of colonic transit was observed after the scintigraphic study, while 15% of subjects showed both qualitatively and GC-estimated normal colonic transit. In men, slowed colonic transit was detected in 78% of examined patients, while 22% of patients had qualitatively normal colonic transit and GC that fell within normal values. In women, the slowing down of colonic transit in the transverse and descending colon predominated, Figures 1 and 2.

Figure 1. Static scintigram in anterior projection, 48 hours after administration of radiofarmaceutical. Female 48 years old, with constipation symptomatology. Qualitatively retention of radiopharmaceutical was observed in transverse and descending colon. GC value was 2,4.

Figure 2. Static scintigram in anterior projection, 48 hours after administration of radiofarmaceutical. Female 43 years old, with constipation symptomatology. Qualitatively retention of radiopharmaceutical was observed predominantly in descending colon. GC value was 2,1.

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In men group of patients there was a noticeable slowing down of colonic transit in the descending colon and rectosigmoidal segment of Figures 3 and 4.

Figure 3. Static scintigram in anterior projection, 48 hours after administration of radiofarmaceutical. Male 37 years old, with constipation symptomatology. Qualitatively retention of radiopharmaceutical was observed predominantly in descending and rectosigmoid part of the colon. GC value was 2,2.

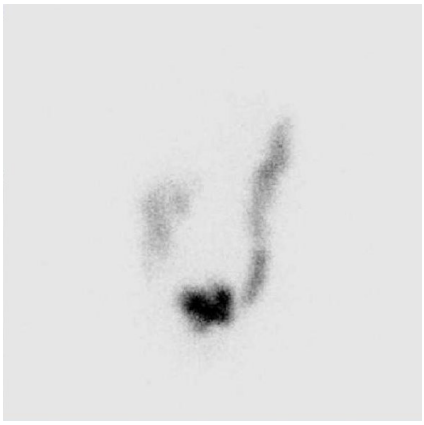

Figure 4. Static scintigram in anterior projection, 48 hours after administration of radiofarmaceutical. Male 41 years old, with constipation symptomatology. Qualitatively retention of radiopharmaceutical was observed predominantly in descending and rectosigmoid part of the colon. In addition retention was observed also in ascending part of the colon. GC value was 2,3.

The findings obtained from the qualitative assessment were in agreement with the results obtained from the GC calculation [6].

Upon further examination, in patients with detected slowed colonic transit, it was detected that the majority of patients had idiopathic constipation. Idiopathic constipation was detected in 85% of women and 88% of men. A smaller number of patients showed the existence of etiological factors for slowed colonic transit. Hypothyroidism caused by Hashimoto's thyroiditis was detected in 11% of women, which was the cause of slowed colonic transit. In 3% of women, the cause of slowed colonic transit was improper diet, while in 2% of the subjects, a disorder of the perineal musculature was detected. Excessive use of coffee and alcohol was detected in 9% of men, misuse of non-steroidal anti-inflammatory drugs in 2% and diabetes mellitus in 1%.

Patients with idiopathic constipation responded positively to a change in the hygienic diet regimen, which included dietary correction, proper hydration, and physical activity. In about 20% of patients of both sexes with idiopathic constipation, drug therapy had to be included in addition to the correction of habits. In one patient, there were no signs of improvement even with drug therapy, so a surgical intervention was performed.

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Patients with recognized etiological factors showed significant improvement after the applied therapy in terms of eliminating the cause of constipation, without the need for further therapeutic procedures.

4. Discussion

Constipation is a significant problem in the general population. Mostly, neither patients nor doctors are aware of the existence of the disorder, practically until the appearance of possible anorectal disorders that are the sequelae of existing constipation [7]. Types of constipation can be divided into several large categories, the most common of which are: Idiopathic constipation, constipation caused by musculature disorders, constipation caused by anatomical disorders, constipation caused by dietary habits, constipation caused by neurological diseases, constipation caused by metabolic and endocrinological causes, constipation caused by the use or abuse of medications and constipation caused by various diseases such as celiac disease, cystic fibrosis, milk allergy and dairy products, inflammatory bowel disease and scleroderma [8].

Examination of colonic motility involves the use of different approaches. The use of radiopaque contrast agents and consecutive x-ray methods implies a greater exposure of patients to radioactive radiation, and at the same time, the use of radiopaque agents such as capsules or radiopaque beads can give wrong information about transit through the large intestine [9]. Nuclear medicine testing of colonic motility is a non-invasive method, which involves the use of a radioisotope-labeled test meal, which enables the evaluation of colonic transit. In addition to the qualitative assessment of the presence of disturbances in the transit of faecal masses, by calculating the geometric center of distribution of radiopharmaceuticals, it is possible to quantify the qualitatively obtained results [10].

Different radioisotopes can be used for colonic transit nuclear medicine testing, depending on the availability and usability in certain nuclear medicine centers.

In this work, we used an approach that involved the use of technetium-labeled DTPA with medical charcoal in combination with an unlabeled solid meal according to the recommendations of the Good Clinical Practice Guide, which achieved a high percentage of labeling, the formation of a solid chelate of the radiopharmaceutical with the test meal, and the existence of a very small amount of free radioisotope.

Various approaches to colonic transit imaging have been reported. Some advocate recording after 24, 48, 72 and 96 hours [11]. Others suggest recording only up to 48 hours. Healthy individuals usually show complete evacuation of the colon within 72 hours. Imaging for up to 72 hours is necessary specifically to diagnose functional obstruction of the rectosigmoid bowel and to localize any sites of functional obstruction in the colon [12].

The use of the test meal with 99mTc-DTPA-medicinal charcoal was simple both for the preparation of the test meal itself and for its application, and the dose of radioactivity used was far less than the legally allowed stay in the general population, so the studies could be performed in outpatient conditions.

The scintigraphic examination required the arrival of the patients at precisely specified time intervals to the center for nuclear medicine, and only the scintigraphic visualization was not time-consuming, and the patients accepted it very well.

The use of the described test meal did not cause any unwanted effects in the patients in terms of nausea or other gastrointestinal complaints, and it was also very well accepted by the patients.

In our work, the majority of subjects referred for examination due to agreement of self-evaluation I using the ROMA IV criteria showed a generalized slowing of colonic transit, which corresponded to the existence of idiopathic constipation. No significant gender difference was observed in the slowing of colonic transit caused by idiopathic constipation. Most patients with idiopathic constipation responded positively to the application of a holistic treatment approach. This approach implied a change in the way of eating, an increased degree of physical engagement in terms of exercise and walks, better hydration, correction of excessive use of coffee or alcoholic beverages.

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A smaller number of patients did not have a good response to the applied measures to correct the diet and lifestyle habits, which is why pharmacological therapy had to be used. Only in one case of a female person was surgery required surgical intervention, as a measure of definitive treatment [13]. In our work, a shortcoming related to the assessment of colonic transit 72 hours after radiopharmaceutical ingestion was observed, which we justified by the half-life of 99mTc used, which is 6 hours. Only in the case of significant retention in the rectosigmoid column was it possible to qualitatively describe the obtained scintigrams and perform quantification by calculating the geometric center. On the other hand, using a technetium-labeled test meal is much simpler than using 111In for labeling [14]. Also, most subjects with normal colonic transit will practically eliminate the radioactive test meal within 48 hours through defecation, and thus the detection of retention of fecal masses in any segment of the large intestine in 48 hours is in itself a diagnostic criterion of slowing of colonic transit.

In this paper, examination of colonic transit with a limit of 48 hours after the ingestion of the test meal was shown to be a sufficient method for the detection of resistance to colonic transit, as well as for the detection of slowing of the segment of the large intestine in which the slowing eventually occurred.

5. Conclusions

Scintigraphic evaluation of colonic transit using 99mTc - DTPA labeled medical charcoal has proven to be an easy to perform, non-invasive method by which it is possible to detect the presence of slowing of colonic transit.

In addition to the qualitative assessment of the obtained scintigrams, quantification by calculating the geometric center enables an even more precise insight into the assessment of the segment of the large intestine in which the slowing of colonic transit occurred.

Conditionally, the lack of methods is the difficult assessment of the distribution of fecal masses 72 hours after ingestion of the test meal, due to the physical properties of the radiopharmaceutical used.

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Data Availability Statement: All data related to manuscript are available from the leading author upon the request.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

GC	the geometric center (GC) of the radiopharmaceutical
FC	Functional Constipation
ROME IV	The ROME IV criteria for constipation

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