COLONIC TRANSIT TIME WITH RADIOPAQUE MARKERS: CASE STUDIES

TIEMPO DE TRÁNSITO COLÓNICO CON MARCADORES RADIOPACOS: SERIE DE CASOS

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SUMMARY

Colonic transit time with radiopaque markers (CTTRM) is a test which evaluates colonic motility in a simple and effective manner. It was first described in 1969 and it is still used as a complementary method of studying patients with constipation. We present 9 patients who underwent this study as part of their clinical constipation diagnosis in 2010; moreover, the technique, diagnostic contributions and indications of the test are reviewed. The exam technique has not been adequately standardized in literature. However, the fact that it helps determine the role of the colon as the cause of constipation in a patient has led to its inclusion in the study guidelines of constipation, which makes the standardization of the study technique and presentation even more important.

RESUMEN

El tiempo de tránsito colónico con marcadores radiopacos (TTCMRO) es un estudio que constituye una manera sencilla y efectiva de evaluar la motilidad del colon. Fue descrito en 1969 y sigue vigente como un método complementario de estudio en pacientes con estreñimiento. Se presentan nueve casos de pacientes en quienes se realizó este estudio como parte del diagnóstico clínico de estreñimiento en 2010; se revisan así mismo la técnica, el aporte diagnóstico y las indicaciones del examen. Aunque en la literatura no hay una estandarización satisfactoria de la técnica de examen, el aporte del estudio para determinar el papel del colon en el estreñimiento de cada paciente ha hecho que se incluya en las guías de trabajo de estreñimiento, lo cual hace aún más relevante la importancia de estandarizar la técnica y la presentación del estudio.

Introduction

Constipation is a complex clinical condition. The statistics of prevalence have a wide range; in the United States, for example, it varies from 3 to 28% (1,2). This difference is explained due to the great discrepancies that for a long time were presented in its definition. In 1999, the Rome II criteria were defined, which helps determine if a patient suffers from constipation (3). These criteria include: less than three bowel movements per week, unusual effort during defecation, prolonged defecation and manual de-impactation (2). In the absence of warning signs (weight loss, bleeding, change of intestinal habits or pain), most patients with constipation suffer from colon or anorectal functional disorders.

Colonic transit time with radiopaque markers (CTTRM) is a diagnostic test which is greatly useful to differentiate between normal and slow colonic transit time, in patients who suffer from constipation, and during the evaluation of unexplained diarrhea, since it measures the approximate time of transit of the entire intestine (3). In order to perform this test, the patient ingests radiopaque markers and afterwards, a radiography of the abdomen is taken with the purpose of evaluating their evacuation. Several methods exist for such a purpose. Three colon motility patterns have been defined, which constitute the test diagnosis: Normal, colonic inertia pattern (slow transit), and obstruction pattern in the exit tract (4).

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Figure 1. Model of the three compartments. The compartments, which are defined at each side of the vertical line, define the right and left column. The compartment under the oblique lines defines the recto-sigmoid compartment.

Figure 4. 66 year old patient with 22 prevalent remnants in the left hemicolon.

Figure 2. 19 year old patient, whose radiography during day 3 shows a total evacuation of all the radiopaque markers.

Figure 5. 60 year old patient with 24 prevalent remnants in the left hemicolon.

Figure 3. 29 year old patient with 19 prevalent remnants in the left hemicolon.

Figure 6. 53 year old patient with 18 remnant markers in all the compartments.

Materials and methods

In 2010, nine people who entered our service with a clinical diagnosis of constipation underwent a procedure where their colonic transit time with radiopaque markers was taken. All of them were women between 19 and 66 years of age.

In our institution, colonic transit time with radiopaque markers is performed by providing a single dose of 24 radiopaque markers; afterwards, simple radiography of the abdomen is taken, 24. 48 and 72 hours after intake, with the purpose of evaluating the evacuation of radiopaque markers in each one of them.

In order to determine the location of the markers, a three compartments model is used (5,6) (figure 1). The L5 spinous process is taken as a repair; oblique lines are drawn from this point to the greater femoral trochanters, and a third line is drawn from the same L5 point upwards, dividing the abdomen in two halves. The compartments at each side of the vertical line and above the oblique lines define the right and the left colon. The compartment defined between two oblique lines is the recto-sigmoid region.

Results

CTTRM was normal in two patients. It showed a colonic inertia pattern in six patients, and an obstruction pattern of the exit tract in one patient (figures 2-8).

Normal Pattern

- Cases 1 and 2. 60 and 19 year old patients, whose radiography during day 3 show a total evacuation of all the radiopaque markers. (figure 2).

Colonic inertia pattern

- Case 3: 29 year old patient with 19 prevalent remnants
- in the left hemicolon in day 3 radiography (figure 3).
- Case 4. 66 year old patient with 22 prevalent remnants in the left hemicolon in day 3 radiography (figure 4).
- Case 5: 60 year old patient with 24 prevalent remnants in the left hemicolon in day 3 radiography (figure 5).
- Case 6. 53 year old patient with 18 prevalent remnants in all the compartments, in day 3 radiography (figure 6).
- Case 7. 32 year old patient with 18 prevalent remnants in the left hemicolon in day 3 radiography (figure 7).
- Case 8: 47 year old patient with 23 prevalent remnants in the left hemicolon in day 3 radiography (figure 8).

Obstruction pattern in the exit tract

Case 9: 21 year old patient with 22 prevalent remnants in day 3, predominantly located in the recto-sigmoid compartment (figure 9).

Discussion

Physiopathology of constipation

The main physiological processes that are produced in the digestive system are secretion, digestion, and absorption. Residue exits through the anus. These last functions are carried out by the contraction and relaxation of the smooth muscle of the food channel and its sphincters in the esophagus, stomach, ileocecal valve and anus (7).

The right colon performs several complex functions which include mixing, fermenting and drying the intraluminal content, in order to create feces. The left column acts as a vessel for drying, and is the fastest transport of fecal matter. The recto-sigmoid region acts as a sensory-motor organ which eases the retention and evacuation of feces, when socially acceptable. Said functions are controlled by neurotransmitters, which include serotonin, acetylcholine, which is a peptide related with the calcitonin gene and substance P, as well as the intrinsic reflexes of the colon and a wide range of reflex and learned mechanisms which control the transport and evacuation of fecal matter (2).

Additionally, the digestive tract is subject to the control of extrinsic nerves which connect it to the brain, such as the vagus nerve and the sympathetic nerve. Similarly, the organization of parts of the brain, exerts control over the digestive function (visceral nervous system or limbic system, including parts of the cerebral cortex which are the oldest phylogenetically.

Digestion is also influenced by endocrine glands; the anterior lobule of the pituitary gland, which has trophic effects in the intestine; suprarenal corticosteroids, which mediate in the transport of water and electrolytes through the intestinal mucus, and thyroid hormones which modify the transit of intestinal content. Similarly, the digestive system depends on the circulatory system for the exchange of gas and nutrients.

Approximately 6 to 11 L of liquid enters the food channel in a normal day. Only 1-2 L, approximately, enter the colon, and less than 200 g of fecal matter exit the rectum. These feces normally contain less than 5 g of fatty acid, and 1.5 g of nitrogen per day, when a diet with 100 g of protein, 300 g of carbohydrates and 120 g of fat is present (7).

The movement of the intestinal current depends on whether the digestive tract contains food which has been recently eaten or whether it is in an inter-digestive period. If the latter is true, depolarization access (migratory motor complex) stretches from the esophagus to the ileocecal valve, with a frequency of one every hour and a half to two hours. Depolarizations coincide with a wave of contractions. The result is a propulsion movement which empties the upper digestive tract to the cecum.

The act of eating overrides the migratory motor complex, which is replaced by irregular contractions which mix the intestinal content and advances the intestinal current towards the colon, in short segments. Two key points exist: The pylorous and the ileocecal valve, where peristalsis is limited. In normal conditions, both sphincters prevent the movement from the distal side to the proximal side. The esophageal sphincters play a similar role. Movement through the colon occurs at much lower velocity. Normal transit time through the food channel is 65 ± 8 hours (7).

The motor functions of the colon are to increase the contact of the intestinal content with the surface of absorption, through mixture or segmentation movements, in order to allow the accumulation of intestinal content and to drive it periodically to the rectum. Normally, the content of the cecum is semi-liquid. Fecal matter only acquires its normal consistency in the descending colon and in the sigmoid colon.

Most of the time, the total transit time in the digestive tract occurs in the colon. Approximately 2 to 3 days can pass before a food residue that enters the cecum is evacuated from the rectum. During this period, propulsive activity is very limited. Generally speaking, once or twice, in a 24 hour period, the intestinal content goes from the right to the left column: it is called "mass movement" (7).

Figure 7. 32 year old patient with 18 prevalent remnants in the left hemicolon.

Figure 8. 47 year old patient with 23 prevalent remnants in the left hemicolon.

Figure 9: 21 year old patient with 22 prevalent remnants in day 3, predominantly located in the recto-sigmoid compartment.

In normal circumstances, fecal matter enters the rectum and the rectum wall stretches. The sensitive fibers in the distal rectum detect this stretch and transmit the nervous impulse to the internal anal sphincter, which immediately and for a short time increase the basal tone. It subsequently relaxes. This is known as inhibitory anal reflex (8).

Normal evacuation indicates the involuntary relaxation of the internal sphincter, as well as the voluntary relaxation of the external anal sphincter and the pelvic floor muscles (paradoxical puborectal contractions), which, in turn, increase the anorectal angle (8).

Constipation, which is one of the most frequent digestive disorders, is polysymptomatic (9). Its prevalence increases with age, especially in persons over 65 years of age, and is more common in patients with irritable bowel syndrome with prevalence of constipation and dyssynergia, than in patients with slow transit constipation (2).

In the absence of warning signs (weight loss, bleeding, change of intestinal habits or pain), or secondary causes such as the use of drugs, metabolic disorders, colon-rectal cancer and painful local lesions such as anal fissure, most patients with constipation suffer from colon or anorectal functional disorders.

Constipation can also result from structural, mechanical or metabolic disorders which directly or indirectly affect the colon or anus-rectum (2). Different organic disorders, as well as a wide range of medications, can cause constipation. Spinal cord lesions represent 9% of all adolescents in untreatable constipation, secondary to the loss of coordination of the digestive tract, and in adults it is more probable that constipation is secondary to renal or endocrine dysfunction (9). At least three types of constipation have been recognized:

Slow transit constipation: Characterized by a prolonged delay in transit of feces through the colon. This may be due to a primary dysfunction of the smooth muscle of the colon (myopathy) or its innervation (neuropathy) (2,10).

Dyssynergic defecation: Known also as obstructive defecation, anism, pelvic floor dyssynergy or exit obstruction, is characterized by the difficulty or inability to expel fecal matter of the anus rectum. Many patients can also suffer from prolonged colonic transit (2,10).

Irritable bowel syndrome with predominant constipation: Abdominal pain with distension or without it is the most important syndrome, along with alteration in intestinal habits. These subjects may or may not have slow transit or dyssenergy (2,10). Even though infrequent defecation has been generally used to define constipation, symptoms such as excessive effort, presence of hard feces or a sensation of incomplete evacuation are equally as important, or even more so.

In order to improve the diagnosis and to develop more even standards during search and treatment, the Rome III criteria were suggested, which define functional primary constipation based only symptoms, while dyssynergic defecation is defined according to symptoms and objective physiological criteria.

Diagnostic criteria for functional constipation must be present during the last three months and must have appeared, at least, six months before diagnosis. These are:

- Two or more of the following: Effort during at least 25% of defecations; b) irregular or hard bowel movements in at least 25% of defecations; c) sensation of incomplete evacuation in at least 25% of defecations; d) manual maneuvers to ease at least 25% of defecations, and e) at least three defecations per week.

- Soft feces rarely present without the use of laxatives.
- Insufficient criteria for irritable bowel syndrome.

Criteria for dyssynergic defecation include that the patients comply with symptomatic criteria for functional constipation, and that constipated patients verify two or more of the following physiological criteria: 1)Dyssynergic defecation pattern, 2) inability to expel a ball or a device similar to feces such as FECOM within a minute, 3) prolonged colonic transit time and 4) inability to expel barium or retention of over 50% of defecography (2).

Regarding physiopathology of constipation through slow transit –also known as colonic inertia–, one must take into account that motor activity of the colon is intermittent, variable and–is influenced by the sleep-waking cycle, food, exercise, physical and emotional stressors and differences in regional colonic motor functions. It has been seen that these patients suffer from an alteration of the phasic colonic motor activity. The gastrocolic response to food and the response to waking up in the morning after sleep are significantly reduced; but the daily variation of colonic motor activity is preserved.

Periodic rectal motor activity is almost always seen at night and is significantly increased, which delays propulsion of feces. Patients who suffer from constipation have less propagated contractions and the speed of propagation is also decreased; moreover, the waves tend to end prematurely and have diminished amplitude.

Constipation may also be associated with autonomic dysfunction, as a lack of Cajal interstitial cells and lymph cells in the myenteric plexus has been demonstrated. It can rarely be related to a more generalized dysmotility and be part of a pseudo-obstruction syndrome. A different and possible hypothesis is excessive absorption of bolus water.

In young adults, it is more common in women than in men. This suggests a possible association with a hormonal or endocrine imbalance. The relationship between menstrual cycle and intestinal transit is still controversial.

Studies of neurotransmitters in the colon wall are also controversial. A decrease in the concentrations of vasoactive intestinal peptide has been informed as an increase in serotonin concentrations. In a study of the contractibility of the smooth muscle, mediated by protein G, the colectomy specimens of women with slow transit constipation showed a relationship between progesterone and contractile G protein, which are due to overexposure of progesterone receptors. This partially explains why some women are more prone to constipation.

More recently, a greater prevalence of methanogenic activity has been observed in constipated patients. It has also been seen that the infusion of methane gas alters muscle contractions. However, more studies are needed to determine when methanogenic activity predisposes a person to develop constipation, or if it is a consequence of altered colonic physiology.

Regarding the physiopathology of dyssynergic defecation, it has been suggested that paradoxical anal contraction or involuntary anal spasm (anism) may be responsible for dyssynergic defecation. This seems to be acquired in two thirds of the population, and most patients show a lack of coordination of the abdominal, anorectal, and pelvic floor muscles during defecation. This failure in rectal anal coordination may consist of several mechanisms which include alteration of the rectal contraction, paradoxical anal contraction or inadequate anal relaxation (2).

It is possible that patients with obstructive defecation suffer from an alteration in the rectal sensation, which is associated with the megarectum or is a result of it, which may be a unique body or part of a more diffuse megacolon disorder. The absence of the inhibitory anal reflex is observed in secondary diseases in the absence of lymph cells. The congenital form of this process is Hirschprung disease, which is more common in newborn children. The adult form is detected during late adolescence and acquired aganglionosis in the rectum is one of the presentation forms of Chagas disease. Even rarer is autosomic dominant myopathy of the internal anal sphincter.

Anatomical abnormalities include rectoceles, sigmoidoceles, enteroceles, prolapses and intussusception, although these are present also in patients with normal defecation.

CTTRM measurement differences between normal colonic transit and slow colonic transit in patients with constipation and in the evaluation of unexplained diarrhea. The test with radiopaque markers measures the transit time of the entire intestine; however, given that most of it reflects the passage through the colon, the test is an approximation of the colonic transit time (3).

Diagnosis due to colonic transit time with radiopaque markers:

In most studies, the average colonic transit time is 30 to 40 h with an upper normal limit of 70 h. In women, the maximum colonic transit time are the longest (70 to 106 h), compared to men (50 h). In a second study, the total colonic transit time in men was 31 h, and 36 h in women, with an estimated inter-observing variation coefficient of 19,4% in men and 42% in women (3).

It has been estimated that total colonic transit time is $35 \pm 2h$, with 11.3 ± 1.1 h for the right colon: 11.4 ± 1.4 h for the left colon, and 12.4 ± 1.1 h for the sigmoid rectum (3). The differences in colonic transit time in the studies are seen in age, gender and methodology (3).

CTTRM consists of the intake of radiopaque markers and radiographies of the abdomen to evaluate their evacuation. Several techniques have been described, among them:

- Twenty-four radiopaque markers in a single dose, with radiography of the abdomen every 24 h until the markers are ejected.
- Twenty-four radiopaque markers in a single dose with radiography of the abdomen between the third and fifth days.
- Twenty-four markers with a single radiography (or fluoroscopy)
- on day 7 (11)
- Ten markers every 24 h, during 3 or 10 days and radiography on day 7 after it has been taken.
- Ten doses: One daily and a barium pill on day 9 (12).

A single dose has been accepted as sufficient to evaluate the transit. Apparently, multiple doses do not contribute additional information, and lengthen the time of study. The technique of multiple radiographies has been criticized due to the high dose of radiation received by the patient.

Three motility patters have been described: 1) Transit time is considered normal if 80% of markers have been eliminated five days after intake (five or less markers remain in the colon). 2) If over 20% of markers remain (over five) in the right or the left hemicolon, then this would be a diagnosis of a pattern of colonic inertia (slow transit). 3) If the remnant markers are located in the anorectal area, an obstruction pattern in the

exit tract is suggested (4). Other others consider it as slow transit if over 44% of markers are retained (13).

Placing a patient in one of these patterns enables the doctor to determine, first, if the patient suffers from functional constipation. In case of colonic inertia patterns or exit obstruction pattern, the probable cause of constipation must be indicated and the subsequent study must be directed in a more focused manner.

Conclusion

Unfortunately, there are deficiencies in the evaluation of CTTRM as a study of constipation. The test has not been adequately standardized, and several techniques have been described. The test allows differentiating if transit is slow or normal. However, in some occasions it does not constitute a precise method to differentiate the two subtypes. Studies with a solid methodology have not been published, as demonstrated by the meta-analysis of Rao and collaborators (13), have not been published. However, these authors conclude that sufficient evidence exists to support its use in the study of constipation. The consensus of the American and European associations of neurogastroenterology and motility (3) also recommends the use of this test, through the technique of a single dose with radiography after five days. However, it also recommends the standardization of the method, the radiological report and the dose of markers.

In our experience, a CTTRM with a single dose of markers and a simple radiography of the abdomen after 72 hours is a low radiation technique with high diagnostic performance. It allows establishing a normal pattern or colon dysfunction with enables the doctor to direct the etiology and focus in future diagnostic tests.

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