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Original article

Measurement of ^{75}Se-SeHCAT Abdominal Retention in the Initial Diagnosis of Bile Acid Absorption (BAM)☆

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ABSTRACT

Aim: To evaluate the usefulness of the ^{75}SeHCAT abdominal retention (AR) measurement in the early diagnosis of diarrhea syndrome (DS).
Methods: Thirty-seven patients with diarrhea syndrome within the first month of evolution were prospectively evaluated. The ^{75}Se-SeHCAT abdominal retention was measured 4 and 7 days post-administration of 0.01 mCi of ^{75}SeHCAT. The test was performed prior to treatment and at 3 months when the baseline study was positive. The test was considered positive if the RA was <25% at 4th and <10% on the 7th day. The patients were followed up at 3 months. Depending on the response, 3 groups were established: (a) complete response: normalization of stool frequency, (b) partial response, decrease of frequency and (c) no response.
Results: Group A: The AR of ^{75}Se-SEHCAT was normal in 21 patients. Six were diagnosed of colonic diverticulosis, 8 of irritable bowel syndrome, 1 of lymphocytic colitis, 1 of post-gastroenteritis syndrome, 1 of celiac disease and 1 of stenosis of the cardia. Four are still under study. Group B: The AR of ^{75}Se-SEHCAT decreased in 16 patients. All showed abnormal AR at day 7 and all but 1 at day 4. Following administration of cholestyramine resin, 8 (50%) presented partial response and 8 presented (50%) complete response. At 3 months, AR had increased at day 4 and 9 at day 7.
Conclusion: The measurement of ^{75}SEHCAT abdominal retention allows the early diagnosis of bile acid malabsorption in 43% of the patients with DS. Measurement at 7 days seems more accurate than that at 4 days.

Medición de la absorción de los ácidos biliares en el diagnóstico inicial de la diarrea crónica

Palabras clave:
^{75}Se-SEHCAT
Diarrea crónica
Absorción de ácidos biliares

RESUMEN

Objetivo: Evaluar la utilidad de la prueba del ^{75}SeHCAT en el diagnóstico precoz del síndrome diarreico (SD). Se evaluaron prospectivamente 37 pacientes con SD de un mes de evolución.
Método: Se midió la retención abdominal (RA) de ^{75}SeHCAT 4 y 7 días post-administración de 0,01 mCi de ^{75}SeHCAT antes del tratamiento y a los tres meses en los pacientes con estudio basal positivo. La prueba se consideró positiva si la RA era: <25% el 4.° y <10% el 7.° días. Los pacientes fueron visitados a los tres meses. Según la respuesta se distinguió: *a*) respuesta completa: normalización del ritmo deposicional; *b*) respuesta parcial, disminución de la frecuencia/consistencia, y *c*) no respuesta.
Resultados: Grupo A: la RA fue normal en 21 pacientes. El diagnóstico fue: 6 divertículos colónicos, 8 síndrome de intestino irritable, 1 colitis linfocitaria, 1 síndrome post-gastroenteritis, 1 enfermedad celíaca, 1 estenosis de cardias y 4 continuan en estudio.
Grupo B: la RA disminuyó en 16 pacientes; todos mostraron una RA baja a los 7 días y solo uno a los 4 días. Tras la administración de resina de colestiramina, 8 (50%) presentaron respuesta parcial y 8 (50%) respuesta completa. A los tres meses, la RA había aumentado en tres pacientes al 4.° día y en 9 al 7.° día.
Conclusión: La medición de la RA de ^{75}Se-SEHCAT permite el diagnóstico precoz de la malabsorción de sales biliares en el 43% de pacientes con SD. La medición a los 7 días parece más precisa que la de los 4 días.

Introduction

Diarrhea is a condition that usually lasts one or two days and that rapidly remits. On other occasions, it lasts longer and is complicated by fever, bed confinement or rectal bleeding. For this reason, 1.5% of the patients who suffer diarrhea require hospital admission.

Diarrhea is defined as a significant variation of the stool characteristics regarding previous bowel movement habits of the patient

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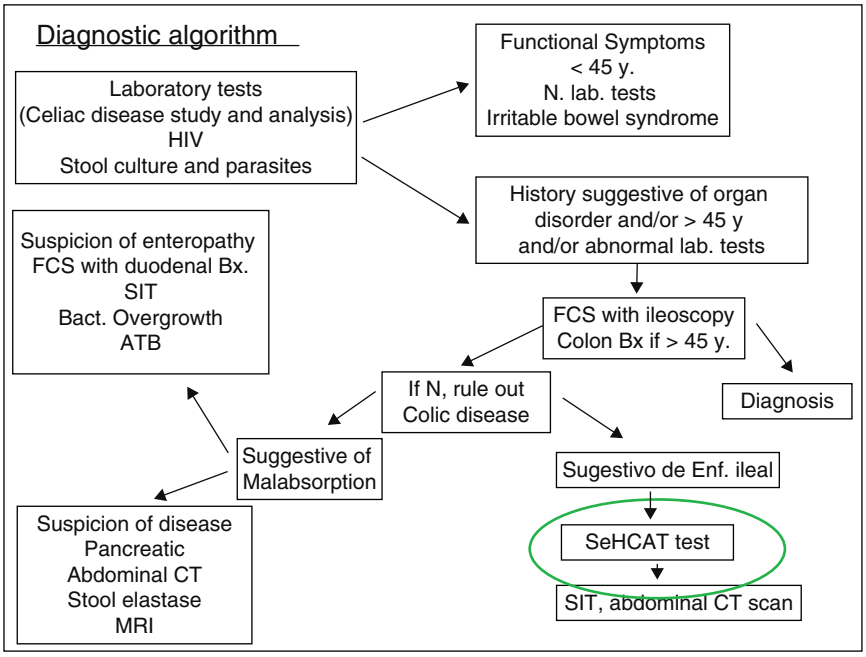

Pbase. Lab. N: normal laboratory tests, FCS: Fibrocolonoscopy, Bx: biopsy, N: normal, TID: small bowel, CT: computed tomography overheating. Bact.: bacterial overgrowth, ATB: antibiotics, RM: MRI.

Fig. 1. Diagnostic algorithm of chronic diarrhea.

as regards to increased volume and/or frequency, with decreased stool consistency. Diarrhea should be distinguished from pseudodiarrhea, in which the frequency is increased but the stools have a solid consistency. In the literature, diarrhea is considered to exist when the stool weight exceeds 200 g/day.[1] However, this definition does not take into account that persons who have high insoluble fiber intake may usually have elevated stool weight (as high as 300 g/day). On the contrary, some subjects who consult due to diarrhea have normal stool weight but with liquid consistency. Arbitrarily, diarrhea is considered to be chronic when it lasts for more than 4 weeks.

It has a 3–5% prevalence in Western countries in the general population and 7–14% in the elderly population.[2] This makes this disorder an important cause of incapacity.

Chronic diarrhea may have multiple etiologies, both malignant and benign.[3] Different pathophysiological mechanisms are distinguished, among which poor absorption of bile salts is included (BAM).

Bile acids secreted to the lumen of the small intestine play a significant role in emulsification and digestion of fatty acids. Under normal conditions, the entry of bile acids into the colon is less than 5% given the combination of the passive diffusion produced in the small intestine and active absorption in the terminal ilium. The remaining 95% undergo enterohepatic circulation approximately 10 times within 24 h.[4] In each recirculation, another 5% of the total circulating acids are eliminated again.

The BAM causes the bile acids to increase in the colon, with the resulting consequence of a reduction in the absorption of electrolytes and water, producing aqueous diarrhea. Another factor that could be altered and therefore have an effect is increase of colonic motility.[5]

Currently, three are three recognized types of BAM. Type 1: due to ileal resection and/or bypass and diseases of the ileum; type 2: the idiopathic or primary BAM which is characterized by not being associated to an organic disorder and by favorably responding to cholestyramine[6,7]; and type 3 which is associated to different conditions, including postcholecystectomy diarrhea, diabetes, post-vagotomy, chronic pancreatitis, cystic fibrosis, celiac disease and some drugs.[8–11]

Medicine nuclear provides a test, this being the quantification of abdominal activity of the ^{75}Se-SeHCAT, for the examination of bile acid absorption. It has demonstrated an 80–90% and 70–100% sensitivity and specificity, respectively.[12–14] SeHCAT is the homotaurocholic acid (23-selena-25-homotaurocholic acid) labeled with ^{75}Se. It has a half life of 120 days and decays emitting gamma radiation of 136 and 265 keV. This radiopharmaceutical behaves like a bile acid, is mostly reabsorbed in the terminal ileum and is resistant to bacterial degradation, there being no false positives due to bacterial overgrowth.

The percentage of patients in whom BAM may be a cause of chronic diarrhea may be greater than 45%.[15] Diagnosis of BAM is not easy. In general, the diagnosis of the cause is delayed for weeks or months due to the performance of different tests in search of a specific diagnosis.

The diagnostic algorithms are based on retrospective studies or small-sized prospective ones (grade C) and on experts' opinion (grade D), since there are currently no controlled and directed studies in the investigation of chronic diarrhea (Fig. 1). These studies place the ^{75}Se-SeHCAT study in the third diagnostic line in spite of the previously mentioned sensitivity and specificity.

Our study has aimed to evaluate the utility of the quantification of abdominal retention of ^{75}Se-SeHCAT as a first-line diagnostic test in the early pathophysiological diagnosis of patients with chronic diarrhea.

Material and methods

Study population

A group of 37 patients (26 women and 11 men) with age range 25–80 years within the period of May 2009 to February 2010 were

studied. All had come to the Nuclear Medicine Service of the Hospital Universitari de Bellvitge referred by the Gastroenterology Service of the same hospital and by the Primary Health Care Center Just Oliveras.

Inclusion criteria

- Having chronic diarrhea of more than one month duration.
- Absence of previous treatment.

Exclusion criteria

- Age under 18 years, pregnancy and breast-feeding.

Type of study and exploratory protocol

A prospective study was performed. The examination consisted in the oral administration after 4 h of fasting of a capsule containing 0.01 mCi (0.37 MBq) ^{75}SeHCAT. The patient had to continue fasting for 3 h more after the test, after which the abdominal activity was recorded. This registry considered the initial activity or zero time (ACT_0). The registry of the abdominal activity was repeated at 4 and 7 days of administration (ACT_4 and ACT_7). All the measurements were performed with the patient in decubitus supine position with the detector centered on the abdominal region, maintaining a constant patient-collimator distance (15 cm) and a 5-min acquisition was made. A dual headed gamma camera with low energy general purpose collimator (LEGP) was used.[16–18] The following measurements were recorded: preacquisition background (B), anterior abdomen (AP), posterior abdomen (PA) and post-acquisition background (B).

After, the percentage of abdomen retention (AR) was calculated at 4 and 7 days.

The formulas used are shown in the following:

$$Act_n = \frac{(AP-B)+(PA-B)}{2}\ Abd\,Ret4 : \frac{Act4}{Act0} \times 100\ Abd\,Ret7 : \frac{Act7}{Act0} \times 100$$

In normal subjects, the AR should be greater than 25% at the fourth day and than 10% on the seventh day.

The dosimeter received by the patient is of 0.3–5.7 mGy/MBq for the whole body and 3.2–11.3 mGy/MBq in the gall bladder.

Interpretation and follow-up

All the patients underwent a clinical follow-up at three and six months. All patients in whom the test was positive for BAM underwent treatment with resin cholestryamine and a new test was conducted at three months.

The patients who received treatment with resin cholestyramine were classified based on response as:

(a) Complete response: normalization of stool rhythm and consistency.
(b) Partial response: decrease of frequency and/or consistency.
(c) No response, without changes or increase in stool rhythm.

Results

Two groups were distinguished in relationship to the test outcome:

Group A: in which abdominal retention of ^{75}SeHCAT was normal in 21 patients (57%). Another diagnosis was confirmed in all of them: 8 patients with irritable bowel, 6 patients with colonic diverticulosis, 1 patient with post-gastroenteritis syndrome; 1 patient with celiac disease and 1 patient with stenosis of the cardia. Four patients currently continue in the study.

Group B: abdominal retention of ^{75}Se-SeHCAT was lower than normality in the remaining 16 patients (43%). All but 1 patient had a low retention index at 4 days and all of them had one at 7 days (Figs. 2 and 3).

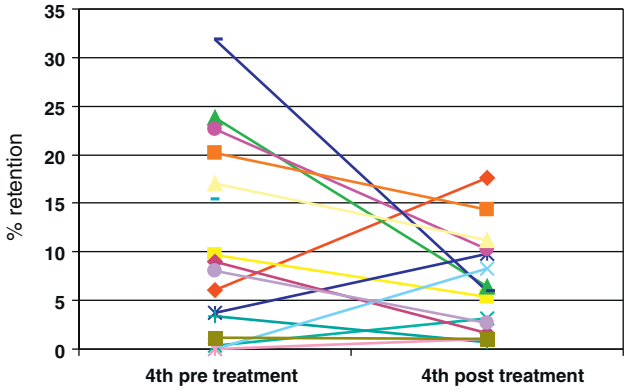

Fig. 2. Retention index on the 4th day pre- and post-treatment with resin cholestyramine.

All of the patients with a positive test began treatment with resin cholestyramine and a new test was conducted 3 months later.

Eight (50%) off the 17 patients who were administered treatment with resin cholestyramine had a total response and 8 (50%) a partial response. In the 3-month control, the retention index increased in 5 of those patients who had a complete response to the resin cholestyramine and decreased in 3. In those having a partial response, it increased in 5 and decreased in 3.

Discussion

Early pathophysiological diagnosis of chronic diarrhea is essential in order to perform adequate management of the disease and to avoid the consequences that it may have. Therefore, a rapid and noninvasive test, such as the study with ^{75}Se-SeHCAT, is necessary. This test has a recognized indication in the diagnostic schema of chronic diarrhea, it usually being found in the third diagnostic line.

The preliminary results of our experience show that 43.2% of the patients have BAM. This percentage agrees with that described in the literature[12] and shows the important utility of the examination in first-line diagnoses. More than 40% of the patients were diagnosed and treated in a much shorter time than if the examination had been performed as a third line test.

As can be observed in the diagnostic algorithm of chronic diarrhea, once the corresponding laboratory tests have been performed, if there is a suspected organic condition or if the laboratory tests are abnormal, a colonoscopy is recommended. Due to this, this technique is considered a first line diagnostic one prior to the ^{75}SeHCAT

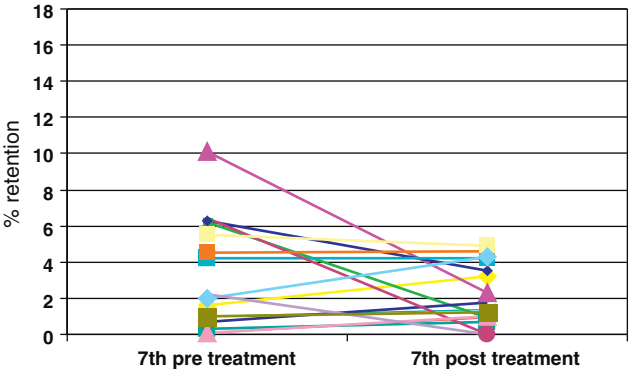

Fig. 3. Retention index on the 7th day pre- and post-treatment with resin cholestyramine.

test. It must be taken into account that the colonoscopy is invasive and requires sedation for the better comfort of the patient. Cardiac and respiratory (more frequent) complications may occur and vary between 2 and 5 per 1000 interventions. Of these, 10% may lead to death.[19] There may also be bleeding, perforation and complications related with the preparation of the colon. These complications occur in approximately 0.3%.[20] In comparison, the test with ^{75}Se-SeHCAT only requires 4 h of fasting and is administered with an oral capsule. It is an easy technique to perform and lacks the complications described. Therefore, in 43.2% of the patients studied, the performance of the colonoscopy as well as the risks entailed was avoided. The radiation dose received by the patient is almost negligible, which makes the risk of the examination even less.

In the baseline examination, 87.5% of the patients had a low AR on the 4th day and 100% on the seventh day. Two readings can be done: either performs the measurement on the fourth day and if it is low, it is not necessary for the patient to return on the seventh day. The second one could be that, given the greater sensitivity, perform the measurement directly on the seventh day. Since it is not an urgent examination, the final option seems more appropriate, and as such, it has been modified in our protocol.

In the examination at three months, the AR at 4 days was normalized in 3 of the 16 patients (18.7%), while at 7 days it was normalized in 9 of the 16 (56.2%). In addition, in those patients who had complete response to resin cholestyramine, the retention index at 7 days increased in 5 and decreased in 3. In those in whom the response was partial, it increased in 5 and decreased in 3. These results suggest that the control at three months is perhaps too early to observe the normalization of the bile acid absorption.

All the patients who received treatment with resin cholestyramine had a favorable response, but only 15% had total remission of the symptoms at three months. It should be considered that given the side effects of resin cholestyramine, especially constipation, many of the patients who, once they achieved a reduction in the number of stools, underwent irregular treatment, on demand, which could affect the results of the examination.

The decrease in the number of stools and consistency of it induced by the specific treatment with BAM improves the quality of life of the patients by reducing or avoiding anxiety, uncomfortableness and emergency accompanying chronic diarrhea.

Conclusion

Measurement of the absorption of ^{75}SeHCAT allows early pathophysiological diagnosis of bile acid malabsorption in 43% of the patients with chronic diarrhea syndrome. It is a relatively inexpensive test, non-invasive and easy to perform. The measurement of the retention index at 7 days seems to be more accurate than that at 4 days.

In this way, the early diagnosis of chronic diarrhea by BAM significantly improves quality of life of the patients and allows for its correct treatment.

Conflict of interest

The authors declare that they have no conflict of interest.

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