

Full Length Research Paper

Evaluation of Microscopic Colitis among Chronic Diarrhea Patients in Shariati Hospital in Isfahan

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Abstract

There are many possible causes of chronic diarrhea such as microscopic colitis (MC). This study evaluates of MC among patients presented with chronic watery diarrhea. It was done colonoscopy for patient with watery diarrhea without known cause. If colonoscopy was normal, multiple mucosal biopsies would be taken from right and left colon. Histological characteristics of lymphocytic colitis and collagenous colitis were assessed in all biopsy specimens. All other patients with normal or uncharacteristic histology were considered as the control group. Demographic characteristics, duration of symptoms and past history of drug intake were compared between the two groups. 33 (27%) had lymphocytic colitis and nobody had collagenous colitis. Mean (SD) duration of symptoms were 8.5 (3.4) and 10.1 (11.1) months in the patients with MC and the control group, respectively. No significant difference in the mean duration of symptoms between the two groups. No significant difference in drug intake between the two groups. The diagnostic lymphocytic colitis frequency was higher than expected. As regard to high rate of MC in patients with chronic watery diarrhea, it is suggest that to be carry out colonic mucosal biopsy for these patients with normal colonoscopy in order to timely diagnosis of MC and its appropriately treatment.

Keywords: Chronic watery diarrhea, Gastrointestinal disease, Microscopic colitis, Lymphocytic colitis, Colonoscopy.

INTRODUCTION

Diarrhea or diarrhoea is the condition of having three or more loose or liquid bowel movements per day (Datta et al., 2009). One of the pathologies presented by chronic non-bloody watery diarrhea in the fifth or sixth decades of life is microscopic colitis (MC) (Tysk et al., 2008). MC, comprising lymphocytic and collagenous colitis, is a syndrome with chronic diarrhea, normal-looking colonic mucosa at endoscopy and specific histological findings (Lazenby, 2005).

Clinically active lymphocytic colitis (LC) and collagenous colitis (CC) were defined as ≥ 3 loose or watery stools/day and/or abdominal pain. The diagnostic

criteria for LC were histological findings of increased numbers of intraepithelial lymphocytes ($\geq 20/100$ surface epithelial cells) in conjunction with surface epithelial cell damage and infiltration of lymphocytes in the lamina propria, but a normal collagen layer (Lazenby, 2005). In CC, in addition to lymphocytic infiltration in the lamina propria and the epithelium, deposition of a subepithelial collagen layer of $\geq 10 \mu\text{m}$ is seen (Lazenby, 2005).

The pathogenesis of microscopic colitis is poorly understood and is thought to be related to a poorly regulated epithelial immune response to luminal or epithelial antigens including bile acids, toxins, or infectious agents (Schiller, 2004).

It is characterized by normal colonoscopy and increased intraepithelial lymphocytes or thickening of subepithelial collagen layer. The former is called lymphocytic colitis whereas the latter is recognized as

collagenous colitis. Medications such as lansaprazole or non-steroidal anti-inflammatory drugs (NSAIDs), thyroid disease or type I diabetes are encountered as suspected etiologies (Abdo and Beck, 2003; Harewood et al., 2005; Trolli, 1999). The diagnosis of MC depends on clinical symptom, endoscopy and histology of multiple colorectal biopsies (Sellin, 2007).

The rate of MC is different in various geographical areas. For example, in North America, it is more common than in Europe (Juckett and Trivedi, 2011; Pardi, 2004; Tangri and Chande, 2009). Very few studies have been implemented to determine its rate in the Middle East. This study was carried out to evaluate of MC among patients presented with chronic diarrhea in Shariati teaching hospital of Isfahan.

METHODS

This cross-sectional study was carried out in Shariati hospital (Isfahan, Iran) from June 2010 to June 2011. It included patients >12 year-old presented with >3 times/day non-bloody watery diarrhea for at least 4 weeks (Yen and Pardi, 2011; Limsui et al., 2009). Patients with 12 year-old presented with >3 times/day non-bloody watery diarrhea for at least 4 weeks were enrolled in this research. Patients diagnosed with underlying gastrointestinal disease such as Celiac disease, bacterial and viral infections, parasites, intestinal diseases, food intolerances and sensitivities, functional bowel and endocrine disorders, reaction to medicines and irritable bowel syndrome were excluded from the study. After taking a detailed history, physical examination and laboratory evaluation were completed. Drug history of patients was proton pump inhibitors, non-steroid inflammatory drugs (NSAIDs) and aspirin.

Patients were enrolled in the study after obtaining written informed consent. Colonoscopy was done and if the result was not normal, the patient would be excluded from the study. Finally 123 patients with chronic watery diarrhea (without known cause) were recruited in this study.

For patients with normal colonoscopy, multiple mucosal biopsies were taken from right and left colon.

Patients underwent colonoscopy by a gastroenterologist using a standard video colonoscope (Fujinon, Japan). The biopsies were fixed in 10% (v/v) neutral buffered formalin and embedded in paraplast. Histopathological examination was performed thereafter; thin sections were prepared, which were routinely stained, using hematoxylin and eosin and Masson's trichrome staining. All histopathological examinations were carried out by one pathologist.

If mononuclear infiltration of mucosal lamina propria, increased intraepithelial lymphocytes >20 in 100 epithelial cells and epithelial damages were observed, the patient would be categorized in lymphocytic colitis group. If the subepithelial collagen layer was thickened

>10 μ m, the epithelial layer was flattened and detached, and the inflammation in lamina propria was mild, the patient would be considered in collagenous colitis group (Garg et al., 1996; Misra et al., 2010; Mohamed et al., 2011). All other patients with normal or uncharacteristic histology were considered as the control group.

This research was approved by the Ethical Committee of the Islamic Azad University Najafabad branch.

Fisher-Exact test and t-test were applied to compare the data between the patients with MC and the control group. SPSS software, version 12 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. P values less than 0.05 were considered significant.

RESULTS

Out of 123 patients with chronic watery diarrhea enrolled in the study, 33 (27%) showed MC on biopsies. Interestingly, nobody had collagenous colitis; all 33 patients had lymphocytic colitis. Male/female ratio was 1/1.36 in patients with MC and 1/1.14 in the control group. The youngest patient was 14 year-old in both groups whereas the oldest ones were 71 and 74 year-old in patients with MC and in the control group, respectively. Independent t-test demonstrated no significant difference in the mean age of patients between the two groups (Table 1).

Minimum and maximum durations of symptoms in patients with microscopic colitis were 2 and 18 months, respectively, whereas in control the group, they were, 1 and 60 months, respectively. Independent t-test revealed no significant difference in the mean duration of symptoms between the two groups (Table 2).

Drug history of patients including proton pump inhibitors, NSAIDs and aspirin was taken. One (2%) and 2 (4%) patients had history of aspirin and NSAIDs, respectively. Fisher-Exact test revealed no significant difference in drug intake between the two groups (Table 3).

DISCUSSION

This is the first study in our country that tried to find the frequency and the type of MC in patients referred to a large teaching hospital. Surprisingly, all 33/123 patients diagnosed with MC had lymphocytic colitis. Given the little inter- and intra-observer variability in histopathological diagnosis (Gonzalez et al., 2010), there are little doubts on validity and reliability of diagnoses. Similarly, in another study in India, all the patients diagnosed with MC showed lymphocytic colitis in biopsies and nobody had collagenous colitis (Cimmino et al., 2010). But, the diagnostic frequency in our study was about four times more than that in India. Single center and multi-center studies demonstrated different

Table 1. Mean age and frequency distribution of age groups microscopic colitis and control groups.

Chronic Watery Diarrhea	Age Groups			Mean (SD)
	< 20 Years	20-50 Years	>50 Years	
Microscopic Colitis	1 (3%)	26 (78.8%)	6 (18.2%)	39.5 (11.5)
Control Group	2 (2.2%)	61 (67.8%)	27 (30%)	40.7 (14.7)
<i>P</i> -value	0.4			

Table 2. Mean age and frequency distribution of durations of symptoms microscopic colitis and control groups.

Chronic Watery Diarrhea	Duration of Symptoms			Mean (SD)
	< 6 Months	6-12 Months	>12 Months	
Microscopic Colitis	11 (33.3%)	20 (60.6%)	2 (6.1%)	8.5 (3.4)
Control Group	42 (46.7%)	33 (36.7%)	15 (16.7%)	10.1 (11.1)
<i>P</i> value	0.086			

Table 3. Comparison of past history of taking medications between microscopic colitis and control groups.

Chronic Watery Diarrhea	Past History of Taking Drugs	
	Yes	No
Microscopic Colitis	3 (6%)	30 (94%)
Control Group	11 (13.3%)	79 (86.7%)
<i>P</i> value	0.3	

diagnostic frequencies in various countries. It was 3.7% in India (Gu et al., 2012), 8.3% in South Africa (Park et al., 2011), 9% in Uruguay (Pironti et al., 2010), 14% in Argentina (Essid et al., 2005), 14.2% in China (Valle Mansilla et al., 2002), 22% in Korea (Gado et al., 2004), 28% in Italy (Fernandez-Banares et al., 1999), 29.3% in Tunisia (Chande et al., 2005), 40% in Peru (Miquel et al., 2001), and 50% in Egypt (Velasco et al., 1992). Lower prevalence of MC in some studies could be attributed to rigid pathological criteria used for diagnosis. The diagnostic frequency of lymphocytic colitis in our center was more than that in Western countries.

The mean age of patients in most Western studies was from 51 to 64 years (Abdo and Beck, 2003; Juckett and Trivedi, 2011; Carmona-Sanchez et al., 2007; Madisch et al. 2005; Limsui et al., 2007). It was 40 in Saudi Arabia (Velasco et al., 1992), 43 in Uruguay (Pironti et al., 2010), 47.5 in Korea (Gado et al., 2004), and 52 in Chile and Mexico (Fernandez-Banares et al., 2011; Chang et al., 2005). The mean age of diagnosis in our study was more than 20 years younger than that in Western countries. This could be due to either earlier exposure to unrecognized risk factors or previous misdiagnoses. The latter is explainable by symptomatic overlap of diarrhea predominant irritable bowel syndrome and MC (Fine et al., 2000). This justifies the necessity of routine biopsy in normal colonoscopies in

patients with IBS (da Silva et al., 2006). The increasing awareness of diagnostic characteristics of MC and development of less rigid criteria has been probably the reasons of its constant increasing rate of incidence since 1980 (Abdo and Beck, 2003; Juckett and Trivedi, 2011; Gebbers and Laissue, 1994).

Some authors have described three more subtypes of MC as follows: minimal change colitis, MC with giant cells and MC not otherwise specified (Chang et al., 2005; Fine et al., 2000; da Silva et al., 2006). Their diagnostic criteria have been illustrated elsewhere. They were not considered in the current study because they may develop later into inflammatory bowel disease (Gebbers and Laissue, 1994; Pokorny et al., 2001). All 33 patients diagnosed with MC will be also monitored to see whether they develop IBD or some other complications.

Further studies are necessary to find out detailed epidemiological features of MC in our geographical area.

CONCLUSIONS

The diagnostic LC frequency was higher than expected. As regard to high rate of MC in patients with chronic watery diarrhea, it is suggest that to be carry out colonic mucosal biopsy for these patients with normal

colonoscopy in order to timely diagnosis of MC and its appropriately treatment.

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