



Correlation between serum serotonin and endoscopy inflammation scores in patients with ileal pouches[☆]

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KEYWORDS

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Abstract

Background: Inflammatory and functional complications are common in patients with inflammatory bowel disease (IBD) after restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA). The pathogenesis of these complications remains poorly understood, and there is discrepancy between the clinical symptoms and objective endoscopic inflammation scores in these patients. While serum serotonin level has been reported to be associated with symptoms of irritable bowel syndrome, its association with ileal pouch disorders has not been studied.

Aim: To investigate the association between serum serotonin level and symptoms and endoscopic inflammation in patients with IPAA.

Methods: A total of 185 consecutive eligible IPAA patients who presented to a specialized Pouchitis Clinic from Jan 2009 to May 2009 were prospectively recruited. Patients were divided into 4 groups: normal pouch, irritable pouch syndrome (IPS), inflammatory pouch disorders (Crohn's disease, acute and chronic pouchitis, and cuffitis), and surgical complications. Serum serotonin level was measured and analyzed for correlation with clinical and endoscopic inflammation scores.

Results: Demographic and clinical variables were evaluated, including age, gender, smoking history, duration of UC, duration of the pouch, and disease category of the pouch. The median fasting serum serotonin level was comparable among the 4 groups: 94.0 ng/ml (interquartile

Abbreviations: CD, Crohn's disease; EC, enterochromaffin; GI, gastrointestinal; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IPAA, ileal pouch-anal anastomosis; IPS, irritable pouch syndrome; NSAID, non-steroidal anti-inflammatory drugs; PDAI, the Pouchitis Disease Activity Index; PSC, primary sclerosing cholangitis; 5-HT, 5-hydroxytryptamine; SERT, serotonin reuptake transporters; UC, ulcerative colitis.

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range [IQR], 70.0, 128.1), 89.2 ng/ml (IQR 54.2, 155.9), 90.3 ng/ml (IQR 49.7, 164.1), 77.9 ng/ml (IQR 54.7, 129.0), for normal pouch, irritable pouch, inflammatory pouch disorders, and surgical complication groups, respectively ($p=0.91$). A significant association between serum serotonin level and the Pouchitis Disease Activity Index (PDAI) endoscopy subscore of the pouch (odds ratio [OR]=1.9, 95% confidence interval [CI]: 1.2, 2.9, $p<0.05$) and total PDAI endoscopy score (OR=1.8; 95% CI: 1.2, 2.8, $p<0.05$) in the inflammatory complication group were noted.

Conclusions: Serum serotonin level appears to correlate with the PDAI endoscopy subscores and total PDAI score in patients with inflammatory complications suggesting that the hormone may be involved in mechanisms of mucosal inflammation. These findings may promote future treatment strategies for patients with pouch inflammation.

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1. Introduction

5-hydroxytryptamine (5-HT) is released through complicated signaling processes which include mechanical, chemical, neural factors, infection, and inflammation in the gastrointestinal (GI) tract. While 5-HT biosynthesis can be altered in disease settings, its availability is also regulated by the degradation process which involves serotonin reuptake transporters (SERT) located at nerve terminals, enterocytes and vascular endothelial cells.¹ 5-HT plays an important role in the pathophysiology of irritable bowel syndrome (IBS). Activation of the mucosal immune system with morphologic changes involving lymphocytes, mast cells, enterochromaffin (EC) cells and enteric nerves by quantitative histologic and ultra-structural analyses is believed to contribute to the pathophysiology of IBS.^{2,3} EC cell hyperplasia has been reported in rectal biopsies in patients with post infectious-IBS.⁴ Blood and tissue 5-HT levels have also been evaluated in IBS patients, and a high blood 5-HT level demonstrated in diarrhea-predominant IBS patients.⁵⁻⁸

There are scant published data on the role of 5-HT in inflammatory bowel disease (IBD), although IBS-like conditions often coexist with IBD.^{8,9} Animal studies have suggested EC cell hyperplasia and increased 5-HT content in the inflamed colon.^{10,11} An increased level of 5-HT in the colon tissue specimens of patients with Crohn's disease (CD) has also been reported.⁸ However, serum 5-HT has not been evaluated in patients with IBD.

Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) has become the surgical treatment of choice for ulcerative colitis (UC) patients who require colectomy. Inflammatory (e.g. pouchitis) and functional (e.g. irritable pouch syndrome [IPS]) complications are common after IPAA surgery. The pathogenesis of these inflammatory and functional pouch disorders is largely unknown. We have previously demonstrated a poor correlation between subjective symptoms and objective endoscopic inflammation scores in patients with pouchitis.¹² One potential explanation for such discrepancy is that some of these patients may have concurrent IPS.¹³ Subsequently, we have demonstrated evidence of visceral hypersensitivity¹⁴ and EC cell hyperplasia¹⁵ in IPS patients. The clinical and pathogenetic role of serum 5-HT in patients with IPAA has not been evaluated. We hypothesized that an alteration in serum 5-HT may contribute to symptoms related to the pouch and mucosal inflammation in patients with IPAA. The aims of this study were to compare serum 5-HT level among patients

with healthy and diseased ileoanal pouch and to assess the correlation between serum 5-HT, clinical symptoms and endoscopic inflammation.

2. Patients and methods

2.1. Patients

This is a prospective study of patients who were seen in our subspecialty Pouchitis Clinic between 2008 and 2010. Demographic, clinical, and endoscopic data were collated in a prospectively maintained, Institutional Review Board (IRB)-approved Pouchitis Database. A total of 185 patients were recruited, and divided into 4 groups: 1) normal pouch; 2) IPS; 3) inflammatory pouch, consisting of CD of pouch, pouchitis, and cuffitis; and 4) surgical complications. The senior investigator B.S. performed all clinical interviews, physical examinations, and pouch endoscopies and biopsies. The protocol was approved by our IRB.

2.2. Inclusion and exclusion criteria

The inclusion criteria included patients who underwent IPAA for underlying IBD, were older than 18 and hence able to give consent, and undergoing diagnostic or surveillance pouchoscopy. Exclusion criteria were patients 1) with IPAA for familial adenomatous polyposis; 2) extraintestinal infection, such as pneumonia, upper respiratory infection, urinary tract infection; 3) systemic disorders, such as chronic renal insufficiency, poorly controlled diabetes, and malignancy; 4) overt gastrointestinal bleeding or extra-intestinal blood loss (e.g. meno- or metrorrhagia).

2.3. Demographic and clinical variables

Demographic and clinical variables were evaluated, including age, gender, smoking history, duration of UC, family history of IBD, extent of colitis, indication for proctocolectomy, extraintestinal manifestations, duration of the pouch, disease category of the pouch, and selective serotonin re-uptake inhibitor (SSR) use as previously described.¹⁵ The 12-point modified Pouchitis Disease Activity Index (mPDAI) consisting of symptoms (range of 0-6 points), and endoscopy (range of 0-6 points) was used to quantify symptoms and pouch inflammation.¹⁶ The mPDAI scoring system is listed in

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