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Association between a Serotonin Re-Uptake Transporter Gene Polymorphism and Mucosal Serotonin Level in Women Patients with Irritable Bowel Syndrome and Healthy Control: A Pilot Study from Northern India

Authors : Sunil Kumar, Uday C. Ghoshal

Abstract : Background and aims: Serotonin (5-hydroxtryptamine, 5-HT) is an important factor in gut function, playing key roles in intestinal peristalsis and secretion, and in sensory signaling in the brain-gut axis. Removal from its sites of action is mediated by a specific protein called the serotonin reuptake transporter (SERT). Polymorphisms in the promoter region of the SERT gene have effects on transcriptional activity, resulting in altered 5-HT reuptake efficiency. Functional polymorphisms may underlie disturbance in gut function in individuals suffering with disorders such as irritable bowel syndrome (IBS). The aim of this study was to assess the potential association between SERT polymorphisms and the diarrhea predominant IBS (D-IBS) phenotype Subjects: A total of 36 northern Indian female patients and 55 female northern Indian healthy controls (HC) were subjected to genotyping. Methods: Leucocyte DNA of all subjects was analyzed by polymerase chain reaction based technologies for SERT polymorphisms, specifically the insertion/deletion polymorphism in the promoter (SERT-P). Statistical analysis was performed to assess association of SERT polymorphism allele with the D-IBS phenotype. Results: The frequency of distribution of SERT-P gene was comparable between female patients with IBS and HC (p = 0.086). However, frequency of SERT-P deletion/deletion genotype was significantly higher in female patients with D-IBS compared to C-IBS and A-IBS [17/19 (89.5%) vs. 4/12 (33.3%) vs. 1/5 (20%), p=0.001, respectively]. The mucosal level of serotonin was higher in D-IBS compared to C-IBS and A-IBS [Median, range (159.26, 98.78–212.1) vs. 110.4, 67.87–143.53 vs. 92.34, 78.8–166.3 pmol/mL, p=0.001, respectively]. The mucosal level of serotonin was higher in female patients with IBS with SERT-P deletion/deletion genotype compared deletion/insertion and insertion/insertion [157.65, 67.87–212.1 vs. 110.4, 78.1–143.32 vs. 100.5, 69.1–132.03 pmol/mL, p=0.001, respectively]. Patients with D-IBS with deletion/deletion genotype more often reported symptoms of abdominal pain, discomfort (p=0.025) and bloating (p=0.039). Symptoms development following lactose ingestion was strongly associated with D-IBS and SERT-P deletion/deletion genotype (p=0.004). Conclusions: Significant association was observed between D-IBS and the SERT-P deletion/deletion genotype, suggesting that the serotonin transporter is a potential candidate gene for D-IBS in women.

Keywords : serotonin, SERT, inflammatory bowel disease, genetic polymorphism
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