Reviewer's report

**Title:** Increased proton pump inhibitor and NSAID exposure in irritable bowel syndrome: results from a case-control study

**Version:** 2  **Date:** 25 June 2012

**Reviewer:** saurabh mukewar

**Reviewer's report:**

The authors have conducted an interesting study to compare use of NSAIDs, PPIs, SSRIs between IBS patients and controls. The authors have concluded that given nature of the study a causal relationship between exposure of these medication and development of IBS cannot be established. However, there was a significant difference between IBS and controls with regards to exposure of these medications.

I have one major concern regarding criteria used for exposure of medications:

All patients having had at least one prescription for a period of four weeks for a PPI/NSAID in the 180 days prior to the time of the index visit were considered exposed – Were the patients included had exposure to PPIs/NSAIDs 6 months before onset of symptoms or 6 months before the time of visit ? Since diagnosis of IBS requires, history of 6 months of symptoms and as mentioned by the authors many patients who were seen were referred to gastroenterologist. These patients may have been exposed to PPIs/NSAIDs after onset of symptoms.

Authors need to clarify this and clearly state that patients with exposure of these medications prior to onset of symptoms were included and not prior to their first visit. Being a tertiary center many patients may have had symptoms for many months prior to being seen in the clinic.

If patients with use of PPIs/NSAIDs after onset of symptoms were included than this study merely shows association between IBS, dyspepsia, chronic pain conditions and medications used for treatment of the same. Based on effects of NSAIDs and PPIs on gastrointestinal permeability and microflora: a better to study would be to compare severity of IBS symptoms between IBS patients taking PPIs/NSAIDs and IBS patients not taking PPIs/NSAIDs.

**Other comments:**

**ABSTRACT**

Results: Should add a statement that PPI use was not significantly correlated after controlling for dyspepsia.

**METHODS**

“In other cases, diagnosis according to Rome III criteria (symptoms for at
least 6 months) was confirmed using questionnaires sent to patients to assess symptom duration following initial symptom onset.” – Unclear what this means. Were these cases with <6 month history of IBS symptoms.

“The control group consisted of 408 individuals randomly selected from the general population in Maastricht, the Netherlands” – Were there 287 controls or 408 controls?

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.