A comparative study on Baclofen and Omeprazole in patients with GERD

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Abstract:
Aim: To compare baclofen and omeprazole in patients with GERD. Materials and Methods: This is an open label prospective study. This study was done in our department from May 2012 to June 2012. We included patients with symptoms of GERD. Total number of patients - 30. Baseline symptoms score was obtained patients were randomized. Baclofen 10mg bd was given for one group and omeprazole 20mg was given for another group. Patients were reassessed after 2 wks. Results: Total number of patients in baclofen group was 15 and in omeprazole group was 14. Heartburn, regurgitation, epigastric pain and belching were graded according to the severity before and after treatment using standard GERD questionnaire. In baclofen group, 66 percent patients had severe belching, moderate heartburn (60 percent), moderate regurgitation (50 percent), whereas in omeprazole group, 57 percent had severe heartburn, severe belching (59 percent), moderate regurgitation (42 percent) and moderate epigastric pain (71 percent). After treatment 93 percent patients in baclofen group had relief from belching compared to 43 percent in omeprazole group and regurgitation decreased in 80 percent with baclofen compared to 55 percent, whereas only 53 percent had relief from heartburn in baclofen group compared to 85 percent in omeprazole group and 71 percent of patients had relief from epigastric pain in omeprazole group (vs 46 percent). One patient had mild drowsiness which didn't need stoppage of baclofen. Conclusion: This study shows that baclofen decreases belching and regurgitation compared to omeprazole whereas as omeprazole is better in controlling heartburn. Drowsiness doesn't limit baclofen use. Hence, Baclofen may be more useful in GERD with predominant belching.

Keyword: Baclofen, GERD, Omeprazole, Belching

INTRODUCTION
Gastroesophageal reflux disease (GERD) is a consequence of the failure of the normal antireflux barrier to protect against frequent and abnormal amounts of gastroesophageal reflux. GERD is a spectrum of disease usually producing symptoms of heartburn and acid regurgitation.
Most patients have no visible mucosal damage at the time of endoscopy (nonerosive GERD), whereas others have esophagitis, peptic strictures, or Barrett's esophagus. GERD is a multifactorial process and one of the most common diseases of mankind. The prevalence of GERD is relatively low among residents of Africa and Asia (1). The prevalence of GERD has been increasing in Western countries over the past 30 years. An explanation for an increased prevalence of GERD in Western populations is the epidemic increase in obesity. Acid suppression has been the mainstay of therapy for GERD over time, with proton pump inhibitors being the treatment of choice. However, despite potent antacid therapies, symptoms can persist in up to 30% of GERD patients. Mechanisms of GERD include incompetence of the lower oesophageal sphincter (LES), decreased oesophageal clearance, impaired resistance of the oesophageal mucosa, and increased transient lower oesophageal sphincter relaxations (TLESRs). Of these, TLESRs have been shown to be a major cause of reflux in healthy patients and in those with GERD(2-3). In this light, GABA B agonists have emerged as an alternative agent for GERD treatment in those patients who have failed antacid therapy. The GABA B receptors are expressed in neurons of the motor nucleus of the vagal nerve and nucleus tract solitarius, and play a central role in TLESRs, while peripheral activation of GABA B receptor inhibit distension related TLESRs (4). Baclofen (4-amino-2 (p-chlorophenyl)-butanoic acid), a selective GABA B receptor agonist, has not only been used traditionally as a muscle relaxant for many years, but has also been shown to reduce TLESRs in both animals and in humans (5&6). Clinical studies of its short term or single dose use have demonstrated its effectiveness in reducing the number of TLESRs, and likewise reducing the number of reflux events.

Data are limited regarding long-term use of baclofen, however, with one study showing an improvement of GERD symptoms over 1 month. Given the paucity of alternative treatment options to antacids for GERD, this study was done to further evaluate the clinical effectiveness of baclofen on GERD and GERD related symptoms as well as to assess its tolerability in light of previously reported side effects.

AIM: To compare baclofen and omeprazole in patients with gastro-oesophageal reflux disease over a 2 week period.

METHODS: Eligible patients seen in the Department of digestive health and diseases, GPH, Anannagar, Chennai were offered enrolment in the study. All patients underwent screening endoscopy. Patients with erosive esophagitis were excluded from the study. All the enrolled patients had normal endoscopy which was suggestive of non erosive reflux disease. This study was done with patients on an outpatient basis. Routine renal function tests were not done because none of them had symptoms of cardiac or renal dysfunction or any other comorbid illness. To be eligible, patients had to meet the following inclusion criteria: 18 years of age or older, symptoms consistent with GERD. Exclusion criteria included prior gastric or oesophageal surgery for the treatment of GERD, severe co-morbid illnesses, history of allergy to baclofen and pregnancy, endoscopic findings of erosive esophagitis. This is an open label prospective study. This study was done in our department from May 2012 to June 2012. We included patients with symptoms of Gerd. Total number of patients - 30.
Baseline symptoms score was obtained using standard GERD questionnaire. Randomisation was done. Baclofen 10mg bd was given for one group and omeprazole 20mg was given for another group. One patient lost follow up. Patients were reassessed after 2wks. Statistical analysis was done using chi-square test.

RESULTS:
Total number of 30 patients were enrolled in this study. Mean age, gender and race distribution were similar between groups. 29 patients completed the study. 1 patient in the omeprazole group was lost on follow up. Total number of patients in baclofen group was 15 and in omeprazole group was 14. Heartburn, regurgitation, epigastric pain and belching were graded according to the severity before and after treatment using standard gerd questionnaire. In baclofen group, 66% patients had severe belching, 60% had moderate heartburn, 50% had moderate regurgitation, and 55% had moderate epigastric pain whereas in omeprazole group, 57% had severe heartburn, 59% had severe belching, 42% had moderate regurgitation and 71% had severe epigastric pain. Statistical analysis was done using chi-square test. After treatment 93% patients in baclofen group had relief from belching compared to 43% in omeprazole group (p<.05) and 53% (p<.05) and 71% of patients had relief from epigastric pain in omeprazole group vs 46% (p>.05). One patient had mild drowsiness in baclofen group which didn’t require stoppage of drug.

BASELINE CHARACTERISTICS:

PERCENTAGE OF IMPROVEMENT AFTER TREATMENT
Discussion: The purpose of this study was to evaluate the role of baclofen in the treatment of patients with typical GERD symptoms over a 2-week period and its tolerability. Baclofen was ingested 30–60 min prior to the meal so that its major effect would occur during the postprandial period, when the frequency of TLESRs is highest. Pharmacologically, oral baclofen results in peak plasma concentrations 2 h following ingestion, with a half life of 6 h(7). Baclofen was administered 30–60 min prior to meals with the thought that it could be taken concurrently with PPIs. Baclofen potentially may have been even more effective if ingested 1–2 h prior to meals. This study clearly shows that baclofen is useful than ppi in patients with predominant belching due to GERD. Interestingly, although belching, regurgitation significantly improved with baclofen, no significant improvement was noted in heartburn.
On the other hand, omeprazole treated patients showed a significant improvement in heartburn. Statistical significance between the two treatment arms in our study may not have been appreciated given our small sample size. Additional studies need to be performed utilising pH/impedance monitoring to fully evaluate the effects of baclofen on both acid and non-acid reflux. Baclofen has several significant side effects including drowsiness and dizziness. Interestingly, our data show that drowsiness was not a significant side effect of baclofen, and this is supported by the fact that there were no dropouts in the baclofen group due to drowsiness. Studies including longer term baclofen use should be performed to determine tolerability of baclofen over time.

This is the first study comparing baclofen and omeprazole in GERD. Cossotino et al (8) randomised 43 patients with GERD to either baclofen 20mg or placebo. This study showed superior efficacy of baclofen over placebo in controlling symptoms of GERD. However in our study the dosage of baclofen is lower than that study. This shows lower dosage of baclofen is adequate in controlling symptoms of GERD. Ciccaglione et al randomised 18 GERD patients to either baclofen 10 mg by mouth four times daily (n = 12) or placebo (n = 6) for 4 weeks and noted a 76% reduction in reflux episodes and a 53% reduction in percent time pH <4 (9). This suggests it may be possible to treat with lower doses of baclofen. Koek et al studied the effect of baclofen in patients who continued to have symptoms in spite of PPI therapy and normal intraoesophageal pH.25 However, all patients in Koek’s study had abnormal duodenogastric reflux as measured by Bilitec probe. Treatment with baclofen 20 mg orally three times daily significantly decreased the total time of bile reflux and overall symptom scores. Several studies that have measured the effect of a single baclofen dose on postprandial reflux parameters also consistently show that baclofen significantly decreases postprandial reflux events and acid exposure time. Although the use of PPIs is sufficient for GERD symptoms in most patients, there is a subgroup of patients who do not have complete symptom relief on PPIs alone. Causes of PPI non-response are varied and include severe reflux due to incompetent LES, oesophageal hypersensitivity and persistent non-acid reflux. Our study did not focus on PPI nonresponders, but these patients may benefit from the addition of baclofen. Combination therapy of baclofen and PPIs has been found to be effective in GERD patients with hiatal hernias.29 Perhaps baclofen should be tested in patients with persistent symptomatic non-acid reflux despite therapy with PPIs. It is possible that the development and FDA approval of new GABAB agonists with fewer side effects will result in a more potent inhibitor of TLESRs with wider acceptance of this form of therapy. A recent phase II study evaluating the use of arbaclofen over a 4-week time frame showed that although it was well tolerated, no significant benefit was seen in GERD symptoms compared to placebo. However, an exploratory subgroup analysis suggested that GERD patients who had previously responded to PPIs had a reduction in weekly heartburn events(10). Other baclofen analogues, lesogaberan (AZD3355) and AZD9343, have been developed as GABAB agonists to likewise decrease TLESRs without the attendant centrally acting side effects (11). In all, while these alternative GABAB agonists have been shown to improve objective reflux parameters, the clinical symptomatic benefit appears to be minimal, if beneficial at all, based on studies to date, and their
use remains limited in the research setting as none are yet FDA approved.

**Conclusion:**
This study shows that **baclofen decreases belching and regurgitation whereas omeprazole is better in controlling heart burn. Drowsiness doesn’t limit baclofen use. Hence, Baclofen may be more useful in GERD patients with predominant belching.**

**REFERENCES:**
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