Role of H₁ and H₂ Blocker in Eradication of Gastrointestinal Malfunctioing

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ABSTRACT

Proton pumps release acids in GIT which result in increased level of alkaline phosphates. The liver irritation by increased alkaline phosphates results in histamine disbalance. H₁ and H₂ blockers act as histamine controlling agents. The bacteria use their flagella to stick in stomach mucosal layer. For bacterial growth optimal conditions include oxygen level b/w 5-15%, approx. CO₂ 5%, availability of some special amino acids, and 30-37°C temperature. Gastro intestinal infections involve a spiral-shaped, gram-negative micro bacterium. It was assumed that earlier no germ might survive in gastric acidic layer, therefore the possibility of microbial colonization of stomach actually was not considered. Thus, the bacterial microenvironment directly surrounds and neutralize the effects of gastric secretions which are corrosive to them and the pathogen escapes. Aim of the present study was to analyze different drugs efficacy which act on certain soft tissue infections specially gastrointestinal tract infections. Non significant results were observed with both qualitative and quantitative measurements of the H₁ and H₂ blockers.

Keywords: H₁ and H₂ Blockers, H. Pylori, Histamine

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INTRODUCTION

Digestive fluids infested with systemic invulnerable and *H. pylori* responded to gastrointestinal infection of *H. pylori* may play a contributory character in upper respiratory tract (URT) (1). Many studies are present on the *H. pylori* which related to upper respiratory tract, but results are variable in different aspects. So the further studies are required because association between *H. pylori* & URT diseases not confirmed. Gastro intestinal infections involve a spiral-shaped, gram-negative micro bacterium. It was assumed that earlier no organism might survive in gastric acidic bilayer of pyloric region due to the high pH, therefore, gastric microbial colonization was not actually considered as possibility of acid suppression. The outcomes of latest studies tell about the risk of early onset allergic disorder and dermatological infection reduced in carriers of *H. pylori* associated with that not infected entities (2) indicating that soft tissue infections can have detrimental and useful properties both in patients suffering from diseases of upper respiratory tract and renal sinuses. A role of antibiotics can bear the resistance of esophageal gastric juice for certain period (3).

Thus microenvironment directly surrounding the bacterium is neutralized and the pathogen escapes the corrosive effects of the gastric secretions. The zoonotic pathogen has no indication of supporting this belief, because animal or environmental reservoirs protect strains that infect humans, despite the separation of *H. pylori* from other animals such as the cat. At this time, it appears that only the

gastric conditions are optimal for growth and capability of the pathogen. Research is being conducted to explain the ways of transmission.

Methodology of the Study

Samples were collected from patients that were observed in Sandman Provincial Hospital, Bolan Medical Complex Hospital and some private hospitals in Quetta, visited for GIT problems. Senior gastroenterologists and private clinics were visited for collection of 140 patients for 12 different diseases (Diarrhea, Dysentery, Entamoeboid infections, Ulcerative enteritis, *Helicobacter pylori*, Irritable bowel syndrome, Gastritis, Heartburn, Gastroesophageal reflux disease, Dyspepsia/Indigestion, Nausea and Vomiting, Peptic ulcer disease, Abdominal pain syndrome and Belching, Bloating, Flatulence) under treatment. Regarding therapeutic treatment of gastrointestinal patients treated and standard mechanism was adopted to ensure eradication of GIT.

Data Collection

Patients from 20 to 50 years of age with both sexes (non-pregnant females) were enrolled in the study. Past history regarding weight loss, fatigue, weakness, anxiety, depression etc was noted by filling a specially designed questioner, written consent from each patient was also obtained with his signature on the same questioner. Patients showing sign or history of clinically important pathological disorders other than GIT were excluded from the study.

Laboratory Work

Drug samples of different H₁ and H₂ blockers were collected and analyzed in provincial drug testing laboratory. Different antibiotics, with another drug that decreases gastric acid and helps the antibiotics to work more efficiently in soft tissues specially in GIT infection, were used. The drugs (PPIs); Ciprofloxacin (dose ranging from 250-500 mg/day), Levofloxacin (dose ranging from 250-500 mg/day), Chlorpheniramine (dose ranging from 250-50 mg/day), Famotidine (dose ranging from 20-40 mg/day), Ranitidine (dose ranging from 150-300 mg/day) and Metronidazole (dose ranging from 200-400 mg/day) were examined in the study.

Comparative Efficacy

Bacteriological efficacy was also observed with eradication of the pathogen in respective drug response, in clarithromycin and azithromycin groups.

RESULTS AND DISCUSSION

Absorption, rate, and excretion H¹ antihistamines were well absorbed after either oral or parenteral administration. The onset of action occurred 15 to 60 minutes after an oral dose. Effects were typically maximal in 1 to 2 hours, with a duration of 4 to 6 hours, although the duration was longer for some agents (Table I). In contrast, most second-generation H¹ antihistamines had a considerably longer duration of action. Loratadine was transformed to an active metabolite with an average elimination half-time of greater than 24 hours, which allows once-daily dosing.

Table I. Classification of H₁ Receptor Blockers

H ¹ Receptor Class	X Substitution on Antihistamine Molecule
Alkylamines	Carbon
Ethanolamines	Oxygen
Ethylenediamines	Nitrogen
Piperazines	Piperazine ring
Phenothiazines	Phenothiazine nucleus
Piperidines	Piperidine ring

Biotransformation of first-generation H¹ antihistamines was terminated by conversion to inactive metabolites through hydroxylation in the liver. Second-generation antihistamines are extensively metabolized in the liver by the CYP^{3A4} microsomal enzyme. In some cases, such as with loratadine, these result in active metabolites. Concurrent administration of other agents metabolized by this same enzyme can reduce the bio-transformation of these particular antihistamines. Other second-generation H₁ antihistamines (e.g. acrivastine and cetirizine) are not metabolized to an active form and are largely excreted unchanged in the urine. Cetirizine is a metabolite of the first-generation agent hydroxyzine.

Analysis of medicines in Laboratory found result oriented for the GIT problems

The effect of H₁ antihistamine, H₂ antihistamine and the combination of the two drugs on both histamine-induced bronchoconstriction and dermal whealing was examined in five patients with mild asthma. Chlorpheniramine 8 mg, cimetidine 300 mg, the combination of both and placebo were administered orally to each patient for a single dose and for seven consecutive doses given every 6 hr after a double-blind randomized protocol. The airway response to inhaled histamine and the wheal size induced by the

intradermal injection of histamine were determined in every patient 2 hr after the final drug dose. The results indicate that a single dose of chlorpheniramine produces a significant increase in the threshold of histamine-induced bronchoconstriction as measured by the provocative histamine dose producing 20% decrease in 1-second forced expiratory volume (PD₂₀-FEV₁) and this effect was significantly enhanced after seven doses.

Cimetidine caused a significant decrease in the threshold of histamine-induced bronchoconstriction, but this was not augmented by seven doses. Only chlorpheniramine, when given for seven doses, improved the baseline FEV₁ and forced expiratory flow during middle half of forced vital H₁ and H₂ and multiple doses and the combination of chlorpheniramine and cimetidine given for seven doses produced a significant inhibition of histamine-induced dermal wheals, whereas cimetidine alone had no effect. These results confirm our previous observation that both H₁ and H₂ receptors are present in the airways of asthmatic patients and that they mediate opposite effects. We also demonstrated a cumulative effect with the repeated administration of chlorpheniramine but not with cimetidine. Finally, the results suggest that the role of H₁ and H₂ receptors differs in the bronchi from that seen in the dermal vessels of asthmatic patients and are in contrast to those of normals. The H₂ receptor effect on histamine-induced skin wheals appears deficient, further supporting earlier suggestions of the presence of an H₂ receptor defect in asthmatic patients.

In this study, it was found that PPIs were superior to H₂ blocker for prevention of Gastrointestinal ulcers, erosions and bleeding. But, among the nine RCTs included, six studies had small samples and had been poorly reported. The partiality of random sequence generation, allocation concealment, blinding method, incomplete outcome data, and other bias in most of the studies were not clear, which means that the results of our analysis should be interpreted with care.

Gastrointestinal infections involve a spiral-shaped gram-negative micro bacterium. It was assumed that earlier no organism might survive in gastric acidic layer, therefore, the possibility of microbial colonization of stomach actually was not considered. Thus the bacterial microenvironment directly surround and neutralize the effects of gastric secretions which are corrosive to them and the pathogen escapes.

In a case-control study, Lanis et al. 2002 discovered that *H. Pylori* infection increased the risk of GI malfunctioning and indicated that *H. pylori* infection was an independent risk factor for LDA-associated GI malfunctioning (4). Only one RCT in our analysis included patients who were negative for *H. pylori*, and one RCT showed *H. pylori* eradication. Most of our studies did not determine *H. pylori* infection status, thus, it is not clear whether infection interacted with LDA to increase mucosal injuries. So, selection bias may have been present in our meta-analysis.

Permanent infection is often acquired early in life (5) many studies show main cause of inflamed stomach, and it's a key factor of gastrointestinal tract pathology include diseases peptic ulcer, gastrointestinal cancer (6) and (7) Zoonotic pathogen has no indication supporting this belief, because animal or environmental reservoirs protect strains that infect humans, in spite of *H. pylori* isolation from other animals such as the cat. At this time, it appears that only the gastric conditions are optimal for growth and capability of the pathogen. Conducting researches to explain the ways of transmission. This review evaluates the role of Gastro intestinal Infections in upper respiratory tract.

In adding to the relations, *H. pylori* damages T cell-mediated immunity through systemic mechanism. Systematic immune and inflammatory responses to *H.*

pylori may be associated to extra-GIT infections (8). Current studies have acknowledged a possible connection among *H. pylori* infection and the pathogenicity of cardiovascular, neurologic, dermatologic, immunologic, hematologic, hepatobiliary, ophthalmic and gynecologic infections, as well as diabetes mellitus (9, 10).

There was no statistical heterogeneity among the results in comparison of incidence of GI malfunctioning (ulcer, erosion or bleeding) in PPI and H₂ groups. And a fixed-effect model was used for this analysis. The result showed that PPIs were superior to H₂ blockers for prevention of GI malfunctioning.

The American College of Cardiology Foundation (ACCF), American College of Gastroenterology (ACG) and American Heart Association (AHA) revised the expert consensus document of 2010 on reducing the GI risks of anti-platelet therapy and NSAID use, which states that H₂ are a reasonable alternative to PPIs for the prophylaxis and treatment of GI injury (11).

We concluded that proton pump inhibitors were better to H₂ receptor antagonists in preventing gastrointestinal erosion ulcers and bleeding. Some of these GI ulcers incorporated in our study were inadequately documented and of lower worth, hence, this study should be construed with great concern.

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