



THERAPEUTIC APPROACHES FOR ACID REDUCTION IN PATIENTS ADMITTED TO INTENSIVE CARE UNITS WITH A HISTORY OF GASTROESOPHAGEAL REFLUX DISEASE AT A TERTIARY CARE HOSPITAL IN PAKISTAN.

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Abstract

Introduction: Although the prevalence of gastroesophageal reflux disease (GERD) in intensive care units is still unknown, the condition is on the rise all over the world. Patients in critical condition are especially susceptible to gastroesophageal reflux disease (GERD) because of the many procedures and underlying illnesses they undergo. Pepsin levels in oral secretions, ambulatory monitoring, and pH measurement are among procedures that can be utilized in the diagnostic process. The most popular treatment methods consist of adjusting one's lifestyle and using medicine, mainly proton pump inhibitors (PPIs).

Methodology: An analysis of data collected from 96 critically sick patients who were getting acid-lowering medication was carried out in retrospective research that was carried out at a tertiary care hospital in AJK, Pakistan between June and December 2023.

Results: Most patients were being treated in medical intensive care units (MICU), and the medications that were prescribed the most frequently were omeprazole and esomeprazole. Omeprazole and antacids were the primary maintenance medications that were administered at the time of discharge. Patients who were diagnosed with gastroesophageal reflux disease (GERD) and those who were undergoing mechanical ventilation made up a sizeable share, with most of them receiving intravenous proton pump inhibitors (PPIs). Both potassium-competitive acid blockers and omeprazole were shown to have equivalent levels of treatment efficacy, according to the findings.

Conclusion: Most of trials in past have established esomeprazole being highlighted as having superiority in certain studies. On the other hand, newer possibilities such as GABA-B agonist baclofen and P-CABs offer potential lines of investigation. Even though developing medicines require more exploration for routine management, intravenous proton pump inhibitors (PPIs) continue to be the primary emergency treatment for gastroesophageal reflux disease (GERD) in critical care.

Keywords: Gastroesophageal reflux disease, Proton pump inhibitors, GERD in ICU, new antacids

Introduction

The incidence and prevalence of gastroesophageal reflux disease, or GERD, are increasing worldwide. The number of individuals with GERD admitted to a critical care unit is unknown. Interventions performed on critically ill patients may increase the risk of reflux and related complications. Certain patient characteristics, coexisting conditions, and interventions used to support critically ill patients, such as sedation, the use of an endotracheal tube, mechanical ventilation, enteral feedings, positioning, and medication make this population more vulnerable to GERD [1].

Individuals in the intensive care unit (ICU) cannot be identified as having reflux using a single, conclusive method. Historically, ambulatory monitoring and oesophageal pH measurement during episodes of reflux have been the most reliable methods for diagnosis. Recordings of reflux episodes are also classified as acid or non-acid. For the next 24 to 48 hours, the pH is continuously monitored after inserting a tiny catheter via the nares into the distal oesophagus. Typically, the pH of gastric contents falls between 1.0 and 4.0; an episode of reflux is typically defined by a pH of less than 4.0. Oesophageal manometry is another technique for diagnosis. Pepsin levels in oral secretions have also been employed as a GERD marker. Pepsinogen, the precursor of the digesting enzyme pepsin that is released from the main cells lining the stomach mucosa, is activated by acid [2]. When 109 patients were tested, salivary pepsin was found to be positive in six control subjects and 13 GERD patients [3].

It is known that one of the key pathogenic factors in GERD is the presence of an acid bubble. Lifestyle interventions like losing weight, quitting smoking, consuming less alcohol, and raising the head of the bed were advised as treatment for GERD, however rigorously avoiding foods or beverages was not. Although proton pump inhibitors (PPIs) were still the go-to treatment for mild-to-moderate GERD, alginates were advised as the first-line treatment for these patients. In cases where PPIs were only partially effective in treating GERD symptoms, alginates were also advised as an adjuvant treatment [4]. The most common signs of gastroesophageal reflux are regurgitation of acid and heartburn. Several therapeutic regimens are available, but due to their effectiveness, safety, and accessibility over the counter, antacids continue to be the go-to medication for treating symptoms associated with gastroesophageal reflux. It is generally advised that adults and children who are at least 12 years old take antacids [5].

Proton pump inhibitors are used to treat GERD. Except for pantoprazole, Sachs, and colleagues' research revealed that all PPIs have a shorter half-life of recovery of acid secretion and, consequently, proton-pump function than anticipated [6]. Even at high dosages, PPIs have demonstrated a very good safety record. There is no indication of a clinically significant shortage in minerals, vitamins, or vital nutrients, except for a modest reduction in vitamin B12 absorption, which is usually always clinically negligible. A group in Glasgow, Scotland, conducted some intriguing research on the impact of PPIs on the bioavailability of vitamin C in food [7].

Several studies compared different proton pump inhibitors with each other most of the studies comparing esomeprazole with other PPIs [8-15]. GABA-B agonist baclofen is a novel treatment under trials [16-18]. Potassium-competitive acid blockers (P-CABs) is another treatment option [19-20].

Methodology

The study was conducted between June and December 2023 at a tertiary care hospital in AJK, Pakistan, with an intensive care unit (ICU) facility in a retrospective manner. The study included all the critically ill patients, who received ICU care at hospital and an acid-lowering treatment. A consecutive sampling method was used to induct patients from surgical ICU and medical ICU. The age of induction was kept being 18 years and older at the time of admission. Patients who had received

intravenous proton pump inhibitors before, pregnant women, patients with a recent episode of gastrointestinal bleeding due to ulcers, patients with active bleeding at the time of admission, and the patients taking treatment for stress ulcers were all excluded. Participants were enrolled after strictly following an inclusion and exclusion criteria.

The electronic medical records from the hospital were used to obtain data of all the patients admitted in ICU. A data collection form was used to collect patients 'data which included demographic details, primary diagnosis, past medical history, past medication details, current medication in the hospital, GERD associated risk factors and factors that could exacerbate the condition, and the prescription at discharge.

All the data was collected on an excel sheet and then transferred to an SPSS sheet. The data was analysed using statistical methods and the descriptive statistics including mean and standard deviation for continuous variables and frequency and percentage for categorical variables were obtained using inferential statistics.

Results

Table 1: Descriptive characteristics of the study population

Variable		Frequency	Percent
Gender	Male	56	58.33
	Female	40	41.67
Past medication	No	85	88.54
	Yes	11	11.46
Mechanical ventilation	No	88	91.67
	Yes	8	8.33
AT Risk patients	No	79	82.29
	Yes	17	17.71
GERD	No	66	68.75
	Yes	30	31.25
Risks	No	75	78.13
	Hydrocortisone	4	4.17
	Sepsis	5	5.21
	Sepsis and Hydrocortisone	3	3.13
	AKI	2	2.08
	Hepatic/Renal Failure	1	1.04
	Sepsis and AKI	3	3.13
	Hepatic Failure And AKI	2	2.08
	Coagulopathy	1	1.04
Number of risk factors	0	73	76.04
	1	16	16.67
	2	6	6.25
	3	1	1.04
ICU	MICU	63	65.63
	MICU(SD)	20	20.83
	SICU	11	11.46
Age	Less Than 60 Years	49	51.04
	More Than 60 Years	47	48.96
LOS	Less Than 3 Days	54	56.25
	More Than 3 Days	42	43.75

The total number of patients in the study was 96, out of which MICU patients were 65.63%, MICU/SD patients were 20.83% and SICU patients were 11.46%. The main descriptive characteristics are given in table 1.

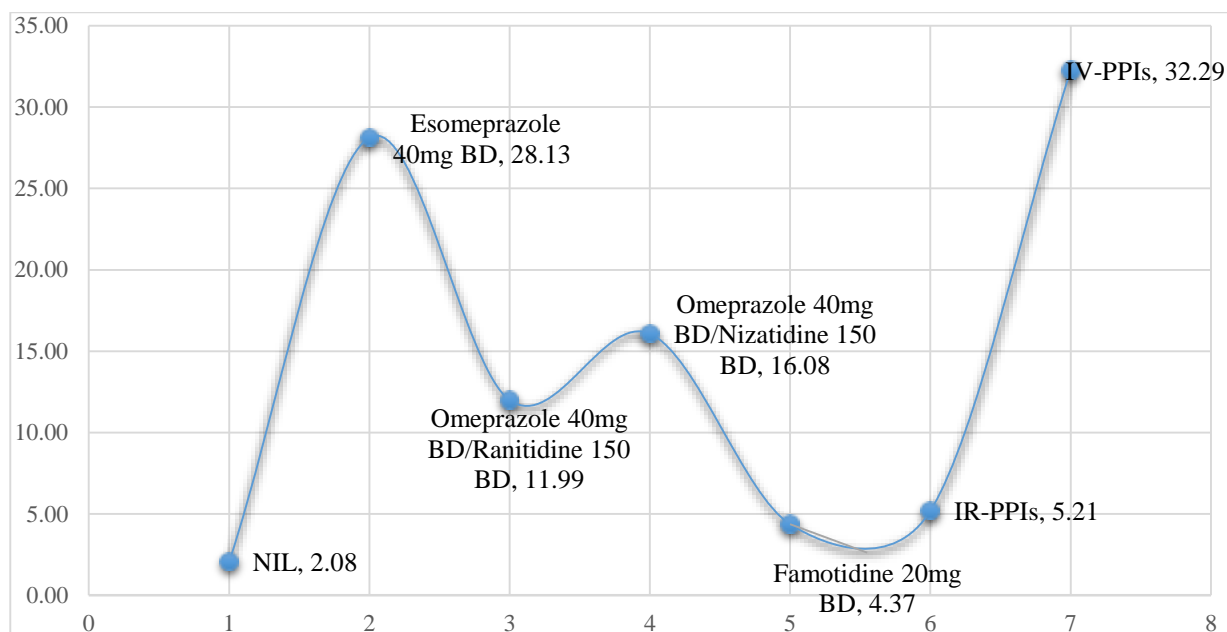
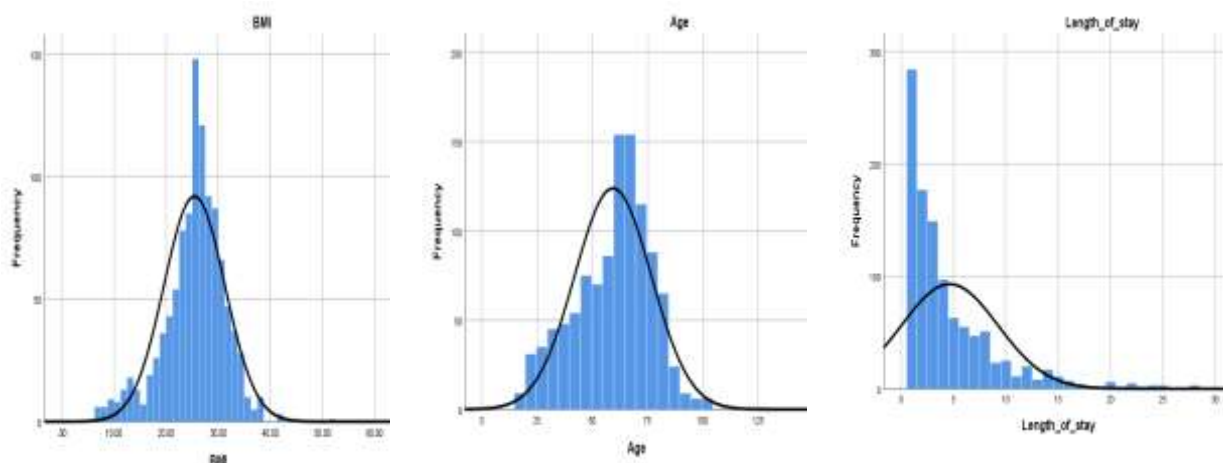


Figure 1: The treatment regimen used inside the intensive care unit. IV: intravenous, IR: instant release, PPI: proton pump inhibitor, BD: two doses a day



Mean BMI: 25.42

Mean age: 59.23 years

Mean hospital stay: 4.62 days

Figure 2: The mean of BMI, age and the length of time patient stayed at the ICU.

The age of the patients admitted at medical ICU and surgical ICU was less than 60 years for 51.04% of the patients. The most common drug used was esomeprazole and omeprazole in 40mg (Table 1, Figure 1).

Table 2: The medicine prescribed at the discharge day as a maintenance therapy for gastric issues.

Medicine Prescribed at Discharge	Frequency	Percentage
Nil	19	19.79
Omeprazole 40mg OD	56	58.33
Pantoprazole 40mg OD	2	2.08
Aluminium/magnesium Hydroxide	17	17.71
P-CAB	2	2.08

The most common drug prescribed at discharge was omeprazole and second common was an antacid like aluminum or magnesium hydroxide.

Table 3: The GERD profile.

GERD			Mechanical ventilation		Total
			No	Yes	
No	Antacid agent	NIL	2	13	15
		Esomeprazole 40mg BD	24	0	24
		Omeprazole 40mg BD or Ranitidine 150 BD	9	0	9
		Omeprazole 40mg BD or Nizatidine 150 BD	12	0	12
		Famotidine 20mg BD	3	0	3
		IR-PPIs	3	0	3
	Total	53	13	66	
Yes	Antacid agent	NIL	0	0	0
		Esomeprazole 40mg BD	3	0	3
		Omeprazole 40mg BD or Ranitidine 150 BD	3	0	3
		Famotidine 20mg BD	1	0	1
		IR-PPIs	1	1	2
		IV-PPIs	0	21	21
	Total	8	22	30	

There were 30 patients who had a history of GERD, and 31 patients who needed mechanical ventilation. There were 22 patients on ventilator who also had a positive GERD history. Of these, 21 patients received an intravenous OD dose of PPIs, and one patient got off from ventilator on second day so after that he was given an instant release PPI (IR-PPI) inside ICU during his stay. Other GERD patients who were not ventilated were given IR-PPI (1), esomeprazole (3), omeprazole (3), or famotidine (1) orally. All the GERD patients received a maintenance treatment with omeprazole 40mg or P-CAB. The patients reported same treatment efficacy with both drugs.

Discussion

The current treatment plan for GERD includes medication, behavioural and lifestyle modifications, and surgery. To identify patients who are both critically sick and at risk for gastric reflux disease (GERD) and to prevent consequences from these illnesses, critical care plays a significant role [1]. There is huge research on the use of drugs for GERD treatment. The drug trials report comparison of different drugs.

In one study,[8] individuals receiving lansoprazole by random showed longer symptom alleviation on day 1 and lower heartburn episode durations than patients receiving omeprazole 20 mg and esomeprazole 40 mg daily. Two additional investigations, however, asserted that esomeprazole was superior to lansoprazole. First of these studies measured intragastric pH in GERD patients randomized to either 30 mg of lansoprazole or 40 mg of esomeprazole daily between days 1 and 5 of treatment. [9] those receiving esomeprazole experienced a substantially higher proportion of time (hours) at intragastric pH > 4.0 on both treatment days (day 1, 40.6% vs. 33.4%; day 5, 57.7% vs. 40.6%, respectively) than those receiving lansoprazole. Patients who took esomeprazole had a much higher chance of maintaining both symptomatic and mucosal remission, according to the study's authors. [10].

In a double-blind, crossover trial, Baisley, and colleagues [11] examined intragastric pH measurements in 27 patients taking 20 mg of rabeprazole and 40 mg of esomeprazole daily. There was no difference in the clinical efficacy of pantoprazole 40 mg or esomeprazole 40 mg daily for 227 patients with erosive esophagitis in a double-blind, randomized, multicentre study [12]. In addition to having similarly high healing rates, both medications were safe and well-tolerated. Two trials assessed how well rabeprazole 10 mg and 20 mg daily relieved Nonerosive Reflux Disease NERD (the condition in 50-70% GERD patients) patients' symptoms [13]. Individuals treated with rabeprazole 10 mg or 20 mg daily or placebo for recurrent bouts of moderate-to-severe heartburn. When compared to placebo, rabeprazole showed a noticeably faster time to the start of the first 24- and 48-hour heartburn-free intervals for both doses. Furthermore, by the fourth week of treatment, a far higher proportion of rabeprazole-treated patients reported total or adequate relief from heartburn.

Rather from being a necessary part of NERD expression, the dyspeptic symptoms in some of the patients are probably an overlap of NERD with functional dyspepsia [14].

In a three-month double-blind, placebo-controlled, randomized crossover experiment, 16 individuals with functional heartburn were randomly assigned to receive either lansoprazole 30 mg twice day or a placebo. None of the metrics used to evaluate symptom improvement showed any difference between the two treatment groups. A subgroup of individuals experienced a statistically significant improvement in their symptom score if they had reported heartburn symptoms for more than a year and experienced the symptoms more frequently than twice a week. [15]

Richard Holloway examined that GABA-B agonist baclofen raises basal lower oesophageal sphincter pressure and blocks 34% to 60% of transient lower oesophageal sphincter relaxation (TLESRs). Furthermore, the medication lowers acid reflux episodes by 40% to 42%. Additionally, there is less exposure to ambulatory oesophageal acid and postprandial acid. Additionally, it seems that this medication prevents reflux, both acidic and nonacidic (including bile). Overall, the adverse effects of this medication are not very severe, and it has no discernible effect on oesophageal peristalsis [16].

Unlike acid secretion inhibitors TLESR reducers target the root cause of GERD. Oesophageal pH readings and the intensity of GERD symptoms significantly improved in one study [17] that comprised a small number of individuals randomized to receive either a placebo or baclofen (10 mg four times day) for a month. Baclofen consistently reduces classic GERD symptoms while also normalizing oesophageal pH readings. GERD-affected children had comparable positive outcomes. Baclofen was well tolerated, did not alter stomach emptying, and significantly decreased the rate of TLESRs and acid reflux episodes as compared to a placebo [18].

the mucosal protectants, which support the physiological protective barrier of the oesophageal mucosa, and the potassium-competitive acid blockers (P-CABs), which offer a quick start, prolonged, and significant acid suppression. The array of innovative therapeutic endoscopic procedures that are being researched or newly launched into the market is increasing, adding to our arsenal of GERD treatment options [19].

Potassium-competitive acid blockers, also known as P-CABs, are medicines that inhibit H⁺, K⁺-ATPase in a way that is both reversible and K⁺-competitive. Furthermore, they show almost full reduction of gastric acid output from the very first dose [20].

Conclusion:

the emergency treatment for GERD is still the intravenous proton pump inhibitor and it provides relief in ICU patients. The newer drugs like GABA-B agonist baclofen, and potassium-competitive acid blockers, also known as P-CABs can be used for regular treatment of GERD and are under trials P-CABs are also approved and they are being used in our country on small scales. But these drugs have not established their efficacy as an emergency treatment regimen.

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