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Prevention of Stress Peptic Ulcer Among Patients Admitted To Intensive Care Unit

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Abstract

Introduction: The understanding of risks and benefits associated with stress peptic ulcers is important and determining current ICU clinical practice of intensivists regarding risk assessment, clinical relevant information, and pharmacologic approaches for stress ulcer prevention. This review aimed to assess the effectiveness of SUPs in intensive care unit.

Methods: An electronic search was conducted in MEDLINE and EMBASE databases resulted in 108 articles and the search in ScienceDirect database yield 14 articles. Thus, the total articles found by this systematic search is 121 articles, then after exclusion of irrelevant, duplicated and reviews, the included articles were 33 articles Data were extracted from these articles using data extraction forms.

Results: Thirteen studies reported bleeding rate was less significant in the treated patients), while one study found that the bleeding rate was higher in the treatment groups than in the control groups. In addition, 12 included studies found that no significant differences in bleeding rate between the groups. Significant effects were reported in rate of bleeding with pantoprazole, ranitidine, cimetidine in comparison to placebo. Significant results were achieved in increasing gastric pH with ranitidine versus placebo, and ranitidine plus antacid when compared to sucralfate. Cimetidine treated patients demonstrated significantly higher mean gastric pH than placebo. Statistically better pH control was found in the famotidine treated groups than in the cimetidine and in rantidine treated groups than in cimetidine. The least reported bleeding rate was reported with antacid suspensions.

Conclusions: This review concluded that the most effective medications in control of gastrointestinal bleeding and gastric pH was rantidine followed by cimetidine. However, the least reported bleeding rate was reported with antacid medications.

Keywords: Stress, Peptic ulcer, ICU, Prophylaxis, Gastric, Bleeding

Introduction

Stress ulcer or stress-related mucosal disease is defined as “acute superficial inflammatory lesions of the gastric mucosa induced when an individual is subjected to abnormally elevated physiologic demands.” Multiple lesions are typically associated with stress ulcers and are usually located in the acid and pepsin secreting mucosa [(1)]. Studies have reported evidence of mucosal damage within 24 hours of admission in 75–100% of intensive care unit (ICU) patients [(2)]. however, these lesions generally heal as the patient’s’ clinical status improves.4 Risk of bleeding from stress ulcers appears to be on the decline, from 20–30% in the 1970s to 1.5–14% in the 1990s. This is largely thought to be due to improvements in the treatment of underlying conditions and the appropriate use of stress ulcer prophylaxis [(3)]. Even with this decline in the risk of

bleeding, however, mortality from stress-related bleeding in critically ill patients approaches 50% [4].

The pathogenesis of stress ulcers in critical illness is linked to many factors, such as hypovolemia, depressed cardiac output, increased vasoconstriction, and importantly, splanchnic hypoperfusion, which contributes to acid back-diffusion and reduction in bicarbonate secretion, mucosal blood flow, and gastrointestinal motility [5]. Although mechanical ventilation is regarded as the most frequent risk factor, several other disease states related to critical illness that contribute to gut ischemia and acute organ failure have also been implicated [6].

The use of proton pump inhibitors (PPIs) and histamine H2-receptor antagonists for the prevention of stress ulcers has been well-defined in critical care patients. In 1999, the American Society of Health-System Pharmacists (ASHP) published guide-lines on the use of stress ulcer prophylaxis in medical, surgical, respiratory, and pediatric ICU patients [7].

Studies have investigated various agents prescribed for stress ulcer prophylaxis (SUP), with histamine-2 receptor antagonists (H2RA) largely identified as efficacious therapy [8]. Despite H2RAs proven efficacy, the armamentarium of possible therapies has expanded to include proton pump inhibitors (PPIs). Superior gastric acid suppression with PPI therapy has been suggested as a reason to select this class of medication for SUP over the H2RA class. This may be related to H2RA-demonstrated tolerance and irreversible acid suppression associated with PPI [9]. Acid suppressive therapy is associated with increased colonization of the upper gastrointestinal tract with potentially pathogenic organisms and may increase the risk of hospital-acquired pneumonia [10].

Thus, understanding risks and benefits of SUP is important and determining current ICU clinical practice of intensivists regarding risk assessment, clinical relevant information, and pharmacologic approaches for stress ulcer prevention. This review aimed to assess the effectiveness of SUPs in intensive care unit.

Methods

An electronic search was conducted in MEDLINE and EMBASE databases using this search strategy (intensive care OR admitted OR hospitalized patients) AND (Stress ulcer) And (prophylaxis OR proton pump inhibitors OR histamine H2-receptor antagonists OR H2RAs OR PPIs). This search resulted in 108 articles. The search (intensive care OR admitted OR hospitalized patients) AND (Stress ulcer) And (prophylaxis OR proton pump inhibitors OR histamine H2-receptor antagonists OR H2RAs OR PPIs) n ScienceDirect database yield 14 articles. Thus, the total articles found by this systematic search is 121 articles. Data were extracted from these articles using data extraction forms (table 1).

Results

The search resulted in 121 articles, then after exclusion of irrelevant, duplicated and reviews, the included articles were 33 articles. All of them were randomized clinical trials, four studies were multicentral studies [11-14]. In addition, 12 trials (37%) used placebo as comparator [12-22], whereas the remaining trials used no prophylaxis. In 7 trials, patients were fed enterally [9, 11, 12, 18, 20, 23, 24].

These 33 included trials enrolled 4441 patients in the ICU ranging from 12 patients in Ketterl, et al. [25] to 1200 patients in Cook, et al.[11]. From which 213 were pediatric in a study of Yildizdas, et al. [26] 160 and Kuusela, et al., (22) 53. Most of adults patients were admitted to general ICUs except for Kantorova, et al. [27], who recruited patients from surgical ICU and Duma [28] who included patients from cardiac unit, while MacDougall, et al. [29] studied patients admitted to liver failure unit and Chan, et al. [15] recruited patients from neurosurgery ward.

Regarding the intervention, four clinical trials evaluated both PPI and H2RA [21, 26, 30] while 10 clinical trials assessed the effect of cimetidine [6, 12, 13, 17-20, 29, 31]. Eleven included trials focused ranitidine [4, 14, 15, 22-24, 27, 32-35] and one clinical trial conducted by Heiselman, et al.[36] assessed the effect of Famotidine, while three trials compared cimetidine with ranitidine [25, 28, 37]. Other studied prophylactic drugs included pantoprazole [38] and famotidine [39]. Only one clinical trial compared cimetidine, ranitidine and famotidine[40]. The most common route of administration in the included studies was intravenous alone in 15 included studies [12-15, 18-22, 24, 27, 28, 36, 37, 39] and either orally or intravenously in 9 trial [6, 9, 11, 23, 29, 31, 32, 34, 41] and orally alone in 8 trials [17, 25, 26, 30, 33, 35, 38, 40].

Regarding the gastrointestinal bleeding, 13 studies reported that the bleeding rate was less significant in the treated patients [11-15, 17, 20, 22, 27, 29, 32-34], while one study found that the bleeding rate was higher in the treatment groups than in the control groups [31]. In addition, 12 studies found that no significant differences in bleeding rate between the groups [6, 19, 21, 23, 24, 26, 28, 35, 36, 38-41]. Levy, et al.[9] reported that the bleeding rate was higher in the group treated with H2RAs than PPIs.

Regarding the effect of prophylactic drugs on GI bleeding, significant effect were achieved in rate of bleeding with pantoprazole in comparison to placebo [38], with ranitidine in comparison to placebo [9, 14, 15], and with cimetidine in comparison to placebo [12, 13, 20]. The included studies reported higher bleeding rate in sucralfate comparison to famotidine and omeprazole [21], and in sucralfate when compared to ranitidine [11], and when compared to ranitidine plus antacids [34]. While, non-significant effects of these drugs on the rate of bleeding reported in the comparison between antacids, cimetidine, and a placebo in Friedman et al. study [17]. In addition, Apte et al. found no significant difference in rate of bleeding associated with ranitidine versus control group [24]. Groll also reported no significant difference between cimetidine and placebo group in incidence of GI bleeding [19].

Significant results were achieved in increasing gastric pH with ranitidine versus placebo [22, 23], and higher gastric pH with ranitidine plus antacid when compared to sucralfate [34]. Cimetidine treated patients demonstrated significantly higher mean gastric pH than placebo [12, 18]. In addition, statistically better pH control was found in the famotidine treated groups than in the cimetidine [40] and in rantidine treated groups than in cimetidine [28, 37, 40]. A higher gastric pH reported in sucralfate treated group in comparison to cimetidine group [41]. The pirenzepine-antacid combination proved to be superior to ensure a gastric pH of more time than the pirenzepine-cimetidine group [6]. However, non-significant effects of these medications on gastric pH were reported few studies such as between Lansoprazole and famotidine [30], between rantidine and cimetidine [25], and between omeprazole, pantoprazole, esomeprazole, and rabeprazole [16].

Concerning the mortality, data were obtained from 8 trials including 2908 patients, all of them showed no significant difference in mortality in patients treated with SUP compared with those treated with placebo or no prophylaxis [11, 19, 21, 26, 34-36, 38]. Finally concerning the occurrence of pneumonia, two trials found that it occurred more in the control group than the treatment group Martin, et al., (41) and Metz, et al., (42). However, four trials reported higher mortality in the treatment group than in the control group [11, 24, 34, 38]. Only one trial reported no significant difference in pneumonia occurrence [13] Karlstadt, et al., (39), while two trials reported a higher incidence of pneumonia in patients treated with H2RAs than PPIs [9, 26] and two trials reported that it occurred more with PPIs than with H2Ras [21, 35].

Table (1): Summary of the findings

Reference	Sample size	Type of patients	Pharmacological prophylaxis of stress ulcer	The effectiveness of the prophylaxis	Complications associated with prophylaxis
(Selvanderan et al., 2016)	214	ICU	Pantoprazole	Administration of pantoprazole was not associated with any difference in rates of overt bleeding (6 vs 3; p = 0.50) Mortality was similar between groups	Three patients met the criteria for either an infective ventilator-associated complication or pneumonia (placebo: 1 vs pantoprazole: 2), and one patient was diagnosed with Clostridium difficile infection (0 vs 1)
(Burgess et al., 1995)	34	Adults with Glasgow coma scale scores < or = 10	Patients were randomized to a 6.25 mg/hr ranitidine continuous infusion or placebo for a maximum of 72 hr	Ranitidine patients maintained a significantly greater mean pH than placebo patients (placebo 2.2, ranitidine 4.1; P < 0.01).	Not-reported
(Brophy et al., 2010)	51	Critically ill patients	Lansoprazole 30 mg suspension via NG/NJ tube daily or famotidine 20 mg IV q12 h for SUP	No significant differences in the percentages of time gastric residual volumes <28 ml. Heme-positive aspirates were present in 18–39% of patients (*P* = NS); one patient receiving famotidine met the criteria for overt bleeding.	Thrombocytopenia occurred in 17% in the famotidine group and 4% in the lansoprazole group (*P* = NS). Thrombocytopenia occurred in 17% in the famotidine group and 4% in the lansoprazole group (P = NS).

(Levy et al., 1997)	67	ICU	Patients were randomized to receive either ranitidine 150 mg (N = 35) intravenously daily or omeprazole 40 mg (N = 32)	31% of patients given ranitidine and (6%) given omeprazole developed clinically important bleeding (P < 0.05).	Nosocomial pneumonia developed in five patients (14%) receiving ranitidine and one patient (3%) receiving omeprazole (P< 0.05).
(Kantorova et al., 2004)	287	Surgical intensive care unit	Compared 3 prophylactic regimens omeprazole 40 mg i.v. once daily, H2 antagonists--famotidine 40 mg twice a day, and sucralfate 1 g every 6 hours, n=69) with placebo (n=75)	Significant stress-related upper gastrointestinal bleeding was observed in 1%, 3%, 4%, and 1% of patients assigned to receive omeprazole, famotidine, sucralfate, and placebo, respectively	Nosocomial pneumonia occurred in 11% of patients receiving omeprazole, in 10% of famotidine patients, in 9% of sucralfate patients and in 7% of controls (p>0.34)
(Darlong et al., 2003)	52	Critically ill	Group I received ranitidine 50 mg (intravenous) 8 hourly, group II received tablet sucralfate 1 g 8 hourly whereas group III was the controls	Ranitidine was more effective in increasing the gastric pH, the incidence of gastric colonization was higher in the ranitidine group compared to the sucralfate group	Not-reported
(Yildizdas et al., 2002)	160	Pediatric intensive care unit	Group (S) sucralfate suspension 60	Overall mortality rate was 22% (35 of 160); it was 21% (8 of 38) in the	VAP rate was 42% (16 of 38) in the sucralfate group, 48%

			mg/kg/d Group (R) received ranitidine 2 mg/kg/d group (O) received omeprazole 1 mg/kg/d and group (P) the controls	sucralfate group, 23% (10 of 42) in the ranitidine group, 21% (8 of 38) in the omeprazole group, and 21% (9 of 42) in the nontreated group.	(20 of 42) in the ranitidine group, 45% (17 of 38) in the omeprazole group, and 41% (17 of 42) in the control group
(Friedman et al., 1982)	36	Patients rec eiving mechanical ventilation	Patients were prophylactically treated with either antacids, cimetidine, or a placebo.	Gastrointestinal bleeding did not occur in any of the six subjects receiving antacids but did occur in one of the 11 subjects receiving cimetidine, in 5 of the 14 control patients, and in 3 of the 5 patients who were unable to tolerate antacids. These differences were not significant	Not-reported
(Cook et al., 1998)	1200	ICU patients wh o required mechanical ventilation	Patients receive d either nasogastric sucralfate suspension (1 g every six hours) and an intravenous placebo or intravenous ranitidine and a nasogastric placebo	Gastrointestinal bleeding developed in 10 of 596 (1.7%) of the patients receiving ranitidine, as compared with 23 of 604 (3.8 %) of those receiving sucralfate (relative risk, 0.44)	In the ranitidine group (19.1 %) had ventilator-associated pneumonia, as compared with (16.2 %) in the sucralfate group

(Kuusela et al., 1997)	53 infants	Neonatal In tensive Care unit	A histamine-2-receptor blocker , ranitidine, was given prophylactically after birth for 4 days to infants	The gastric mucosa was visually classified as normal in 14 (61%) infants as compared with five (20%) of 25 controls (p < .004)	Not-reported
(Thomason et al., 1996)	242	Mechanical ly ventilated p atients adm itted to the trauma inte nsive care unit	Patients were randomized: sucralfate, n = 80; antacid, n = 82; and ranitidine, n = 80.	The death rate in patients with pneumonia was not statistically different among the three groups.	There was no statistically significant difference in pneumonia rates among the treatment groups (p = 0.875).
(Halloran et al., 1980)	50	Patients with severe head injury	A placebo or 300 mg of cimetidine, was given as intravenous bolus dose every 4 hours 26 patients were randomly placed in the Cimetidine group and 24 in the control group.	19% of the 26 patients in the cimetidine group had gastrointestinal bleeding. In contrast, 18 (75%) of the 24 control patients had bleeding	Not-reported
(Heiselman et al., 1995)	40	ICU patient s	ICU patients at risk for stress ulcerat ion were randomly assigned to	Clinical outcomes, including evidence for gastrointestinal bleeding and hospital mortality, did not differ significantly between groups	Not-reported

			receive either famotidine 20 mg intravenous bolus followed by 1.67 mg/h infusion or famotidine 20 mg intravenously every 12 h		
(Prod'hom et al., 1994)	244	Mechanically ventilated ICU patients	Antacid (a suspension of aluminum hydroxide and magnesium hydroxide), 20 mL every 2 hours; ranitidine, 150 mg as a continuous intravenous infusion; or sucralfate, 1 g every 4 hours	Patients who received sucralfate had a lower median gastric pH (P < 0.001) and less frequent gastric colonization compared with the other groups (P = 0.015). Gastric bleeding was observed in 10%, 4%, and 6% of patients assigned to receive sucralfate, antacid, and ranitidine, respectively (P > 0.2).	The incidence of early-onset pneumonia was not statistically different among the three treatment groups
(Vargas et al., 1993)	56	Critically ill patients receiving mechanical ventilation	Randomly assigned to receive famotidine 40 mg/day (n = 27) or ranitidine 150 mg/day (n = 29) during 5 days	Famotidine had higher mean gastric pH (6.3 +/- 0.2 and 93% of measurements over 5 vs 5.8 +/- 0.6 and 83% of measurements over 5 (p < 0.05). No patient had evidence of gastrointestinal bleeding	Not-reported
(Martin et al.,	131	ICU	Patients were	Cimetidine-	Of the 56 cimetidine-

1993)		patients	randomized to receive cimetidine (n = 65) as an iv infusion of 50 to 100 mg/hr or placebo (n = 66).	patients experienced significantly less upper GI hemorrhage than placebo patients. Cimetidine patients demons trated significantly higher mean intragastric pH (5.7 vs. 3.9), and had intragastric pH values at > 4.0 for a significantly higher mean percentage of time (82% vs. 41%) than placebo patients	infused patients and 61 placebo-infused patients who did not have pneumonia at baseline, no cimetidine-infused patient developed pneumonia while four (7%) placebo-infused patients developed pneumonia
(Apte et al., 1992)	34 tracheot omized patients with tetanus	ICU	Sixteen patients received iv ranitidine to increase gastric pH greater than 4 (ranitidine group), while 18 patients received no prophylaxis f or upper gastrointestinal bleeding (control group)	There was no difference in the frequency of upper gastrointestinal hemorrhage in the two groups	Pneumonia occurred (81%) received ranitidine, 3 days and in (50%) of control patients (p less than .01) 5 days after tracheal intubation (median, range 3 to 14; p less than .01)
(Lamothe et al., 1991)	57	CCU patients wit h elective coronary artery bypass	There were four treatment groups, each with similar demographics (age and sex). Cimetidine-treated group	Agents were compared for efficacy of gastric pH control, statistically better pH control was found in the famotidine- and ranitidine-treated groups (P less than 0.003) than in the cimetidine-treated group	Not-reported

			consisted of 15, famotidine-treated group of 18, ranitidine-treated group of 19, and antacid-treated group of 5 patients.	(pH less than or equal to 4.0).	
(Duma, 1986)	100	ICU patients with cardio-surgery	Cimetidine and Ranitidine	The gastric 8 o'clock pH-level of group A (Cimetidine) during this intensive therapy was significantly (p = 0.0001) higher than the respective level of group B (Ranitidine). Acute gastro-	Not-reported
(Groll et al., 1986)	221	ICU patients	One hundred and fourteen received cimetidine and 107 placebo patients	Only 8% of the patients bled with no significant difference between the two groups (6/114 cimetidine, 11/107 placebo; p = 0.16)	Thirteen patients died in each study group, resulting in overall mortality of 12%
(Tryba et al., 1985)	100	High-risk patients in an intensive care unit	1 g of sucralfate every four hours or 2 g of cimetidine intravenously. All patients also received 50 mg of pirenzepine by intravenous infusion each day	The intragastric pH was less than 4 significantly more often in patients treated with sucralfate than in patients treated with the other agents, but in the latter two treatment groups, the probability of bleeding correlated with the incidence of pH values below 4	Not-reported

(More et al., 1985)	48	ICU patients	Cimetidine versus ranitidine	Cimetidine was successful in maintaining the intragastric pH above 4, for the duration of the intensive care admission, in five of 28 patients. Ranitidine was successful in 10 of 20 patients. The difference between these two groups was statistically significant	Not-reported
(Van den Berg and Van Blankenstein, 1985)	34	Critically ill patients on assisted ventilation	14 on cimetidine versus 14 on placebo	Although cimetidine produced a markedly lower number of days with a gastric pH below 3.5 (17.4% vs. 72.2%) 5 patients on cimetidine bled as against 1 on placebo	Not-reported
(Tryba, 2001)	33	ICU patients	Pirenzepine intravenously as a basic medication and alternatively 2000 mg. cimetidine i.v or 2-hourly 10 ml. antacid	The pirenzepine-antacid combination proved to be superior to ensure a gastric pH of more than 3.5 than the pirenzepine-cimetidine group. Two stress bleedings could be detected in each group	Not-reported
(Ketterl et al., 1984)	12	ICU patients	300 mg/die Ranitidine versus 2000 mg Cimetidine/die	Ranitidine 300 mg, a prophylactic sufficient control, yet not a complete control of intragastric pH-value was accomplished. With Cimetidine as monotherapy, however, even under 2000 mg/die, no	Not-reported

				successful control of the intragastric pH could be achieved	
(Weigelt et al., 1981).	77	ICU patients	Antacids and various doses of cimetidine	Cimetidine and antacids treated patients adequately neutralized. Stress bleeding occurred in three (5%) patients treated with cimetidine and in no patient treated with antacids	Reversible thrombocytopenia developed in (26%) of patients treated by cimetidine
(MacDougall et al., 1977)	75	Patients with hepatic failure	Antacids versus Cimetidine	Stress related GI bleeding was 3% in antacids group versus 1% in Cimetidine group	Not-reported
(Karlstadt et al., 1990)	87	ICU patients	Fifty-four patients received cimetidine and 33 received placebo.	One (2%) of the 54 patients receiving cimetidine had upper GI hemorrhage and 7 (21%) of the 33 patients receiving placebo had upper GI hemorrhage (p = 0.002)	Only one patient (cimetidine) developed pneumonia during the study, but it was not considered to be related to drug therapy
(Martin et al., 1993)	131	Critically ill patients	Patients were randomized to receive cimetidine (n = 65) as an iv infusion of 50 to 100 mg/hr or placebo (n = 66).	Cimetidine patients demons trated significantly (p = .0001) higher mean intragastric pH (5.7 vs. 3.9), and had intragastric pH values at > 4.0 for a significantly (p = .0001) higher mean percentage of time (82% vs. 41%) than placebo patients.	Of the 56 cimetidine-infused patients and 61 placebo-infused patients who did not have pneumonia at baseline, no cimetidine-infused patient developed pneumonia while four (7%) placebo-infused patients devel oped pneumonia.

(Metz et al., 1993)	167	Patients with severe head injury, defined as having a Glasgow Coma Score of < or = 10	Ranitidine 6.25 mg/hr or saline placebo was administered by continuous infusion for a maximum of 5 days	Bleeding developed in 15 (19%) of 81 placebo-treated patients vs. three (3%) of 86 ranitidine-treated patients (p = .002)	Pneumonia occurred in 19% of the placebo-treated patients vs. 14% in the ranitidine treatment group
(Reusser et al., 1990)	40	Critically ill neurosurgical patients who required prolonged mechanical ventilation	19 patients were randomized to receive ranitidine plus antacids if necessary to maintain gastric pH at greater than or equal to 4. The remaining 21 patients were given no drug prophylaxis.	Gastric pH was significantly (p less than .001) higher in the treated group: 78% of pH readings were at greater than or equal to 4 as compared to 32% in the control group. No patient experienced clinically relevant upper GI bleeding.	Not-reported
(Gursoy et al., 2008)	75	ICU patients	Group C (n = 15), saline 100 mL; group O (n = 15), omeprazole 20 mg; group P (n = 15), pantoprazole 40 mg; group E (n = 15), esomeprazole 20	No statistically significant difference in gastric pH was seen among the groups before or 2, 4 or 6 hours after saline or PPI administration. At hours 2, 4 and 6, gastric pH in the pantoprazole, esomeprazole and rabeprazole groups increased significantly,	Not-reported

			mg; and group R (n = 15), rabeprazole 20 mg.		
(Chan et al., 1995)	101	Patients with nontraumatic cerebral disease (Neurosurgery)	Either ranitidine (50 mg every 6 hours) or placebo. 52 patients received ranitidine and 49 received a placebo preoperatively	30 developed overt GD bleeding; nine of these received ranitidine and 21 received a placebo. Ranitidine significantly reduced the incidence of bleeding ($p < 0.05$)	Not-reported

Discussion

Stress-related prophylaxis of GI bleeding has involved two ways: reduction of gastric acidity and mucosal protection. Mucosal protection has been done with prostaglandins [(42)]. However, in old trials prostaglandins were not as compelling as antacids and no way better than fake treatment, and have not been sought after. Most considers of GI bleeding in ICU patients have not been powered suitably to look at the chance of nosocomial pneumonia, and results have been contradicting, with most studies appearing no noteworthy distinction between treatment arms. Most thinks about of GI dying in ICU patients have not been fueled suitably to look at the hazard of nosocomial pneumonia, and results have been contradicting, with most considers appearing no critical distinction between treatment arms. A meta-analysis in 1991 proposed that acid-reducing drugs were really related with a somewhat diminished hazard of pneumonia [(4)]. A more later meta-analysis performed in 2000 proposed that there was no contrast between patients getting placebo and those accepting ranitidine or sucralfate, but comparisons of the dynamic specialists, appeared that ranitidine was related with an unassuming increment in hazard (OR 1.35, CI 1.07–1.7) 48).

In this review stress ulcer prophylaxis was not statistically significantly different from placebo or no prophylaxis in terms of GI bleeding, mortality and pneumonia in critically ill patients in the ICU [(11, 21, 30, 35, 36, 38)]. Clinical trials with adequate random sequence generation, allocation concealment and blinding did not support these findings. Consequently, an inflated point estimate in the analysis can be suspected with no subgroup differences. Considering the high risk of bias and sparse data, a genuine benefit of SUP on the risk of GI bleeding in adult ICU patients may be addressed.

The mortality analysis revealed neither benefit nor harm of SUP with all agents. The analysis confirmed the finding in the conventional meta-analysis. Critically, appeared that it is improbable that SUP will result in a relative mortality diminishment of 20 % in the event that encourage trials are conducted in adult ICU patients. Concurring to the chance of bias appraisal , all trials had a high hazard of bias. Hence, investigations may be affected by the destitute quality of existing trials, which could result in inflated point estimates and in this way, make

elucidation troublesome. Moreover, increments the chance of overestimating the impact of SUP [43]. No measurably noteworthy advantage or hurt of stress ulcer prophylaxis on the hazard of hospital-acquired pneumonia. The generally high chance of bias in the trials warrants cautious translation of the results since of an expanded chance of falsely expanded estimates.

We prohibited trials just announcing non-patient-centered results in arrange to make the results important for clinical practice. Trials with satisfactory versus insufficient irregular grouping generation, assignment concealment and blinding might have brought about in spurious discoveries. Be that as it may, the heterogeneity of the included trials was significant. Most of the included trials have been conducted in high-risk patients, which must be kept in intellect when interpreting the results.

In general, heterogeneity did not appear to be an enormous issue. Connection to other audits and suggestion for future inquire about No past efficient audits have been distributed on PPIs versus fake treatment or no prophylaxis, and as it were a few orderly surveys have assessed H2RAs versus placebo or no prophylaxis. In 2010, Marik and colleagues recommended that in patients who are encouraged enterally, SUP does not diminish the chance of GI dying from push ulcers and may indeed increment the hazard of pneumonia and death [44]. These issues may have contributed to the inconsistencies in connection to the present review. In 1996, Cook and colleagues conducted a careful and comprehensive precise audit of SUP in critically sick patients [8]. However, the utilization of PPIs in the treatment of peptic ulcer illness started after 1996.

Conclusions

This review concluded that the most effective medications in control of gastrointestinal bleeding and gastric pH was rantidine followed by cimetidine. However, the least reported bleeding rate was reported with antacid medications.

Conflict of interests

The author declared no conflict of interests.

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