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A comparative study to assess effect of discontinuation of proton pump inhibitors (PPIs) after 48 hours on admission in critical care unit on incidents of nosocomial pneumonia

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Abstract
Aim and Background: The aim of this study was to determine whether the use of gastric acid-suppressive agents increases the risk of NP in Critical care.
Methods: The methodology adopted for experimenting with the effectiveness of PPI use in two study groups and evaluated the result with the help of APACHE II and CPIS calculator. The researcher divided patients into two groups after initiation of enteral feeding on a random basis, one group of patients with PPI and another group without PPI. Both of the groups were evaluated for the risk of suspected HAI with the guidance of APACHE-II, GCS, and CPIS.
Results: Overall, out of 60 patients, further divided into two groups Pre-operative ICU mortality for patients from PPI group (11.13) was lower than patients from No PPI group (12.77). Mean Post-operative ICU mortality for patients from the PPI group (5.43) was lower than patients from No PPI group (6.77). Mean APACHE II score for patients from PPI group (7.83) was lower than patients from the No PPI group (9.13). CPIS I score for patients from PPI group (1.83) was lower than patients from No PPI group (2.13). From findings, an unpaired t-test was done to compare. There was no significant difference between the two groups (p>0.05) indicating very few cases of NP.
Conclusion: In short, prior use of a PPI did not correlate increase in the risk of developing NP. Apart from PPI, there are a plethora of treatments, and nursing care received by critical patients with various physical illnesses and symptoms.

Keywords: Proton pump inhibitor, clinical pulmonary infection score, nosocomial pneumonia

Introduction
The goal of this study was to determine whether the use of gastric acid-suppressive agents increases the risk of nosocomial pneumonia (NP) in a medical intensive care unit/ Critical Care population. Several studies have stated that pharmacological stress ulcer prophylaxis with sucralfate is safer than H2 blockers respecting VAP. Proton pump inhibitors are more effective in causing community-acquired pneumonia (CAP) and HAP in patients without mechanical ventilation. Despite their good safety profile, PPIs have potential adverse effects, yet they are often overprescribed and without a clear indication.
This risk was higher with the administration of sedatives or neuromuscular blockers, increased disease severity, and placement of a central venous catheter. This intervention may be beneficial for both patients and the hospital. The rate of hospital-acquired nosocomial Infection Rate may be reduced without increasing the risk of antimicrobial resistance.

Aim and objective
The aim of this study was to determine whether the use of gastric acid-suppressive agents increases the risk of nosocomial pneumonia (NP) in the Critical care unit population.

Materials and Methods
This study was conducted to find out Holding PPIs (Proton Pump Inhibitors) after 48 hours of hospitalization among patients admitted in Critical Care Unit of Krishna Hospital, Karad will help to reduce Nosocomial Pneumonia (NP)/VAP Rate.

Stopping PPIs will reduce adverse effects associated with Proton Pump Inhibitors. Assessment of Acute Physiology and Chronic Health Evaluation score (APACHE II) is a severity-of-disease classification system (Knaus *et al*., 1985) [17], one of several ICU scoring systems. It is applied within 24 hours of admission of a patient to an intensive care unit (ICU): an integer score from 0 to 71 is computed based on several measurements; higher scores correspond to more severe disease and a higher risk of death. The advantage of the APACHE is that it can be used throughout the patient's hospital course in monitoring the patient's response to therapy, especially PPI drugs. The clinical pulmonary infection score evaluates objective data in patients suspected of ventilator-associated pneumonia (VAP) and stratifies the risk of a positive diagnosis.

Clinical pulmonary infection score - CPIS calculator helps the clinician decide whether the patient in question would benefit from a pulmonary culture testing. By using the CPIS, unnecessary antibiotic administration due to treatment of colonized patients is prevented and the incidence of misdiagnosed VAPs is lowered. The score also helps clinicians determine which patients may benefit from pulmonary culture testing. This means that the administration of the score not only facilitates diagnosis but also helps reduce unnecessary tests and antibiotic administration, thus reducing the incidence of misdiagnosed VAP. Each of the six variables in the score is awarded a number of points, depending on its predictive value and contribution towards the risk of a positive diagnosis. The total CPIS varies between 0 and 12, where 0 means normal function with little risk of VAP and 12 means high risk.

The original study introduces a cut-off value at 6 points, where scores below 6 indicate a low risk of pulmonary infection while scores of 6 and above indicate a high likelihood of VAP diagnosis.

A comparative study was carried out of a total of 66 samples from January 2021 to October 2021 by using a random sampling method by using experimental design.

Methodology and Procedure

Step 1: Methodology adopted: An experimenting method with respect to the effectiveness of proton pump inhibitors in two study groups.

Step 2: Identification of target and accessible population: - The researcher identified 200 bedded multi-critical care units that included 60 critically ill patients from January 2021 to October 2021 at Krishna Hospital, Karad.

Step 3: Research Design: - The researcher performed an experimental study with a non-probability purposive sampling technique.

Step 4: The researcher divided patients into two groups after initiation of enteral feeding on a random basis, one group of patients with PPI and another group without PPI.

Step 5: Both of the groups were evaluated the risk of suspected HAI with the guidance of medical classification tools, APACHE-II, GCS, and CPIS at the time of admission and followed by consequent times irrespective of their diagnosis and treatment.

Results

Section A: Distribution of Demographic variables of critical care patients

Table 1: Frequency and Percentage distribution of demographic variables on subjects in study group (n=60)

Sr. No.	Demographic Variables	Group				Total	
		PPI		No PPI			
		F	%	F	%	F	%
1	**Age**						
	< 19 years	7	23.33	8	26.67	15	25.00
	31-40 years	7	23.33	4	13.33	11	18.33
	41-50 years	2	6.67	2	6.67	4	6.67
	51-60 years	6	20.00	3	10.00	9	15.00
	61-70 years	8	26.67	13	43.33	21	35.00
2	**Gender**						
	Males	19	63.33	19	63.33	38	63.33
	Females	11	36.67	11	36.67	22	36.67
3	**Religion**						
	Hindu	30	100.00	30	100.00	60	100.00
4	**Residential Background**						
	Urban	5	16.67	3	10.00	8	13.33
	Rural	25	83.33	27	90.00	52	86.67
5	**Marital status**						
	Married	24	80.00	23	76.67	47	78.33
	Unmarried	6	20.00	7	23.33	13	21.67
6	**Type of Family**						
	Joint	12	40.00	15	50.00	27	45.00
	Nuclear	18	60.00	15	50.00	33	55.00
7	**Education**						
	Higher secondary and higher studies	8	26.67	2	6.67	10	16.67
	Secondary	5	16.67	8	26.67	13	21.67
	Primary	11	36.67	12	40.00	23	38.33
	Illiterate	6	20.00	8	26.67	14	23.33
8	**Economic Status**						
	Low	11	36.67	8	26.67	19	31.67
	Average	19	63.33	22	73.33	41	68.33

9	**Occupation**						
	Housewife	10	33.33	11	36.67	21	35.00
	Not known	20	66.67	19	63.33	39	65.00
	Total	30	50.00	30	50.00	60	100.0

Table 2: Incidence of patients who had an Acute Physiology and Chronic Health Evaluation score (APACHE II) of less than 25. (n=60)

Apache II	PPI		No PPI		Total	
	Frequency	%	Frequency	%	Frequency	%
0	1	3.3	0	0.0	1	1.7
1	1	3.3	0	0.0	1	1.7
2	3	10.0	1	3.3	4	6.7
3	2	6.7	2	6.7	4	6.7
4	3	10.0	2	6.7	5	8.3
5	2	6.7	2	6.7	4	6.7
6	2	6.7	3	10.0	5	8.3
7	4	13.3	5	16.7	9	15.0
8	3	10.0	3	10.0	6	10.0
9	1	3.3	1	3.3	2	3.3
10	1	3.3	1	3.3	2	3.3
11	1	3.3	2	6.7	3	5.0
12	1	3.3	3	10.0	4	6.7
14	0	0.0	1	3.3	1	1.7
15	2	6.7	1	3.3	3	5.0
17	1	3.3	0	0.0	1	1.7
20	0	0.0	1	3.3	1	1.7
21	0	0.0	1	3.3	1	1.7
23	1	3.3	0	0.0	1	1.7
24	1	3.3	1	3.3	2	3.3
Total	30	100.0	30	100.0	60	100.0

From table no. 2, it was clear that all patients from both groups 30 (100%) admitted in the critical care unit of selected hospital had APACHE II score <25.

Section C: Findings related to the calculation of Clinical Pulmonary Infection Score (CPIS) to confirm VAP/NP (if a score of 7 out of 14 need to obtain).

Table 3: Clinical Pulmonary Infection Score (CPIS) I to confirm VAP/NP (if a score of 7 out of 14 need to obtain). (n=60)

CPIS I	PPI		No PPI		Total	
	Frequency	%	Frequency	%	Frequency	%
0	9	30.0	10	33.3	19	31.7
1	3	10.0	4	13.3	7	11.7
2	11	36.7	7	23.3	18	30.0
3	3	10.0	5	16.7	8	13.3
4	2	6.7	0	0.0	2	3.3
6	1	3.3	2	6.7	3	5.0
7	1	3.3	0	0.0	1	1.7
9	0	0.0	1	3.3	1	1.7
10	0	0.0	1	3.3	1	1.7
Total	30	100.0	30	100.0	60	100.0

Table 3 depicts that according to CPIS I score, there were 1(3.3%) patients from PPI group and 2 (6.6%) patients from no PPI group who suffered from VAP/N

Table 4: Clinical Pulmonary Infection Score (CPIS) II to confirm VAP/NP (if a score of 7 out of 14 need to obtain). (n=60)

CPIS II	PPI		No PPI		Total	
	Frequency	%	Frequency	%	Frequency	%
0	9	30.0	9	30.0	18	30.0
1	3	10.0	4	13.3	7	11.7
2	8	26.7	9	30.0	17	28.3
3	4	13.3	5	16.7	9	15.0
4	2	6.7	0	0.0	2	3.3
5	1	3.3	1	3.3	2	3.3
6	1	3.3	1	3.3	2	3.3
7	1	3.3	0	0.0	1	1.7
9	0	0.0	1	3.3	1	1.7
10	1	3.3	0	0.0	1	1.7
Total	30	100.0	30	100.0	60	100.0

Table 4 depicts that according to CPIS II score, there were 2(6.6%) patients from PPI group and 1 (3.3%) patients from no PPI group who suffered from VAP/NP.

Table 5: Clinical Pulmonary Infection Score (CPIS) III to confirm VAP/NP (if a score of 7 out of 14 need to obtain). (n=60)

CPIS III	PPI		No PPI		Total	
	Frequency	%	Frequency	%	Frequency	%
0	9	30.0	9	30.0	18	30.0
1	3	10.0	3	10.0	6	10.0
2	9	30.0	10	33.3	19	31.7
3	3	10.0	5	16.7	8	13.3
4	2	6.7	1	3.3	3	5.0
5	1	3.3	0	0.0	1	1.7
6	1	3.3	1	3.3	2	3.3
7	1	3.3	0	0.0	1	1.7
9	0	0.0	1	3.3	1	1.7
10	1	3.3	0	0.0	1	1.7
Total	30	100.0	30	100.0	60	100.0

Table 5 depicts that according to CPIS III score, there were 2 (6.6%) patients from PPI group and 1 (3.3%) patients from no PPI group who suffered from VAP/NP.

Section D: Findings related to the comparison between patients with Proton Pump Inhibitors (PPI) till discharge and study group stopping of Proton Pump Inhibitors (PPI) after 48 hours.

Table 6: Comparison between patients with Proton Pump Inhibitors (PPI) till discharge and study group stopping of Proton Pump Inhibitors (PPI) after 48 hours.

Group Statistics	Group	N	Mean	Std. Deviation	t statistic	p value
Pre-operative ICU mortality	PPI	30	11.13	10.08	0.62	0.54
	No PPI	30	12.77	10.37		
Post-operative ICU mortality	PPI	30	5.43	7.45	0.66	0.51
	No PPI	30	6.77	8.24		
APACHE II	PPI	30	7.83	5.98	0.89	0.38
	No PPI	30	9.13	5.38		
CPIS I	PPI	30	1.83	1.76	0.53	0.60
	No PPI	30	2.13	2.58		
CPIS II	PPI	30	2.23	2.37	0.59	0.56
	No PPI	30	1.90	2.02		
CPIS III	PPI	30	2.20	2.37	0.53	0.60
	No PPI	30	1.90	1.97		

Unpaired t test was done to compare between patients with Proton Pump Inhibitors (PPI) till discharge and study group stopping of Proton Pump Inhibitors (PPI) after 48 hours. There was no significant difference between two groups for any of the scores (p>0.05).

- Mean Pre-operative ICU mortality for patients from PPI group (11.13) was lower than patients from No PPI group (12.77).
- Mean Post-operative ICU mortality for patients from PPI group (5.43) was lower than patients from No PPI group (6.77).
- Mean APACHE II score for patients from PPI group (7.83) was lower than patients from No PPI group (9.13).
- Mean CPIS I score for patients from PPI group (1.83) was lower than patients from No PPI group (2.13).
- Mean CPIS II score for patients from PPI group (2.23) was higher than patients from No PPI group (1.90).
- Mean CPIS III score for patients from PPI group (2.20) was higher than patients from No PPI group (1.90).

Discussion

The chapter attempts to discuss the significant findings. This chapter discusses with the findings of data analysis in accordance with the objectives and stated hypotheses of the present study. The statement of problem was "A comparative study to assess effect of discontinuation of proton pump inhibitors (PPIS) after 48 hours on admission in critical care unit on incidents of naso comial pnumonia".

Findings of the study

The findings of the study were analyzed by using frequency, percentage distribution and unpaired test to find out the level of significance and proving the hypothesis.
Major findings were as follows:

Demographic Variables

- Among 30 patients of PPI group, 7 (23.33%) of them were in the age group <19 years, 7 (23.33%) of them were in the age group 31-40 years, 2 (6.67%) were there in the age group of 41-50 years and 6 (20%) were in the age group of 51-60 years. 8 (26.67%) were above 60 years of age. Among 30 patients of no PPI group, 8 (26.67%) of them were in the age group <19 years, 4 (13.33%) of them were in the age group 31-40 years, 2 (6.67%) were there in the age group of 41-50 years and 3 (100%) were in the age group of 51-60 years. 13 (43.33%) were above 60 years of age.
- Among 30 critical care patients of PPI group, 19 (63.33%) of them were males and 11 (26.67%) were females. Among 30 critical care patients of no PPI group, 19 (63.33%) of them were males and 11(26.67%) were females.
- Among 30 critical care patients of PPI group, all 30(100%) of them were Hindu. Among 30 critical care patients of no PPI group, all 30 (100%) of them were Hindu.
- Among 30 critical care patients of PPI group, 5 (16.67%) of them were living in urban area and 25 (83.33%) were from rural area. Among 30 critical care patients of no PPI group, 3 (10%) of them were living in urban area and 27 (90%) were from rural area.
- Among 30 critical care patients of PPI group, 24 (80%) of them were married and 6 (20%) were unmarried. Among 30 critical care patients of no PPI group, 23 (76.67%) of them were married and 7 (23.33%) were unmarried.

- Among 30 critical care patients of PPI group, 12 (40%) of them were from joint family and 18(60%) were from nuclear family. Among 30 critical care patients of no PPI group, 15 (50%) of them were from joint family and 15 (50%) were from nuclear family.
- Among 30 critical care patients of PPI group, 8 (26.67%) of them have completed higher secondary and higher studies, 5 (16.67%) have completed secondary education. 11 (36.67%) have completed primary education. 6 (20%) were illiterate. Among 30 critical care patients of no PPI group, 2 (6.67%) of them have completed higher secondary and higher studies, 8 (26.67%) have completed secondary education. 12 (40%) have completed primary education. 8 (26.67%) were illiterate.
- Among 30 critical care patients of PPI group, 11 (36.67%) of them were from low economic status and 19(63.33%) were from average economic status. Among 30 critical care patients of no PPI group, 8 (26.67%) of them were from low economic status and 22 (73.33%) were from average economic status.
- Among 30 critical care patients of PPI group, 10 (33.33%) of them were housewife and 20 (66.67%) patients occupation was not known. Among 30 critical care patients of no PPI group, 11 (36.67%) of them were housewife and 20 (51.28%) patients occupation was not known.

Findings related to patients who had an Acute Physiology and Chronic Health Evaluation score (APACHE II) of less than 25

All patients from both groups 30 (100%) admitted in the critical care unit of selected hospital had APACHE II score <25.

Findings related to Clinical Pulmonary Infection Score (CPIS) to confirm VAP/NP (if a score of 7 out of 14 need to obtain)

According to CPIS I score, there were 1 3.3%) patients from PPI group and 2 (6.6%) patients from no PPI group who suffered from VAP/NP.

According to CPIS II score, there were 2 (6.6%) patients from PPI group and 1 (3.3%) patients from no PPI group who suffered from VAP/NP.

According to CPIS III score, there were 2 (6.6%) patients from PPI group and 1 (3.3%) patients from no PPI group who suffered from VAP/NP.

Findings related to comparison between patients with Proton Pump Inhibitors (PPI) till discharge and study group stopping of Proton Pump Inhibitors (PPI) after 48 hours

Unpaired t test was done to compare between patients with Proton Pump Inhibitors (PPI) till discharge and study group stopping of Proton Pump Inhibitors (PPI) after 48 hours. There was no significant difference between two groups for any of the scores (p>0.05).

- Mean Pre-operative ICU mortality for patients from PPI group (11.13) was lower than patients from No PPI group (12.77).
- Mean Post-operative ICU mortality for patients from PPI group (5.43) was lower than patients from No PPI group (6.77).
- Mean APACHE II score for patients from PPI group (7.83) was lower than patients from No PPI group (9.13).
- Mean CPIS I score for patients from PPI group (1.83) was lower than patients from No PPI group (2.13).

Organization of Review of Literature

The results were supported by many of the studies.

According to A study conducted by Mathieu Beaulieu MSc, (2008) on to determine whether the use of gastric acid-suppressive agents increases the risk of nosocomial pneumonia (NP) in a medical intensive care unit population. The risk for patients who received proton-pump inhibitors (adjusted hazard ratio [AHR] 0.63; 95% CI 0.39-1.01) was not significantly different than in non-exposed patients.

Prior use of a proton-pump inhibitor did not correlate with a significant increase in the risk of developing NP. This risk was higher with the administration of sedatives or neuromuscular blockers, increased disease severity, and placement of a central venous catheter.

Mathieu Beaulieu, David Williamson, Carole Sirois Jean Lachaine, Do proton-pump inhibitors increase the risk for nosocomial pneumonia in a medical intensive care unit? Journal of Critical Care Volume 23, Issue 4, December 2008, Pages 513-518

A study conducted by Alan B R Thomson, Michel D Sauve, Narmin Kassam, Holly Kamitakahara published in PUB MED on dated 2010 with subject of Safety of the long-term use of proton pump inhibitors. It stated that, the proton pump inhibitors (PPIs) as a class are remarkably safe and effective for persons with peptic ulcer disorders

PPIs may result in rebound symptoms requiring further and even continuous PPI use for suppression of symptoms. As with all medications, the key is to use PPIs only when clearly indicated, and to reassess continued use so that long-term therapy is used judiciously. Thus, in summary, the PPIs are a safe class of medications to use long-term in persons in whom there is a clear need for the maintenance of extensive acid inhibition.

Thomson, Alan & Sauve, Michel & Kassam, Narmin & Kamitakahara, Holly. (2010). Safety of the long-term use of proton pump inhibitors. World journal of gastroenterology: WJG. 16. 2323-30.

A study conducted by Emmae N Ramsay and published on 24 June 2013- Proton pump inhibitors and the risk of pneumonia: a comparison of cohort and self-controlled case series designs. It showed an increased risk of hospitalizations for pneumonia in the three defined risk periods following initiation of proton pump inhibitors compared to baseline. With the highest risk in the first 1 to 7 days. Exposure to a proton pump inhibitor increases the likelihood of being admitted to hospital for pneumonia, with the risk highest in the first week of treatment.

Ramsay, E.N., Pratt, N.L., Ryan, P. *et al.* Proton pump inhibitors and the risk of pneumonia: a comparison of cohort and self-controlled case series designs. BMC Med Res Methodol 13, 82 (2013). https://doi.org/10.1186/1471-2288-13-82

To conclude, VAP is a common nosocomial infection occurring in mechanically ventilated patients.

Summary
The primary aim of the study was to assess effect of discontinuation of proton pump inhibitors (PPIs) after 48 hours on admission in critical care unit on incidents of nosocomial pneumonia

The objectives of the study were
1. To assess patients who had an Acute Physiology and Chronic Health Evaluation score (APACHE II) of less than 25.
2. To calculate Clinical Pulmonary Infection Score (CPIS) to confirm VAP/NP (if a score of 7 out of 14 need to obtain).
3. To compare between patients with Proton Pump Inhibitors (PPI) till discharge and study group stopping of Proton Pump Inhibitors (PPI) after 48 hours on incidence of Nosocomial Pneumonia (NP) or after initiation of enteral feeding.

The main study was conducted in Krishna Institute of Medical Sciences in Deemed to Be University Karad among 60 patients on mechanical ventilator for more than 48 hours were enrolled for the study. The samples were assigned using a purposive sampling technique.
Semi structured questionnaire was used to collect data. Questionnaire consists of socio demographic data sheet which includes variables like age, gender, religion, residential background, marital status, education, economic status and occupation. Checklist was used for assessing risk factors related to Ventilator associated pneumonia (VAP). Clinical pulmonary infection score (CPIS) for diagnosing Ventilator-associated pneumonia on clinical background was used.
The collected data was organized, tabulated, analyzed and interpreted using descriptive and inferential statistics. Descriptive Statistics used were frequencies, percentage to describe the data. Inferential Statistics used to test the hypothesis and to draw conclusions. Unpaired t test was done to compare between patients with Proton Pump Inhibitors (PPI) till discharge and study group stopping of Proton Pump Inhibitors (PPI) after 48 hours. The findings were organized and presented in four parts with tables and figures.

Conclusion
- Long time use of a proton-pump inhibitor (only) did not correlate with a significant increase in the risk of developing Nosocomial Pneumonia (NP).
- There was no significant difference between the two groups for any of the scores (p>0.05) indicating very few cases of nosocomial pneumonia in Krishna hospital, Karad in the selected group.

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