In the name of God

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Comparison of Oral Pantoprazole and Famotidine on Gastric Volume and Ph in Elective Surgeries

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Abstract:

Objectives: Perianesthesia aspiration is a threatening side effect, whose severity depends on pH and volume of aspirated gastric juice. Because of the loss of consciousness while anesthesia, the protective reflexes disappear and expose the person in the risk of aspiration. Pharmacological attempts have been made to eliminate the risk of pulmonary aspiration. The aim of this study was to compare oral pantoprazole and famotidine on gastric volume and pH in elective surgeries.
Methods: In a double-blind randomized clinical trial, 120 candidates of elective surgery were randomized into 3 groups (control or C, pantoprazole or P and famotidine or F groups). The patients in group C ،P and F were given placebo ،pantoprazole 40mg and famotidine 40mg orally at 11 pm a night before surgery respectively. After induction of anesthesia, gastric contents were aspirated and analyzed for the pH and volume.
Results: PH values were 2.87 ± 0.92 in group C, 4.53 ± 1.29 in group P and 3.79 ± 1.97 in group F. There was statistical difference between groups C, P and F ($P < 0.05$). The results showed a considerable decrease in the gastric volume in groups P and F comparing to group C. ($P < 0.05$).
Conclusion: We concluded that oral pantoprazole is effective in reducing gastric pH comparing to famotidine and placebo،and famotidine is effective in reducing gastric volume comparing to pantoprazole.

Keywords: Gastric pH, Pantoprazole, Famotidine,

Introduction:

Aspiration syndrome is still a threatening complication during Anesthisia and its severity depends on PH and Volume of gastric fluids aspirated and it is associated with mortality and pulmonary morbidity after surgery.(1-3) General anesthesia is a major risk factor due to lack of airway protective reflexes during anesthesia which makes the patients vulnerable to aspiration.

Pharmacologic preventive approach is the basis of airway protection.(4) Gastric fluid volume of more than 0.4 mg/kg and PH less than 2.5 increases the risk of aspiration.(5) Regurgitation and vomiting are associated with other complications such as laryngospasm and bronchospasm in addition to aspiration. In case of PH less than 2.5, aspiration may lead to Mendelson syndrome. Mendelson described etiology of pulmonary aspiration in 1946.(6)

A lot of patients are in risk of aspiration including patients who are not NPO (nil per os), patients with diabetes, high ICP (intra cranial pressre), hiatus hernia, gastrointestinal obstruction, obesity, lithotomic and head down positions and laparoscopic surgeries and the last but not the least, the use of LMA (laryngeal mask airway) instead of tracheal tube in airway management increases aspiration risk due to gastric insufflations.(7)

Pharmacologic preventive measures include H2 receptor antagonist, Proton pump inhibitors (PPI) and antacids to reduce or eliminate the risk of pulmonary aspiration through decreasing volume and acidity of gastric fluid.(6) Pantoprazole is a long acting PPI which is used in oral and intravenous forms to treat peptic ulcer and other acid dyspepsia of GI tract and has been proved not to interact with other antacids, anti febrile, Caffeine, Carbamazepine, Diclofenac, nifedipine, warfarin, phenytoin and …(8) No repeated doses are needed in 24 hours if 40 mg tablets are used. Famotidine is a long acting H2 receptor blocker which usually does not interact with other medications and has rare side effects and long half life. Hence the goal of this study is to compare the effect of single 40 mg oral famotidine and pantoprazole dose the night before operation on reducing gastric fluid volume and acidity in elective surgeries. PH > 2.5 and gastric fluid volume < 0.4 during anesthesia induction decrease aspiration risk. Knowing that gastric fluid secretions increase and gastric emptying delays the night before operation due to stress, probably administration of these medications the night before operation is more efficient than before induction in reducing gastric fluid volume and acidity. Considering long acting characteristic of Famotidine, not having medical interactions and side effects compared to other H2 antagonists and the long acting characteristic to Pantoprazole compared to other PPIs, the night before surgery dose seems to be sufficient. This study will clarify which of the studied medications are effective in reducing gastric fluid volume and acidity.

Route and Method:

This study is a placebo- control double blind prospective randomized clinical trial. The sample volume was 120 people, all adults in the age range of 16-65 years and physical condition of ASA (American society of an-

esthesiologist) I and II from both gender candidates for elective surgery under general anesthesia.

Exclusion Criteria:

patients having upper GI (gastrointestinal) dyspeptic syndromes, previous gastric or intestinal operation, confirmed hiatus hernia and obese patients (body mass index) BMI > 30 kg/m2, Patients being treated by medications affecting secretions and movements of gastrointestinal tract, patients having addiction, patients having had difficult intubation, patients having partial or complete intestinal obstruction, patients with diabetes mellitus and existence of biliary salts or blood in contents aspirated from stomach. Studied groups' description:

Group C or placebo or control: 40 patients were in this group and the goal of this group is to determine gastric fluid PH and volume in candidates for elective surgery under general anesthesia and tracheal intubation. In this group, placebo (a small piece of starch) was placed in an empty capsule and given to the patients with 20 ml of water at midnight the night before operation.

Group P or Pantoprazole: 40 Patients were in this group, Pantoprazole 40 mg was placed in an empty capsule with the same color without being crushed or halted and was given to the patients at midnight the night before operation.

Group F or Famotidine: 40 Patients were in this group, famotidine 40mg was placed in an empty capsule with the same color without being crashed of halted and given to the patients at midnight the night before operation.

A person who did not have any role in recording, patient evaluation and anesthesia placed medications and placebos in the capsules with same color and placed each in a bag coding them: medication 1, medication2 and medication 3. The night before operation, the patients were asked to select one of the bags (Randomization). The person draining stomach and determining gastric fluid PH and volume was unaware of premedication type and the patient was also unaware of medication he or she was given (double blind). In the end and after recording, premedication type was revealed.

The patients in all three groups underwent general anesthesia under similar standard monitoring in operation room. A tracheal tube lubricated using gel was inserted esophagus orally through F 18 NGT (nasogastric catheter) to enter stomach when anesthesia was deep enough. To measure appropriate nasogastric tube length, the distance between xyphoid process to earlobe and from earlobe to nose were measured and marked on the tube. After tube entering stomach, its placement in stomach was confirmed using 20 ml syringe and air. Gastric contents were aspirated as much as possible using 60 ml syringe in supine and trendelenberg positions associated with epigastrium pressing and then in right lateral position followed by left lateral position. Suctioning was done while NGT was being extracted. The blind aspiration volume underestimated true total gastric volume by an average of 14.7 (17) ml. Although in this method probably not all gastric contents could be emptied, as this is the same method in all pa-

tients of both groups, it would not affect results.(9) This method is simple, cheep, and easy to perform and has been widely used in similar studies. Aspirated contents were measured in biochemistry laboratory by an expert regarding acidity using PH meter. Volumes were measured by a syringe. Volume less than 1 ml was considered as empty stomach. Hay's sulphur quality test was used to determine bile existence in gastric fluid. To perform this test, gastric fluid less than 1 ml is enough. In this test, sulphur powder is added to gastric fluid. Sulphur deposits if there are biliary salts in gastric fluid and deposition degree depends on bile content. NPO duration and gastric fluid PH and volume were recorded. Patients having PH < 2.5 and gastric fluid volume more than 25 ml are at risk of aspiration.

Data analysis Method: Obtained data including demographic information, operation type, gastric fluid volume and PH and premedication were analyzed using SPSS. 12 software and results were demonstrated by percentage and mean ± SD.

To compare weight, height, age, Volume, PH, NPO duration and BMI two tailed student test was used. To compare ASA, Aspiration risk fisher's exact test was used. To analyze quantitative data between three groups, one way Anova test was used and to compare qualitative data between three groups Chi- square test was used. $P < 0.05$ was considered significant.

Results:

120 adult candidates for elective surgery from three wards of ENT, neurosurgery and urology were studied.

Demographic information of the patients, NPO duration and BMI are brought in table 4-1 and there was no significant difference between groups. There was no significant difference between three groups regarding age, gender, ASA, height, BMI and NPO duration in our study, From 120 patients, 117 cases had aspirable secretions and in 3 cases secretions could not be aspirated from which 1 case was in pantoprazole group and 2 other cases were in famotidine group. In patients of placebo group secretions were aspirable. From 117 patients with aspirable contents 27 patients had biliary salts in their gastric fluid and were distributed equally between three groups. Cases in which gastric fluid was mixed with biliary salts were not included in statistical calculations of determining pulmonary aspiration risk.

In our study deodenogastric reflux significantly influenced gastric fluid volume in all three groups by increasing it. Gastric fluid volume without bile (14, 23±7.2) and gastric fluid volume mixed with bile (28±21.7) in pantoprazole group showed significant difference (P=0.001). In Famotidine group, gastric fluid volume with bile (10.79 ± 7.1) and gastric fluid volume mixed with bile (27.44 ± 23.55) had significant difference (P = 0.002). There was also a significant difference in placebo group (P = 0.035). However, There was no significant difference between both groups regarding gastric volume and PH. Gastric fluid PH was 4.56 ± 0.97 in gastric fluid without bile and 4.44 ± 2.12 in gas-

tric fluid with bile in pantoprazole group which was not a significant difference (P = 0.808). PH in famotidine group was amlordingly 3.11 ± 0.88, 3.22 ± 01.01with P = 0.209 which was not significant. This difference was significant in placebo group. In this study there was a significant difference between gastric fluid volume in two groups of pantoprazole (14.23 ± 7.2) and famotidine (10.72 ± 7.1) groups which is suggestive of better efficacy of famotidine in reducing gastric fluid volume.gastric content without bile in pantoprazole and famotidine groups showed a significant difference with placebo group. Total gastric fluid volume (with and without bile) showed significant difference between three groups: pantaprazole group 17.5 ± 13.39 famotidine group 14.46 ± 14.789 and placebo group 36.61 ± 19.7. In this study, volumes less than 25 ml and more than 25 ml were evaluated in all three groups and in pantoprazole group there were 34 cases (85%) with volume less than 25 ml and 6 cases (15%) with volume more than 25 ml. In Famotidine group there were 32 cases (80%) with volume less than 25 ml and 8 cases (20%) with volume more than 25 ml which shows that there is no significant difference between two famotidine and pantoprazole groups regarding gastric fluid volume less than 25 ml (P = 0.56) whereas there was significant difference between pantoprazole and placebo groups (P = 0.0019) and also famotidine and placebo groups (P = 0.0013) regarding total volume less than 25 ml. Total gastric fluid PH was reported 4.53 ± 1.29 in pantoprazole group, 3.89 ± 0.97 in famotidine group and 2.87 ± 0.99 in placebo group.

There was a significant difference comparing PH in pantoprazole and famotidine groups (P = 0.035). This difference was also significant comparing PH in pantaprazole, famotidine and placebo groups (P = 0.000). There was also significant difference in all three groups regarding PH of gastric fluid without bile. In pantoprazole group, PH below 2.5 was reported in 6 People (12.87%) and more than 2.5 in 33 people (87.2%) In famotidine group PH less than 2.5 was reported in 7 people (18.4%) and more than 2.5 in 31 people (81.6%) and in placebo group 19 (17.5%) people were reported to have PH less than 2.5 and 21 (52.2%) people more than 2.5. There was no significant difference comparing PH Less than 2.5 in pantoprazole and famotidine groups however there was a significant difference in both pantoprazole and famotidine groups and placebo group regarding PH.

To determine pulmonary aspiration risk based on a defined criteria (PH > 2.5 and volume < 25 ml), PH < 2.5 and volume > 25ml in non biliary secretions were measured. Patients having both PH < 2.5 and volume > 25 ml are at pulmonary aspiration risk. 6 people in pantoprazole group (20%), 52 people in famotidine group (17%) and 13 people in placebo group (41%) had PH < 2.5 in non biliary secretions. 5 people (16%) in pantoprazole group, 6 people (20%) in famotidine group and 28 people (90%) in placebo group had volumes more than 25 ml in non biliary secretions. There were 4 patients with PH < 2.5 and volume > 25 ml in non

biliary secretions (13%) in pantoprazole group, 5 people (17%) in famotidine group and 13 people (41%) in placebo group. There was no significant difference between pantoprazole and famotidine groups regarding aspiration risk (P = 0.67). However There were significant differences between pantoprazole and famotidine groups and placebo group accordingly P = 0.02 and P = 0.03 respectively.

Table 1. Physical Characteristics of Patients

Variable	Group P	Goup F	Group C	P Value
Age	3/14 ± 35/37	15/13 ± 35/35	5/13 ± 35/38	299/0
Weight(kg)	79/8 ± 15/74	98/7 ± 72/72	48/8 ± 95/71	1029/0
Height(cm)	98/8 ± 95/171	29/7 ± 95/169	36/7 ± 85/170	7507/0
Male (72%)	(73%) 29	(75%) 30	(68%) 27	48/0
Female (28%)	(27%) 11	(25%) 10	(32%) 13	
BMI	23/2 ± 3/26	6/2 ± 47/26	3/2 ± 8/26	2002/0
ASA				
Class I	(80%) 32	(80%) 32	(70%) 28	
Class II	(20%) 8	(20%) 8	(30%) 12	
NPO time(min)	15/130 ± 61/824	5/125 ± 5/830	2/137 ± 52/829	8463/0

Table 2. Features of Gastric Content in 3 Groups

Variable	Group P	Group F	Group C
Samples mixed with bile(ml)	(9) 7/21 ± 28	(9) = n 55/23 ± 44/27	(9) = n 5/14 ± 44/78
Samples with no bile	(30) 2/7 ± 23/14	(29) 1/7 ± 79/10	(31) 5/19 ± 03/33
PV	001/0	002/0	035/0
Ph samples with no bile	97/0 ± 56/4	88/0 ± 44/3	78/0 ± 73/2
Ph samples with bile	12/2 ± 44/4	07/0 ± 22/3	2/1 ± 33/3
PV	808/0	209/0	087/0
Samples with no gastric content	1	2	0

Table 3. Comparison of Volume and PH between Groups (Content with and without Bile)

Volume	Group P	Group F	Group C
Gastric content volume	39/13 ± 5/17	46/14 ± 789/14	7/19 ± 61/36
PH of gastric content	29/1 ± 53/4	97/0 ± 79/3	99/0 ± 87/2

Comparison of Volume between Groups P and F, P and C, F and C pv Consequently (P = 0.001,0.000,0.000)
** Comparison of Volume between groups P and F, P and C, F and C pv Respectively (0.35,0.00,0.00)

Table4. Comparison of the Volume Less than 25 ml and More than 25 ml between Groups

Volume	Group P	Group F	Group C
Volume < 25 ml	(%85) 34	(%80) 32	(%5/17) 7

Volume > 25 ml	(%15) 6	(%20) 8	(%5/82) 33

Comparison of the Volume Less than 25 ml between Group P, F and C, pv Respectively (0.56 ,0.0019 ,0.0013

Table5. Comparison of the pH Less than 2.5 and more than2.5 between Groups

Ph	Group P	Group F	Group C
Ph < 2.5	(%8/12) 6	(%4/18) 7	(%5/47) 19
Ph > 2.52	(%2/87) 33	(%6/81) 31	(%5/52) 21

Comparison of the PH Less than 2.5 and more than2.5 between P, F and C, pv Consequently (0.049,0.001 ,0.01)

Table 6. Patients at Risk of Pulmonary Aspiration

PH	Group P	Group F	Group C
PH < 2.5	30 = n (20%) 6	29 = n (17%) 5	31 = n (41%) 13
PH > 2.5	(%16) 5	(%20) 6	(%90) 28
PH < 2,5 volume >25ml	(13%) 4	(17%) 5	(41%) 13

Comparison of the Risk of Aspiration between Group P, F and C, PV Respectively (0.67 ,0.1 .0.03)

Discussion:

Regurgitation, vomiting and silent and unexpected aspiration can happen during anesthesia and lead to serious complications. Regurgitation and aspiration happen in 5% of the patients undergoing general anesthesia.(10)

In a study, Hett et all used lansoprazole, 30 mg and 60 mg at 10 p.m. the nigh before surgery in patients undergoing elective surgery. Gastric fluid PH and volume using lansoprasol 30 mg were accordingly 2.46 and 27.3 ml and in 33% of the patients PH was less than 2.5 and gastric fluid volume was more than 25 ml.(11)

In our study we used pantoprazole and famotidine. Mean PH and volume were reported as PH = 4.53 ± 1.29 and volume = 17.5 ± 13.39 ml in pantoprazole group which is in the same pharmacologic group as lansoprazole. The results confirmed better efficacy for pantoprazole compared to lansoprazole. Nishina et al studied the efficacy of lansoprasol, Omeprazole and ranitidine in different doses for reducing secretions before stomach surgery in adult patients undergoing elective surgery. In lansoprasol group, mean and SD of gastric fluid PH and volume were accordingly 2.7 ± 1.3 and 0.31 ± 0.28 ml/kg. Patients having PH < 2.5 and content volume > 0.4 ml/kg are at risk of regurgitation and aspiration. This risk was 24% in the study of Nishina.(12)

In our study, PH and gastric fluid volume were 4.53 ± 1.29 and 17.5 ± 13.39 ml in pantoprazole group and 3.79 ± 0.97 and 14.78 ± 14.46 ml in famotidine group which revealed better results than Nishina's study. The reason can be the effectiveness of the medications used in this study or our study method.

In a study carried out by Nishina et all, comparative effect of Rabeprazol, Lansoprazole

and Ranitidine were studied, ranitidine was the most effective medicine in reducing gastric fluid acidity and volume.(13) This study also revealed that single dose of ranitidine was the most effective of all above mentioned medications in controlling gastric fluid acidity and volume. Gastric fluid acidity and volume using ranitidine were accordingly 5.3 ± 1.9 and 0.1 ± 0.09 ml/kg and Rabeprazol was in second place after ranitidine. The aspiration risk was reported zero for ranitidine and Rabeprazol in this study.

In our study PH was 3.79 ± 0.97 and volume was 17.5 ± 13.39 ml in pantoprazole group and PH was 3.79 ± 0.97 and volume was 14.789 ± 14.46 ml in famotidine group. The aspiration risk for the patients in pantoprazole and famotidine groups were accordingly 13% and 17%. This study revealed that Rabeprazol was more effective in reducing volume and acidity of gastric fluid compared to famotidine and pantoprazole.(13)

Dilek Memis et al compared intravenous pantoprazole and ranitidine regarding reducing gastric PH and volume and showed that there is no significant difference between them and both medications are effective in reducing gastric fluid acidity and volume when used intravenously as well as orally compared to placebo group.(14)

Also in our study famotidine and pantoprazole were more effective in reducing gastric fluid acidity and volume compared to placebo group. Pantoprazole was more effective than famotidine reducing acidity whereas gastric fluid volume decreased more in famotidine group compared to pantoprazole group.

Our study differed from Dilek Memis study regarding method, the time and the route of medication administration. Famotidine is a long acting H2 receptor blocker and pantoprazole is a long acting PPI which does not need to be repeated during the day in case of being used 40 mg. In patients waiting for operation, gastric fluid volume increases due to stress and gastric contents empty with delay especially in conditions like pregnancy and bulky abdominal masses in which the night before prophylaxis seems to be more logical.(15)

Conclusion:

This study focuses on the comparison of effects of famotidine (40mg) from H1 blocker group with pantoprazole (40mg) from PPIs group in two IV and oral forms. This study showed that when using oral pantoprazole (40mg) the night before operation and oral famotidine (40mg) the night before operation, pantoprazole was more efficient than famotidine and placebo in reducing acidity and famotidine was more effective than placebo, and pantoprazole in reducing gastric fluid volume and famotidine is better than placebo in reducing gastric fluid acidity. Aspiration risk during anesthesia decreases as these two medications reduce both gastric fluid volume and acidity.

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