Effect of Preanesthetic Famotidine on Gastric Volume and pH

Takahiko OKUDA, Touru TAKATSU, Osamu KUMODE,
Yasuhiro SHIOKAWA and Keita SUEKANE

The effect of preanesthetic 20 mg of famotidine on gastric fluid volume and pH were studied in patients scheduled for elective surgery. One hundred and twenty-eight patients were divided into four groups-control, intravenous, intramuscular and oral with 32 patients in each group. Patients in placebo group received no famotidine and served as control. Patients in the intravenous and intramuscular groups were administered famotidine one hour before surgery. Patients in the oral group were administered famotidine the night before and on the morning of surgery. Gasric volume in the control group was 19.1 ± 10.8 ml; in the intravenous group, 7.4 ± 6.4 ml; in the intramuscular group, 7.3 ± 6.9 ml; and in the oral group, 7.1 ± 6.9 ml. Gastric pH was 3.4 ± 2.3, 6.8 ± 1.1, 6.9 ± 1.6, and 6.7 ± 1.2 in groups one through four, respectively. When compared to the control group, famotidine significantly decreased gastric volume and increased gastric pH. There were no statistical differences among the different modes of administration. No adverse effects were observed in this study. It is concluded that preanesthetic management of 20 mg of famotidine reduced the risk of acid aspiration pneumonitis. (Key words: acid aspiration syndrome, preoperative premedication, famotidine)

(Okuda T, Takatsu T, Kumode O et al.: Effect of preanesthetic famotidine on gastric volume and pH. J Anesth 2: 17–21, 1988)

Pulmonary aspiration of gastric contents is one of the most feared complications associated with the induction of general anesthesia. Volumes of gastric aspirate of more than 25 ml and gastric pH levels less than 2.5 generally produce a severe pulmonary injury. To protect against the adverse effect of gastric aspiration syndrome, various methods have been suggested to reduce the volume and acidity of gastric contents. H_2-receptor antagonists such as cimetidine and ranitidine have been recently used as a premedication. Preoperatively administered cimetidine or ranitidine is partially effective in lowering gastric volume and decreasing gastric acidity thereby decreasing the risk of aspiration pneumonitis[1–6]. Famotidine, a new histamine H_2 receptor antagonist developed in Japan, is more potent than ranitidine and cimetidine and is presumed to have minimal side effects[7–9]. Noguchi has reported that intramuscular administration of famotidine is a useful drug for premedication by reducing the risk of acid aspiration pneumonitis[10].

The purpose of this double blind study was to compare the effect of famotidine and placebo when administered before surgery by the intravenous, intramuscular or oral route on gastric fluid volume and pH, and to determine whether it would be effective for the prophylaxis of acid aspiration pneumonitis at the time of intubation.

Department of Anesthesiology, Kinki University School of Medicine, Osaka-fu, Japan

Address reprint requests to Dr. Okuda: Department of Anesthesiology, Kinki University School of Medicine, 377-2 Oonohigashi, Osakasayama-shi, Osaka-fu, 589 Japan

Table 1. Age, weight and sex distribution of patients

Group	n	Age (yr)	Weight (kg)	Sex (F/M)
Control	32	40±13	57±10	18/14
Intravenous Drugs	32	39±13	56±9	15/17
Intramuscular Drugs	32	40±14	57±5	17/15
Oral Drugs	32	40±13	57±8	17/15

Mean Values ± SD

Table 2. pH and volume of gastric contents

Group	n	pH	Volume (ml)
Control	32	3.4±2.3	19.1±10.8
Intravenous Drugs	32	6.8±1.1*	7.4± 6.4*
Intramuscular Drugs	32	6.9±1.6*	7.3± 6.9*
Oral Drugs	32	6.7±1.2*	7.1± 6.9*

Mean Values ± SD

*Within analysis of variance, significantly different from the control group ($P<0.001$)

Methods

This study was carried out 124 adult patients scheduled for elective surgery under general anesthesia with endotracheal intubation. All patients were ASA class 1 and 2, aged 18 to 74 years, and weighed between 38 and 70 kg. Patients were excluded from the study if they had gastrointestinal disease and were receiving drugs likely to affect gastric pH or volume. They were randomly divided into four groups-control, intravenous, intramuscular and oral with 32 patients in each group. Patients in the control group received no famotidine and served as a control. Patients in the intravenous and intramuscular groups were administered famotidine one hour before surgery. Patients in the oral group were administered famotidine the night before and on the morning of surgery. All patients fasted at least eight hours before induction of anesthesia and were premedicated with intramuscular atropine and hydroxydine 30 min before the induction of anesthesia. Anesthesia was induced with thiopental and suxamethonium and continued with nitrous oxide and enflurane or halothane. If necessary, neuromuscular blocking agents were used. A nasogastric tube (#16 Salem sump tube) was inserted into the stomach immediately after tracheal intubation. The contents of the stomach were aspirated and the volume and pH measured. The pH of the sample was measured using a pH meter. Patient with gastric pH below 2.5 and gastric volume over 25 ml were defined as being at risk of pulmonary damage in the event of aspiration. Student's t test was used for the analysis of gastric pH and volume. Chi square analysis was used to compare the proportion of patients at risk of acid aspiration pneumonitis in the famotidine groups with the control group. The level of $P<0.05$ was considered significant.

Results

The characteristics of the patients in the four groups are shown in table 1. The four groups were similar with respect to age, weight and sex. The duration of fasting time was similar in all groups. The values of the mean gastric pH and volume in the four groups are shown in table 2. The mean gastric pH was significantly higher in the famotidine groups than in the control group ($P<0.001$). The mean gastric volume was significantly less in the famotidine groups than in the control groups ($P<0.001$). There were no statistical differences between the intravenous, intramuscular and oral administration in gastric volume and pH. Table 3 shows the distribution of high risk patients. Twenty five percent of the patients in the control group were considered to be at risk of acid aspiration pneumonitis, but in famotidine groups, the percentage of patients with a pH of less than 2.5 and gastric volume over 25 ml were significantly lower than the control. There were no patients at risk in intravenous group. Only one patient in the intramuscular and oral groups, respectively, was at risk of acid aspiration pneumonitis.

Discussion

In this study, the preoperative administration of 20 mg of famotidine was found

Table 3. Distribution of high risk patients

Group	No. of patients (%) with		
	pH<2.5	Volume>25ml	pH<2.5 and Vol.>25ml
Control	18(56)	10(31)	8(25)
Intravenous Drugs	1(3)*	3(9)*	0(0)*
Intramuscular Drugs	1(3)*	2(6)*	1(3)*
Oral Drugs	2(6)*	3(9)*	1(3)*

*Significantly different from the control group ($P<0.001$) using Chi-square analysis.

to decrease gastric fluid volume and increase gastric fluid pH significantly. There were no patients at risk in the intravenous group. Only one patient was at risk at the time of intubation in the intramuscular and oral famotidine groups, respectively. These results revealed that the dosage of famotidine (20 mg) appeared to be sufficient to decrease the risk of acid aspiration penumonitis.

It is generally agreed that a gastric pH below 2.5 and gastric volume over 25 ml are considered to be risk factors in acid aspiration pneumonitis. However, the critical volume of buffered aspirate has not been determined. Christopher demonstrated that in the interaction between gastric aspirate pH and volume, even low volumes have a high mortality rate if the pH is very low, whereas if gastric fluid is effectively buffered, then much higher volumes than previously thought can be tolerated[11].

H_2-antagonists such as cimetidine and ranitidine have been shown to be effective in increasing the pH of gastric contents and in decreasing the gastric volume. It has been extensively studied that the prophylactic administration of these drugs minimizes the risk of acid aspiration pneumonitis during anesthesia by reducing the gastric volume and acidity[1-6].

Famotidine is a new highly selective H_2 receptor antagonist. When compared to the effect of cimetidine, famotidine is at least 20 times or more potent than cimetidine in antisecretory potency[7-9]. It is reported that ranitidine is five times more potent than cimetidine, so that famotidine is perhaps more potent than ranitidine. The duration of action of 20 mg of famotidine has been shown to last for more than 10 hours[9].

When comparing the mode of administration, there was no significant difference between in intravenous, intramuscular and oral administration. In this study, the time interval between oral administration and induction was about 10 hours, but the antisecretary action of famotidine was sufficient to decrease the risk of acid aspiration pneumonitis. Parenteral administration may lower the time required to achieve this effect because it achieves a higher blood level faster[12]. Gastric acid secretion was inhibited after one hour in the intramuscular or intravenous administration of famotidine, but the antisecretory activities of oral administration are exhibited between 2 and 3h after dosing. Therefore, parenteral administration is recommended in emergency cases. It may not, however, always be useful for the management of patients undergoing emergency surgery because of a full stomach due to too short a fasting time. The use of any H_2 antagonist and metoclopramide[13,14] or sodium citrate[15,16] may reduce the incidence of aspiration pneumonitis, but these agents cannot completely prevent the possibility of pulmonary damage if aspiration should occur. Therefore, the usual precautions should still be observed for patients at risk, in particular, emergency, obstetrical and the morbidly obese patients and in emergency abdominal surgery.

No adverse effects were observed in this study. Side effects have been reported with both intravenous and oral use of cimetidine. It is now recognized that cimetidine may

reduce hepatic blood flows[17,18] and inhibit microsomal oxidative formation in the liver. Therefore, in long-term cimetidine treatment patients, it must be kept in mind that there is the possibility of prolonging the metabolism of diazepam[17], propranolol[18], lidocaine[19] and a host of other drugs. Ranitidine is not believed to cause this potentiation because it does not inhibit microsomal oxidation[20] and famotidine caused little effect on hepatic blood flow[21]. Cardiac dysrhythmias such as hypotension, bradycardia or sinus arrest have been reported after the use of intravenous and oral cimetidine[22,23]. Omote reported that ranitidine and famotidine did not produce remarkable hemodynamic changes in ICU patients, although cimetidine produced a significant decrease in MAP due to peripheral vasodilation[24]. Famotidine is considered to be safer than cimetidine with regard to side effects.

We conclude that famotidine should be recommended as a routine premedication for prophylaxisis of aspiration pneumonitis because of its reliable effect, longer duration of action, ease of administration and minimal incidence of adverse reactions.

(Received Oct. 12, 1987, accepted for publication Nov. 27, 1987)

References

1. Aromaa U, Kalima TV: Ranitidine and prevention of pulmonary aspiration syndrome. Acta Anaesthesiol Scand 30:10–12, 1986
2. Harris PW, Morison DH, Dunn GL, Fargas-Babjak AM, Moudgil GC, Smedstad KG, Woo J: Intramuscular cimetidine and ranitidine as prophylaxis against gastric aspiration syndrome- a randomized double-blind study. Can Anaesth Soc J 31:599–603, 1984
3. Francis RN, Kwik RSH: Oral ranitidine for prophylaxis against Mendelson's syndrome. Anesth Analg 61:30–32, 1982
4. Morison DH, Dunn CL, Fargas-Babjak AM, Moudgil GC, Smedstad K, Woo J: A double-blind comparison of cimetidine and ranitidine as prophylaxis against gastric aspiration syndrome. Anesth Analg 61:988–992, 1982
5. Andrews AD, Brock JG, Downing JW: Protection aganst pulmonary acid aspiration with ranitidine. Anaesthesia 37:22–25, 1982
6. Durrant JM, Strunin L: Comparative trial of the effect of ranitidine and cimetidine on gastric secretion in fasting patients at induction of anaesthesia. Can Anaesth Soc J 29:446–451, 1982
7. Takagi T, Takeda M, Maeno H: Effect of a new potent H_2-blocker, 3-[[[2-[(diaminomethylene) amino]-4-thiazolyl] methyl]-thio]-N2-sulfamoyl propionamidine (YM-11170) on gastric secreation induced by histamine and food in conscious dogs. Arch. int. Pharmacodyn. 256:49–58, 1982
8. Takeda M, Takagi T, Maeno H: Kinetics of antisecretory action of a new H_2-antagonist, YM-11170, in conscious dogs. Eur J Pharmacol 91:371–376, 1983
9. Miwa M, Tani N, Miwa T: Inhibition of gfastric secretion by a new H_2-antagonist, YM-11170 in healthy subjects. Inter J Clini. Pharma Ther and Toxi 22:214–217, 1984
10. Noguchi J, Yamamoto H, Inada Y, Yamamoto T, Kobayashi K, Amaha K, Mima T: A double-blind evaluation of famotidine for pre-anesthetic intramuscular administration. Masui 36:592–603, 1987
11. James CF, Modell JH, Gibbs CP, Kuck EJ, Ruiz BC: Pulmonary aspiration-Effects of volume and pH in the rat. Anesth Analg 63:665–668, 1984
12. Lam AM, Grace DM, Phil D, Penny FJ, Vezina WC: Prophylactic intravenous cimetidine reduces the risk of acid aspiration in morbidly obese patients. Anesthesiology 65:684–687, 1986
13. Manchikanti L, Colliver JA, Marrero TC, Roush JR: Ranitidine and metoclopramide for prophylaxis of aspiration pneumonitis in elective surgery. Anesth Analg 63:903–910, 1984
14. Wyner J, Cohen SE: Gastric volume in early pregnancy: Effect of metoclopramide. Anesthesiology 57:209–212, 1982
15. Dewan DM, Floyd HM, Thistlewood JM, Bogard TD, Spielman FJ: Sodium citrate pretreatment in elective cesarean section patients. Anesth Analg 64:34–37, 1985
16. Gibbs CP, Spohr L, Schmidt D: The effectiveness of sodium citrate as an antacid. Anesthesiology 57:44–46, 1982
17. Klotz U, Reimann I: Delayed clearance of diazepam due to cimetidine. N Engl J Med 302:1012–1014, 1980
18. Feely J, Wilkinson GR, Wood AJJ:

Reduction of liver blood flow and propranolol metabolism by cimetidine. N Engl J Med 304:692–695, 1981

19. Kim KC, Tasch MD: Effects of cimetidine and ranitidine on local anesthetic central nervous system toxicity in mica. Anesth. Analg 65:840–842, 1986
20. Zeldis JB, Friedman LS, Isselbacher KJ: Ranitidine-a new H_2 receptor antagonist. N Engl J Med 309:1368–1373, 1983
21. Takagi T, Takeda M, Fujihara A, Yashima Y: General pharmacolpgical properities of a new potent H2-blocker, Famotidine (YM-11170). Pharmacometrics 26:599–611, 1983
22. Lineberger AS, Sprague DH, Battaglini JW: Sinus arrest associated with cimetidine. Anesth Analg 64:554–556, 1985
23. Mehta AB, Goldman JM: Cimetidine and cardiac dysrhythmias. Ann Int Med 97:283–286, 1982
24. Omote K, Namiki A, Sumita S, Takahashi T, Ujike Y, Hagiwara T: Comparative studies on hemodynamic effect of intravenous cimetidine, ranitidine and famotidine in intensive care unit patients. Masui 36:940–947, 1987