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Cimetidine, Antacids, and Pulmonary Aspiration

IT IS DISTURBING to learn from the most recent published figures that in 1976–1978 there were 11 maternal deaths in England and Wales following pulmonary aspiration of gastric contents under anesthesia and nine of these deaths were attributed to Mendelson's syndrome.[1] In the previous triennium there were 13 maternal deaths from aspiration, and, again, nine resulted from Mendelson's syndrome.[2] In the 6 years from 1973–1978 anesthesia caused 61 maternal deaths, and pulmonary aspiration caused at least 23 of them. The incidence of nonfatal Mendelson's syndrome is unknown. In 1973–1978, oral antacids (usually magnesium trisilicate mixture) had been given during labor to at least 12 of the 18 mothers who died of Mendelson's syndrome in the United Kingdom.

It is evident from these statistics that oral antacids, and magnesium trisilicate mixture in particular, always do not prevent fatal aspiration pneumonitis. Before condemning all antacid therapy outright, some possible reasons for this failure should be examined. Experience suggests that failure to administer the antacid is not unusual either because of a lapse in routine or refusal by the patient. Antacid may have been administered and later vomited. Thorough mixing with stomach contents is necessary for complete effectiveness. Layering is common with particulate antacids.[3] Although mixing can be promoted by rolling the patient through 360°,[3] this is not always practicable. Where the volume of gastric content is unusually large, then the standard dose of antacid will be ineffective. The use of narcotic analgesia during labor is a potent cause of delayed gastric emptying and high gastric volume. There remains the possibility that pneumonitis may have been caused by the entry of a particulate antacid into the lungs. Gibbs and his colleagues[4] demonstrated that Kolantyl Gel® (a suspension of aluminum and magnesium hydroxides) caused functional and histologic changes in the lungs of dogs comparable to those induced by acid. The changes induced by the alkali persisted for longer than those caused by acid and this is attributed to the foreign body reaction to the antacid particles. Clinical reports suggest that particulate antacids have caused or aggravated aspiration pneumonitis in humans.[5,6]

Clear antacids probably are safer, being less likely to cause pneumonitis if aspirated,[4] and mixing with gastric juice is more effective.[3] The risk of pulmonary irritation from inhaled food particles remains, of course. Unfortunately, the efficacy of sodium citrate as an alkalinizing agent is a matter of concern. Early work by Lahiri *et al.*[7] suggested that 15 ml of 0.3 M sodium citrate raised gastric *p*H above 3.0 in 95% of women in labor. Not all subsequent work is in agreement with this observation, and it is possible that gastric samples were contaminated with alkali in the series by Lahiri *et al.* Two other groups of workers recorded a gastric *p*H below 2.5 in 19 and 53% of patients with this dosage.[8,9] Dewan *et al.* found that 30 ml of 0.15 M sodium citrate was completely ineffective.[10] In contrast, 30 ml of 0.3 M solution was effective.[11] Timing of administration and perhaps the volume probably are important. When given immediately before the induction of anesthesia, the gastric *p*H was above 3.5 in all 15 patients a few minutes later.[12] While a larger series would be welcomed, pragmatism suggests that this may be the preferred regimen and that the volume could be increased to 20 or 30 ml.[13]

The need to increase gastric *p*H safely is confirmed by the finding that 43% of women who received no antacid in labor had a *p*H below 2.5[14] and would be liable to develop Mendelson's syndrome if sufficient gastric juice entered the alveoli. The minimum quantity of gastric juice needed to cause Mendelson's syndrome is thought to be about 0.4 ml/kg body weight. Filtered

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gastric juice causes pneumonitis, which is rendered more severe by the presence of food particles.

An alternative to the administration of an antacid is the use of an H_2-receptor antagonist such as cimetidine or ranitidine. These agents inhibit the secretion of acid by the stomach by blocking gastric histamine receptors. The volume of gastric juice is reduced by the volume of acid no longer secreted. There is, of course, no alkalinizing effect upon acid already present within the stomach. Cimetidine has been used successfully and extensively to treat peptic ulcers and allied conditions. Even after prolonged therapy, side effects are uncommon and unlikely to be serious. Sedation, confusion, and vertigo have been reported, however. Delayed hypersensitivity reactions and biochemical disturbances such as raised serum creatinine and prolactin have been recorded. Cimetidine can inhibit hepatic enzyme systems and potentiate the actions of other drugs such as anticoagulants and phenytoin. Potentiation of anesthetic agents has not been reported. Cimetidine is excreted mainly unchanged in the urine, and caution should be observed if renal function is impaired severely. Cimetidine has a molecular weight of 252, a *p*K of 6.8 and is poorly bound to serum proteins. For these reasons unrestricted placental transfer can be predicted and this has been demonstrated by Howe *et al.*[15] and Hodgkinson *et al.*,[16] who observed peak maternal-fetal concentration ratios (0.84) between 90 and 120 min after intravenous injection of 200 mg cimetidine. Hodgkinson and his colleagues have confirmed free placental transfer in a study reported in this issue.[15] Cimetidine appears to be free of any adverse effects on newborns as assessed by Apgar scores and neurobehavioral evaluations.[16–18] Blood loss in the third stage appears to be unaltered by cimetidine.[17]

The efficacy of cimetidine in increasing gastric *p*H and in reducing gastric juice volume depends upon the route of administration, the dose, and the interval of time following administration. When cimetidine 300 mg was given orally in the evening before or 60–90 min before surgery, gastric *p*H was above 2.5 in 75–84% of surgical patients after the induction of anesthesia.[19–21] An intramuscular injection of 300 mg cimetidine was as effective as an oral antacid in a small series of elective cesarean sections, six of eight patients having a gastric *p*H above 2.5 with each treatment.[19] An intravenous injection of cimetidine 45 min before anesthesia resulted in 90–92% of surgical patients having a gastric *p*H above 2.5.[22,23] Intravenous injections of cimetidine should be given very slowly and even then cannot be recommended unreservedly because of the risk of bradycardia, hypotension, arrhythmias, and even cardiac arrest.[24,25] A combination of oral cimetidine on the night before surgery and an intramuscular injection at least 1 hour before operation raised gastric *p*H above 2.5 in all patients in Weber and Hirshman's series.[26] A similar combined oral and intramuscular regimen was very successful when used by Hodgkinson and his colleagues[15] as a preparation for elective cesarean section. All of 48 mothers who received 300 mg cimetidine orally on the evening before operation and a further 300 mg im 1–3 h before surgery had a gastric *p*H above 2.5 when sampled 30 min after induction of anesthesia. In contrast, only 88% of 41 mothers who received an antacid (Mylanta-II®) had a gastric *p*H above 2.5. The volume of gastric juice was lower in those who received cimetidine.

There is now justification for the replacement of oral antacids by cimetidine before elective cesarean section, especially if a combined oral and intramuscular regimen is followed. Cimetidine 300 mg should be given orally in the evening before operation, and a further 300 mg should be injected intramuscularly 1–3 h before anesthesia is induced. It is important that an hour should be allowed for gastric *p*H to rise. If surgery is not completed within 4 hours it would be wise to repeat the injection. Ranitidine 50 mg is undergoing assessment as an alternative to cimetidine.[23] A potential advantage is a longer duration of action of 6–8 h. Timing of the intramuscular injection of ranitidine could be from 1–6 h before anesthesia, and *p*H changes are probably comparable to those observed with cimetidine.[23]

The situation is more complex when emergency obstetric anesthesia is required. A single intramuscular injection of cimetidine requires 60 min to be effective in nonemergency circumstances, and, even then, gastric *p*H may not be above 2.5 in 10% of cases. Where opiate analgesics have been given in labor, a substantial prolongation of gastric emptying time is likely and existing acid may remain in the stomach for several hours. Cimetidine cannot be relied upon in this situation. The possible effects of uterine contractions, oxytocin infusions, and maternal acid-base alterations upon the action of cimetidine are unknown. Therefore, it is recommended that an oral antacid such as sodium citrate be used before emergency obstetric anesthesia. If cimetidine also is used, it should be regarded as a supportive measure designed to inhibit further acid secretion and thereby to diminish the consequences of pulmonary aspiration during emergence from anesthesia.

There is a risk that anesthesiologists may have become unduly obsessed with the concept of a "safe" gastric *p*H. There is, as yet, no hard evidence that the use of antacids or cimetidine reduces maternal anesthetic mortality from pulmonary aspiration. Indeed, the administration of magnesium trisilicate mixture has failed to prevent death in well-documented cases.[1,2] Nevertheless, pharmacologic methods of raising *p*H are worth-

while if they are free of intrinsic danger. Cimetidine and antacids do not decrease the possibility of regurgitation and aspiration, they only can make the consequences less serious. Neither can these agents prevent the entry of food particles into the lungs, and acid is not the sole cause of pneumonitis. Other particles, such as those found in many antacids, are potential irritants. If the number of maternal deaths from aspiration pneumonitis is to be reduced, then many measures in addition to the reduction of gastric acidity will be required. Most of these are well known by now but are not always implemented. They include the administration of obstetric anesthesia by, or under, the supervision of adequately experienced anesthesiologists, the provision of proper equipment and assistance, the use of regional anesthesia whenever appropriate, the avoidance of heavy sedation in labor, and perhaps the use of drugs to reduce gastric volume, promote gastric emptying, and to increase the tone of the gastroesophageal sphincter. Cricoid pressure, when correctly applied, is of great value.

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References

1. Tompkinson J, Turnbull A, Robson G, et al: Report on Confidential Enquiries into Maternal Deaths in England and Wales 1976–1978. London, Her Majesty's Stationery Office, 1982, pp 79–80
2. Tompkinson J, Turnbull A, Robson G, Cloak E, Adelstein AM, Weatherall JAC: Report on Confidential Enquiries into Maternal Deaths in England and Wales 1973–1975. London, Her Majesty's Stationery Office, 1979, pp 80–81
3. Holdsworth JD, Johnson K, Mascall G, Roulston RG, Tomlinson PA: Mixing of antacids with stomach contents. Anaesthesia 35:641–650, 1980
4. Gibbs CP, Schwartz DJ, Wynne JW, Hood CI, Kuck EJ: Antacid pulmonary aspiration in the dog. ANESTHESIOLOGY 51:380–385, 1979
5. Bond VK, Stoelting RK, Gupta CD: Pulmonary aspiration syndrome after inhalation of gastric fluid containing antacids. ANESTHESIOLOGY 51:452–453, 1979
6. Heaney GAH, Jones HD: Aspiration syndrome in pregnancy (correspondence). Br J Anaesth 51:266–267, 1979
7. Lahiri SK, Thomas TA, Hodgson RMH: Single-dose antacid therapy for the prevention of Mendelson's syndrome. Br J Anaesth 45:1143–1146, 1973
8. White WD, Clark JM, Stanley-Jones GHM: The efficacy of antacid therapy. Br J Anaesth 48:1117, 1976
9. Hester JB, Heath ML: Pulmonary acid syndrome: should prophylaxis be routine? Br J Anaesth 49:595–599, 1977
10. Dewan DM, Writer WDR, Wheeler AS, et al: Sodium citrate premedication in elective caesarean section patients. Can Anaesth Soc J 29:355–358, 1982
11. Foulkes E, Jenning LC: A comparative evaluation of cimetidine and sodium citrate to decrease gastric acidity and effectiveness at the induction of anaesthesia. Can Anaesth Soc J 28:29–32, 1981
12. Viegas OJ, Ravindran RS, Shumacker CA: Gastric fluid pH in patients receiving sodium citrate. Anesth Analg (Cleve) 60:521–526, 1981
13. Gibbs CP, Spohr L, Schmidt D: In vitro and in vivo evaluation of sodium citrate as an antacid. ANESTHESIOLOGY 55:A311, 1981
14. Taylor G, Prys-Davies J: Prophylactic use of antacids in the prevention of the acid-pulmonary-aspiration syndrome (Mendelson's syndrome). Lancet 1:288–291, 1966
15. Howe JP, McGowan WAW, Moore J, McCaughey W, Dundee JW: The placental transfer of cimetidine. Anaesthesia 36:371–375, 1981
16. Hodgkinson R, Glassenberg R, Joyce TH, Coombs DW, Ostheimer GW, Gibbs CP: Comparison of Cimetidine (Tagmet®) with antacid for safety and effectiveness in reducing gastric acidity before elective cesarean section. ANESTHESIOLOGY 59:86–90, 1983
17. Dundee JW, McGowan WAW, Moore J: Cimetidine in the first stage of labour. Preliminary results. Anaesthesia 34:118, 1979
18. Husemeyer RP, Davenport HT: Prophylaxis for Mendelson's syndrome before elective caesarean section. A comparison of cimetidine and magnesium trisilicate mixture regimens. Br J Obstet Gynaecol 87:565–570, 1980
19. Pickering BG, Palahniuk RJ, Cumming M: Cimetidine premedication in elective caesarean section. Can Anaesth Soc J 27:33–35, 1980
20. Stoelting RK: Gastric fluid pH in patients receiving cimetidine. Anesth Analg 57:675–677, 1978
21. Coombs DW, Hooper D, Colton T: Acid-aspiration prophylaxis by use of pre-operative oral administration of cimetidine. ANESTHESIOLOGY 51:352–356, 1979
22. Coombs DW, Hooper D, Colton T: Pre-anesthetic cimetidine alteration of gastric fluid volume and pH. Anesth Analg (Cleve) 58:183–188, 1979
23. 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
24. Cohen J, Weetman AP, Dargie HJ: Life threatening arrhythmias and intravenous cimetidine. Br Med J 2:768–770, 1979
25. Shaw RG, Mashford ML, Desmond PV: Cardiac arrest after intravenous injection of cimetidine. Med J Aust 2:629–630, 1980
26. Weber L, Hirshman CA: Cimetidine for prophylaxis of aspiration pneumonitis: Comparison of intramuscular and oral dosage schedules. Anesth Analg (Cleve) 58:426–427, 1979