Prophylaxis for aspiration pneumonitis

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It would be extremely misleading to leave the impression that pharmacological prophylaxis is a substitute for sound judgement and good anaesthetic technique. Yet, existing reports demonstrate that significant morbidity and occasional death all too commonly still arise secondary to the unpredictable event of aspiration.[1] The primary purpose of this refresher course is to review the pharmacology, efficacy and safety of those drugs which are utilized clinically to alter the volume and/or character of gastric fluid contents. Although documentation is lacking, it is hoped that administration of these drugs will lessen either the incidence or severity of aspiration pneumonitis.

Factors affecting the severity of aspiration

The acidity of the aspirate is probably the most important factor contributing to the severity of pneumonitis. In numerous animal models, increasing acidity, whether alone or in combination with food particles, results in increasing tracheal mucosal and lung parenchymal damage.[2–4] The literature has been replete, however, with the suggestion that an aspirate with a pH greater than 2.5 is relatively benign. Several anecdotal reports as well as recent animal work refute this concept.[5–7] In fact, the initial physiologic derangement may be just as severe and potentially as lethal. Nevertheless, recovery and healing rates appear to be faster if acidity is reduced.

In this same light, there has been propagation in our literature of the notion that a volume of aspirate less than 0.4 $ml \cdot kg^{-1}$ (20 to 25 ml in an adult) is relatively safe. Perhaps just as misleading is the converse of this statement – that an aspirate volume exceeding this derived number if uniformly fatal. The concept of a "critical" volume was based on work done in rhesus monkeys in which the aspirated fluid was highly acidic.[8] In fact, recent work in rats demonstrated that the critical volume depends on the pH of the apirate. Even low volumes have a high mortality rate if the pH is low; whereas higher volumes than noted above can be tolerated if the gastric fluid is effectively buffered.[9]

Aspiration of particulate matter such as partially digested food particles has also been known for some time to result in severe pulmonary physiologic derangements.[10] Such aspirates, in addition to increasing shunt fraction and decreasing arterial oxygen tension, often result in alveolar hypoventilation with accompanying hypercarbia. In the long term, a granulomatous response develops around these particles. Similarly, bacterial contamination of an aspirate, as may occur in a patient with a bowel obstruction, is associated with a very high mortality rate.[11]

Finally, experience in both fresh and salt water drowning victims have demonstrated the importance of the tonicity of an aspirate. Recent work in dogs reconfirmed that as osmolarity of the aspirate increases, so too does the degree of pulmonary physiologic derangement.[12] It thus becomes apparent that multiple factors influence the significance of an aspirate.

Who is at risk?

One should ask not only who is at risk for aspiration but also who is at risk for developing a severe pneumonitis should aspiration occur? Clinical experience and common sense tells us that the "prepared", fasted adult or paediatric patient does not present the same risk for aspiration as patients with known anatomic or physiologic disturbances. This group of high risk patients would include patients with reduced levels of consciousness, abnormalities in their swallowing mechanism, oesophageal pathology, incompetence of the gastroesophageal junction, delayed gastric emptying,

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or with material in the stomach. A very high percentage of prepared patients however present to surgery with gastric contents of a volume and acidity which would result in significant pneumonitis should aspiration occur.[13] In considering the following discussion you should weigh the unpredictability of aspiration in the perioperative period and the potential beneficial effects of various pharmacologic modalities against the potential risk associated with the drugs themselves. Is aspiration a preventable iatrogenic event? Does every patient deserve some type of pharmacologic prophylaxis in addition to our best anaesthetic technique and judgement?

Drugs used for prophylaxis

Anticholinergics

Although anticholinergics are of no value in neutralizing acid present in the stomach at the time of their administration, they should block ongoing gastric acid production since it is in part controlled through an acetylcholine effect. Thus, their inclusion with preoperative medicants would conceivably decrease gastric fluid volume and acidity at the time of induction of anaesthesia. In fact, their efficacy has proven to be dose- and time-dependent, greatest with glycopyrrolate, and most effective in paediatric and obstetrical patients.[14–16] Their efficacy in clinically accepted doses in adult patients scheduled for elective surgery has proved to be of limited benefit. Although potentiation of the inhibitory action of cimetidine on gastric acid secretion by simultaneous administration of anticholinergics has been reported in patients with duodenal ulcers, this interaction has not been demonstrated in elective surgical patients.[17,18] Interestingly, markedly beneficial effects have been demonstrated when anticholinergics were given with antacids.[19]

With regard to the overall prevention of aspiration, anticholinergics have some potential drawbacks associated with their administration. First, they may decrease lower oesophageal sphincter pressure, thus increasing the likelihood of regurgitation. This effect is dose-related and most pronounced after intravenous administration.[20] Second, anticholinergics can counteract the desirable effects of metoclopramide on gastric peristalsis and the lower oesophageal sphincter.[21]

Antacids

Many investigators have demonstrated that particulate antacids are effective in raising gastric fluid pH in a high percentage of both obstetrical and surgical patients.[8,22,23] Indeed, their effectiveness in raising pH depends on (1) the volume and pH of the gastric contents present at the time of their administration, (2) the frequency and timing of antacid administration, (3) the type and amount of antacid given, (4) what manoeuvres, if any, are done to promote mixing of the antacid with the gastric contents, (5) the intrinsic gastric motility present at the time of antacid administration, and (6) the rate of ongoing gastric acid production.

Despite their overall effectiveness in raising gastric fluid pH, particulate antacids have come under criticism in the last few years for two primary reasons. First, their administration may increase gastric volume. As an example, routine q2–4 hour dosing with antacids became common practice on many obstetrical wards because of the unpredictability of emergency induction of anaesthesia as well as concern over acid rebound (an increase in pH over basal levels four or more hours following antacid neutralization). This practice has fallen into disfavour since it has been appreciated that in the labouring patient (particularly those receiving narcotics for pain), gastric motility is slowed.[24] Thus, such a practice could lead to significant increases in gastric volume. Yet, the impact of a single dose of an antacid on gastric volume in an individual patient is highly variable. In fact, in patients with normal gastric motility, antacids not only may not change volume but may decrease it, because the duodenum can accept neutral gastric contents more rapidly than highly acidic contents.[25]

The second major criticism is that particulate antacid aspiration not only results in initial pulmonary derangement as severe as a highly acidic aspirate but also histologic abnormalities for as long as one month following aspiration.[26] In fact, these chronic granulomatous responses were not noted in study groups with acid aspirates.

Thus an intense interest has been sparked in soluble antacids. The two soluble antacids most investigated clinically to date are 0.3 molar sodium citrate (not available commercially, thus it must be prepared by your hospital pharmacy) and Bicitra (Willen Drug Co). These two antacid preparations contain approximately the same amount of sodium

citrate and despite differing pH's (Bicitra is more acidic since it contains citric acid in addition to sodium citrate) they have similar neutralizing capacities.[27]

Are these compounds as effective as particulate antacids in raising gastric fluid pH and are there any advantages for their use? The preponderance of evidence suggests that soluble antacid are as effective as particulate antacids in raising gastric fluid pH in both elective and emergency surgical patients, if given within 15 to 60 minutes of induction of anaesthesia.[28–33] In the reports where their efficacy has been questioned, the interval between their ingestion and the induction of anaesthesia (gastric sampling) usually has been greater than 60 minutes.[33–35] Recent work has demonstrated that this is most likely due to the fact that if normal gastric motility is present at the time of antacid administration, the soluble antacids may pass on through the gastrointestinal tract (thus their effect dissipates) while gastric acid production continues.[36]

Are there advantages? Soluble antacids mix with gastric contents more readily than particulate antacids.[37] Thus, the need to have the patient roll from side to side to promote mixing of gastric contents with the antacid may be lessened. In addition, some studies have indicated that aspiration of soluble antacids, compared with particulate antacids, though resulting in just as severe initial pulmonary physiological derangements, may be associated with more rapid recovery and less long-term histologic changes.[38,39]

Histamine H2 receptor antagonists

It is well documented that the H2 blockers decrease nocturnal, basal, and meal stimulated gastric acid production by competitively inhibiting the action of histamine on the H2 receptor of the gastric parietal cell. In contrast, they have no apparent effect on gastric emptying time or on lower oesophageal sphincter pressure. Such findings, as would be expected, sparked an absolute plethora of work on the efficacy of these compounds in increasing gastric fluid pH or decreasing gastric volume using multiple approaches and in numerous subsets of surgical patients. The following comments attempt to summarize this mass of data on cimetidine (Tagamet-Smith Kline & French), the most widely studied H2 blocker.

First, the preoperative administration of cimetidine has in a dose related manner, been shown to decrease significantly the acidity of gastric contents in samples taken immediately following the induction of anaesthesia.[40] Second, timing of administration is important. Oral administrtion takes 60 to 90 minutes before a significant effect can be demonstrated and this effect seems to wane by four to six hours.[41] In contrast, intravenous administration has been demonstrated to be efficacious 45 to 60 minutes following injection although the duration of action is not necessarily any longer than following oral administration.[42] Parenteral administration results in earlier and higher initial blood levels and results in a higher percentage of patients with pH values greater than 2.5 at induction of anaesthesia.[43] Multiple dose regimens (a dose the evening before and the morning of surgery) are more effective than single morning doses.

One- or two-dose cimetidine therapy has an excellent safety record. Such short-term administration inhibits the mixed function oxidase system and decreases liver blood flow.[44,45] These effects can result in higher blood levels and more pronounced effects of drugs which depend on the liver for their clearance. Indeed, it is well documented that co-administration of cimetidine will prolong the elimination half-lifes of warfarin, diazepam, theophylline, phenytoin, and possibly propranolol. Likewise, there are a few reports in which cimetidine has been purported to contribute to delayed awakening from anaesthesia by this mechanism.[46,47] There is a theoretical, if not real, concern that cimetidine therapy can aggravate bronchospasm in asthmatics by allowing histamine to have an unopposed H1 effect.[48] Finally, rapid intravenous administration of relatively large doses (600 mg) of cimetidine has been reported to cause hypotension and dysrhythmias.[49]

Cimetidine has also proved to be safe in obstetrical patients. Two reports have not demonstrated any maternal complications attributable to cimetidine treatment nor have any adverse effects been noted in infants whose mothers received cimetidine (based on Apgar and neurobehavourial scores).[50,51]

Does the newly available H2 antagonist – ranitidine (Zantac – Glaxo) – offer any significant advantages over cimetidine? Purported advantages are ranitidine's greater potency, longer duration of action (six to eight hours), lower incidence of side effects, and lesser degree of inhibition of the mixed

function oxidase system.[44] Its onset of action is probably no more rapid than that of cimetidine and therefore it suffers from the same limitations in the emergency situation. Its efficacy in raising gastric pH has proven to be similar to or slightly better than that of cimetidine.[52–55] The prolonged duration of action is well documented and offers a distinct advantage. A dose on the eve of surgery should suppress acid production throughout the night while a morning dose should last long enough to provide good conditions well into the emergence/recovery period. It seems increasingly obvious however that the latter claims of fewer side effects and less inhibition of the mixed function oxidase system may be overstated.[56]

Co-administration of antacids or metoclopramide with H2 blockers has been shown to reduce the bioavailability of the H2 antagonist secondary to reduced absorption.[57,58] Nevertheless, co-administration of H2 blockers and metoclopramide has been shown to have greater efficacy in favourably altering both the pH and volume of gastric fluid than either drug alone.[59–62]

Metoclopramide

Metoclopramide (Reglan – A.H. Robins) is a chlobenzamide derivative which possesses three characteristics which make it potentially very useful in anaesthesia. It increases the lower oesophageal sphincter pressure, speeds gastric emptying time, and has antiemetic properties.[63,64] It has no direct effect on gastric fluid pH. As such it represents a markedly different approach to aspiration prophylaxis than the drugs discussed above.

Several investigators have noted that either oral or parenteral administration of metoclopramide to patients scheduled for elective or emergency surgery decreases the volume of gastric contents.[65–68] Others have not been able to duplicate these findings.[69] Some of the discrepancies may be dose-related. Another factor which comes into play is the highly variable blood levels attained following oral administration, due to the wide range in first pass hepatic metabolism of metoclopramide. Differences in observed effects may also arise from differences in the basal state of gastrointestinal motility present at the time of administration of metoclopramide. That is, it is probable that metoclopramide is most effective in modifying gastric motility when this is already impaired by other factors.

Of interest to anaesthetists is the observation that metoclopramide may not reliably reverse narcotic-induced inhibition of gastric motility.[70] Similarly, metoclopramide may be more effective at emptying a "light" or liquid meal than a solid meal.[71] Although a significant decrease in gastric volume can be demonstrated within 20 minutes of administration of metoclopramide, it is recommended to wait at least 30 minutes after a "light" meal and up to 75 to 90 minutes after "heavier" meals for a reliable effect following metoclopramide.

Likewise, it has been demonstrated that metoclopramide increases lower oesophageal sphincter pressure and barrier pressure (the pressure difference between intragastric pressure and lower oesophageal sphincter pressure) in both nonpregnant and pregnant women with and without symptoms of oesophageal reflux.[72] Thus, the likelihood of passive regurgitation should be reduced following metoclopramide. The efficacy of metoclopramide as an antiemetic in anaesthesia has proven to be highly variable.

In the dose range commonly employed (10 to 20 mg), metoclopramide is relatively safe. Higher dosages, particularly in children, have been associated with agitation, irritability and extrapyramidal symptoms.[73] To date, when given to parturients, metoclopramide has been shown not to impede the progress of labour nor adversely affect Apgar neurobehavioural scores.[74]

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