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Review Article

Gastro-esophageal reflux in mechanically ventilated patients: The "oil well" analogy

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Abstract. From a conceptual and clinical point of view, a comprehensive interpretation of risk factors leading to gastro-esophageal reflux (GER) is translated in this review into an *"oil well" analogy: w*hereas gastric contents represent the oil deposit, groups of "on-off" events reflect the presence or absence of specific risk factors and events, respectively, similar to opening and closing a drilling tower. In this dynamic analogy for both the risk and magnitude of GER, we emphasize that generalization of GER risk factors in clinical settings is extremely relevant but fraught with complexity, difficulties and limitations. Therefore, the primary purpose of this review is to examine the effect of the interaction between body positioning, gastrointestinal function, tube feeding, drugs and additional factors on the aspiration risk in critically ill, tube-fed patients.

Keywords: Gastro-esophageal reflux, intensive care, risk, mechanical ventilation, pneumonia, morbidity, mortality, prevention

The "oil well analogy" as a comprehensive interpretation of factors leading to gastro-esophageal reflux

Gastro-esophageal reflux (GER) is a multifaceted disease presenting with both esophageal and extra-esophageal clinical manifestations in critically ill patients. Despite a relative plethora of information regarding clinical relevance of GER, the mechanisms that underlie this reflux in patients receiving mechanical ventilation (MV) have not been completely characterized. Although aspiration is common, the clinical consequences of GER are variable because of differences in the nature of the aspirated material and individual host responses. Moreover, the incidence of aspiration in MV patients has been difficult to determine due to methodological limitations (i.e. differences in definitions, assessment monitors and clinical recognition).

The mechanisms that underlie GER and risk of aspiration in critically ill patients differ substantially from those in awake or asleep patients with reflux disease. A group of defense mechanisms normally present in the upper aero-digestive system that protect against aspiration become compromised by clinical events associated with MV, submitting the patient to increased risk of GER. However, assessment of specific physio-pathological bases of MV-associated GER has methodological limitations. Firstly, GER is not exclusive to critical care settings. Its high prevalence of GER in the general population, even in the absence of significant acute or chronic comorbidity, raises a critical concern related to confounders and interactions between variables in critically ill individuals submitted to MV. Secondly, risk factors for GER can appear, disappear, interact and synergize during clinical evolution of the illnesses or during administration of MV (e.g. tube feeding, sedation, body positioning, etc.).

From a conceptual and clinical point of view, a comprehensive interpretation of risk factors leading to GER is translated in this review into an *"oil well analogy"* (Fig. 1). Gastric contents represent the oil deposit; "on-off" events reflect the presence or absence of specific risk factors and events, respectively, similar to opening and closing a drilling tower. In this dynamic analogy for both

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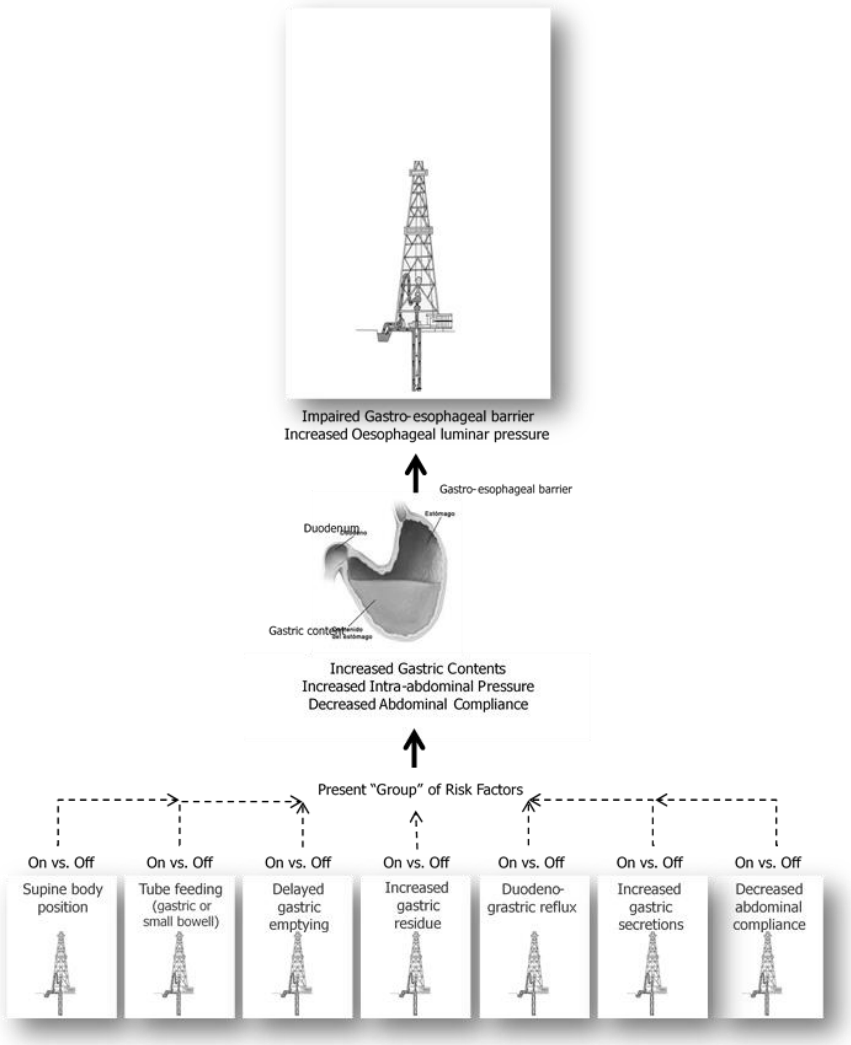

Figure 1 Schematic representation of risk factors for gastro-esophageal reflux using the "Oil Well Analogy" in patients receiving mechanical ventilation (MV). The mechanisms that underlie GER reflux in critically ill patients differ substantially from those in awake or asleep patients with reflux disease. The critically ill are at risk for aspiration for a number of reasons. A group of defense mechanisms normally present in the upper aerodigestive system that protect against aspiration become compromised by clinical events associated with MV, submitting the patient to increased risk of GER. Individual risk factors for GER can appear, disappear, interact and synergize either during clinical evolution of the illnesses or while receiving MV (e.g., tube feeding, sedation, body positioning, etc.). From a conceptual and clinical point of view, a comprehensive interpretation of risk factors leading to GER is translated into the "oil well analogy." This analogy reflects that, whereas gastric contents would represent the oil well, opening and closing drilling towers ("on-off" events) would represent presence or absence of specific risk factors and events, respectively. Using this dynamic interpretation of both risk and magnitude of GER, we underline that generalization of risk factors for GER in clinical settings is extremely relevant but also complex, difficult and limited.

the risk and magnitude of GER, we emphasize that generalization of GER risk factors in clinical settings is extremely relevant but fraught with complexity, difficulties and limitations. Therefore, the primary purpose of this book chapter is to examine the effect of the interaction between body positioning, gastrointestinal (GI function, tube feeding, drugs and additional factors on the aspiration risk in critically ill, tube-fed patients.

Lessons from gastro-esophageal reflux in general population

GER is more than a simple descriptive characteristic of interrelated esophagus and stomach functions. It has both clinical and pharmaco-economic relevance. In fact, GER increases the workload of both the gastroenterologist and family physician due to its high prevalence in the general population [1]. Research on risk factors, pathophysiological mechanisms and therapeutic modalities in critical care could focus on a unified strategy to address GER in the general population rather than individually evaluating each phenotypic presentation of gastro-esophageal reflux disease (GERD) [2].

GERD arises from contact of the esophageal epithelium with acidic gastric contents. For this to occur, gastric contents must move across the esophago-gastric junction (reflux) to enter the esophageal lumen. In conscious and

non-sedated patients with GER disease, the major reflux mechanism is transient lower esophageal sphincter relaxation (TLESR). However, we must bear in mind that absent lower esophageal sphincter (LES) pressure at baseline is an important mechanism in a substantial minority of patients, particularly those with hiatal hernias [3]. Straining, associated with increased abdominal pressure or deep inspiration, is a contributory factor in 20-30% of reflux episodes.

Several components of the esophago-gastric junction enable it to function effectively as an anti-reflux barrier (Table 1). The intraluminal pressure of this zone is significantly higher (10 to 30 mmHg) than in either the gastric lumen (+5 mmHg) or esophageal lumen (+5 mmHg) and, as such, constitutes an anti-reflux barrier. Notably, at various times, different components contribute more or less to the barrier function. For example, during exercise the crural diaphragm is a key component of anti-reflux barrier function; during swallowing, the phreno-esophageal ligament and acute angle of His become more important; at rest, the LES generates the most pressure. Noteworthy from a protective standpoint, the esophago-gastric junction is, by nature, an imperfect anti-reflux barrier; even healthy subjects exhibit multiple episodes of gastro-esophageal (acidic) reflux, and do so virtually every day. Thus, the esophago-gastric junction serves its protective function, not by complete prevention of reflux but by limiting the frequency and modulating the circumstances under which gastric juice enters the esophagus.

Despite increased awareness among clinicians and researchers on the importance of GER as a pathological condition, a number of unsolved problems persist in conventional clinical management [4]. Many authors suggest that the disease be modeled as a spectrum encompassing a broad range of clinical manifestations due

TABLE 1
STRUCTURAL COMPONENTS OF THE ESOPHAGO-GASTRIC JUNCTION:
ANTI-REFLUX GER BARRIER FUNCTION IN HUMANS

1. Lower esophageal sphincter
2. Mucosal rosette
3. Intra-abdominal segment
4. Acute angle of His
5. Phreno-esophageal ligament
6. Crural diaphragm

to the retrograde flow of gastric contents into the esophagus. Another school of thought believes that GER disease might be divided into three categories – non-erosive GERD (or NERD), erosive GERD (or ERD) and Barrett's esophagus – with little or no transition from one category to the other. However, some authors believe that any model based on a classification of the disease into three separate, mutually exclusive subgroups is misleading. In mechanically ventilated patients, the physiological environment differs substantially from that in the awake subject. These questions and lessons regarding GER in general population must be kept in mind when defining endpoints in critical care because, in fact, they represent confounders and interactions in the study analyses.

Role of impaired reflexes as risk factors for GER

Gag and upper airway reflexes.

Many mechanically ventilated patients have a decreased level of consciousness that tends to be associated with depressed cough and gag reflexes, making it difficult to protect the airway [5]. Two studies have demonstrated this increased risk. Saxe et al. [6] found significantly reduced LES pressures in 16 head-injured patients with Glasgow Coma Scale scores ranging from 3 to 11 within 72 hours of admission. Drakulovic et al. [7] found that a Glasgow Coma Scale score of less than 9 was a significant risk factor for pneumonia in nasogastric tube (NGT)-fed patients. These findings imply that a decreased level of consciousness might predispose to aspiration due to its effect on LES pressure and the need for tube feeding, since accumulated oropharyngeal secretions and regurgitated gastric contents can be aspirated into the lungs in the absence of normal safeguards to protect the airway [8].

Impaired function of the lower esophageal sphincter

Esophageal function may be influenced by a variety of extrinsic factors [9]. Anesthesia and sedation inhibit the triggering of TLESR [10], which would be expected to decrease the rate of reflux events. MV substantially alters the pressure profile across the gastro-esophageal junction and affects esophageal motility. However, basal LES pressure may be decreased through the effects of sepsis [11] and shock [12], thereby potentially increasing the likelihood of reflux.

Role of esophageal and gastric dysfunctions as risk factors for GER

Non-pharmacological factors associated with esophageal dysfunction

GER has been found to be enhanced in mechanically ventilated patients maintained in the supine body position and in patients fed by NGT, because these factors appear to increase the permeability of the LES [13]. Most critically ill, tube-fed patients have cuffed endotracheal tubes in place for MV; although these cuffed tubes are designed to seal the lower airway and prevent the entry of materials from the upper airway, they often fail to provide consistent barrier against aspirated materials. It is controversial whether the feeding site (gastric vs. small bowel) affects aspiration; however, many authors believe that gastrointestinal (GI) motility has a major impact on the degree of risk [10-12, 14-17].

Non-pharmacological factors associated with risk of gastric dysfunction

The underlying disease or injury associates with

decreased gastric motility in critically ill patients. Gastric dysfunction can range from a mild delay in gastric emptying to marked gastroparesis. Neurologically impaired patients with an elevated intracranial pressure (ICP) are at especially high risk. Mechanically ventilated patients disclose a decreased frequency of contractions, as shown by manometry. The loss of peristaltic activity is greater in the stomach than in the duodenum. This cause-effect relationship has been confirmed in experimental studies showing suppression of gastric and duodenal contractions by 60-80% after elevation of ICP [18]; when ICP decreased to normal, the animals' GI motility returned to normal.

Role of gastric volume as a risk factor for GER

Increased gastric contents also associated with small bowel feeding

Gastric secretions are significantly increased by the infusion of nutrients into the duodenum or jejunum [19], presumably in response not only to gastric but also biliary and pancreatic stimulation. The mean 24-hour gastric volume may even double after nasojejunal feedings are started. Aspiration has been documented at a rate of 5.9% and presumably is related to the accumulation of gastric secretions. Although gastric volume increases during small bowel feedings, the potential increase is significantly lower than that associated with gastric feedings [20]. In addition, patients fed through the stomach have a higher incidence of a single gastric residual volume (GRV) >150 mL than do those fed through the jejunum.

Increased gastric contents associated with duodenogastric reflux

Although a small degree of reflux from the small bowel into the stomach occurs in healthy persons, more significant reflux may occur in critically ill, tube-fed patients. Schindlbeck et al. [21] demonstrated that intragastric bile acid concentration in critically ill patients is greater than in healthy controls, whether fasting (mean 1.3 vs. 0.3 mmol/L) or fed through a gastric tube (1.3 vs. 0.4 mmol/L, $p< 0.05$). The increase in gastric bile acid is attributed to duodenogastric reflux. The degree of duodenogastric reflux is apparently related to the volume of nutrients delivered into the GI tract. Phillips et al. [22] found evidence that intestinal infusions of 5 to 15 mL (1 mL/min) of a liquid diet (3% glucose in saline) refluxed into the stomachs of rats; the degree of reflux was volume dependent. Given that fluid refluxed from the duodenum into the stomach adds to the already increased gastric volume, even small bowel feedings can pose a risk for aspiration if motility of the entire GI tract is significantly slowed.

Delayed recovery of gastric function as a risk factor for GER

Gastric motility is decreased after surgery or trauma, and time to recovery varies, in part based on the extent of injury. Carlin *et al* [23] found that seven days after admission the trauma patients studied had only limited improvement in gastric emptying. On the other hand, Avrahami et al. [13] studied patients who were submitted to aortic aneurysm surgery and found that gastric emptying was satisfactorily restored within 18 hours. These differences between patients and settings further support the proposed "oil well analogy" for interpreting the risk of GER in the context of multiple and dynamic events.

Pharmacological risk factors for GER

Pharmacological factors associated with risk of gastric dysfunction and GER

Commonly used medications (e.g. propofol, low-dose dopamine, and opioids) adversely affect gastric emptying. Propofol has a relaxing effect on visceral smooth muscle; although this effect is probably insignificant in healthy persons, it may be a consideration in patients receiving other medications that slow gastric emptying, especially when hyperglycemia is present [24]. Low-dose dopamine slows gastroduodenal motility in mechanically ventilated, critically ill patients [25]. Opioids are associated with slow gastric emptying, presumably through both a central and peripheral mechanism [26]. The enteral administration of opioid antagonists has been suggested as a possible method to improve gastric emptying and decrease the frequency of aspiration in mechanically ventilated patients receiving opioid analgesia. Moreover, enteral administration of naloxone may allow selective blockage of intestinal opioid receptors without producing central antagonist effects on analgesia. Opioid blockage is associated not only with a lower gastric tube volume in the naloxone group but also a decreased frequency of pneumonia (34% vs. 56%, $p=0.04$).

Role of gastrointestinal feeding as a risk factor for GER

Effect of feeding site on aspiration

Controversies still exist regarding the optimal feeding site for critically ill patients. Some investigators advocate feeding through the small bowel, whereas others are equally convinced that most can tolerate gastric feedings. However, a review of 10 randomized clinical trials of critically ill patients that compared small bowel and gastric feedings [27] concluded that small bowel feeding may be associated with a reduction in GER and a lower rate of ventilator-associated pneumonia (VAP). Several studies have found that small bowel feedings are better tolerated than gastric feedings and thus allow better (i.e. higher) caloric intake [28]. Similar conclusions were reported in the Consensus Statement issued by the North American Summit on Aspiration in the Critically Ill Patient (Table 2) [29]; this group recommended that feeding tubes be placed distal to the stomach. Further, positioning the tip beyond the ligament of Treitz may be superior to simple postpyloric placement in reducing aspiration risk in critically ill patients. A single answer to the question of the preferred feeding site is not likely to be found because aspiration risk exists to some extent in all tube-fed patients,

TABLE 2
RECOMMENDATIONS FOR PRACTICE ACCORDING TO NORTH AMERICAN SUMMIT ON ASPIRATION IN THE CRITICALLY ILL PATIENT: CONSENSUS STATEMENT

Assessment of gastric residual volume
Stop feedings abruptly when overt regurgitation or aspiration occurs.
Withhold feedings and reassess the patient's tolerance when GRVs greater than 500 mL are found.
GRVs in the range of 200 to 500 mL should prompt careful bedside evaluation and initiation of approaches to reduce aspiration risk.
Although GRVs less than 200 mL seem to be well tolerated, there should be ongoing evaluation of risk.
Methods to decrease risk of aspiration
Place the feeding tube distal to the stomach. Positioning the tip of the feeding tube beyond the ligament of Treitz may be more effective in reducing aspiration risk than simple postpyloric placement.
Reassess need, level, and choice of agents used for sedation.
Reevaluate the need for opioid analgesia, and minimize the use of narcotics.
Keep the head of the bed elevated to more than 30° to 45°; if not possible, position the patient in reverse Trendelenburg.
Consider the use of prokinetic agents (egg, metoclopramide and erythromycin).
Change formula delivery method from bolus/intermittent to continuous.
Regularly assess feeding tube placement to ensure that the tube has remained in the correct position.
Consider use of continuous aspiration of subglottic secretions.

depending on GI dysmotility patterns and individual patient characteristics. However, regardless of the feeding site, it is regurgitated gastric contents that are aspirated into the lungs. For this reason, the assessment of gastric emptying is of greatest interest for tube-fed patients.

Gastric tube feedings as a risk factor for GER

Gastric tubes are easier and less expensive to place than those required for distal small bowel feedings. Therefore, intra-gastric feedings are favored over small bowel feedings when gastrointestinal motility is normal [17]. When motility is only mildly impaired, intra-gastric feedings may be tolerated at a less than desirable flow rate. When gastric motility is moderately or seriously impaired, feedings accumulate in the stomach along with gastric secretions and predispose the patient to reflux and aspiration.

Small bowel feedings as a risk factor for GER

Small bowel function usually returns before gastric or colonic activity is re-established following trauma or surgery [30]. Similarly, small bowel activity may be less adversely affected than either gastric or colonic function in acute medical conditions, such as pancreatitis [31]. When gastric motility is significantly slowed, small bowel feedings are preferred. Although small bowel motility often is greater than gastric motility in critically ill patients, feeding through the small bowel may also be associated with aspiration of gastric contents. This results from increased gastric secretions during small bowel feedings and reflux of duodenal contents into the stomach.

The role of body position as a risk factor for GER in mechanically ventilated patients

In 1992, the supine body position and the duration of the time spent in the supine position were associated with an increased risk of aspirating gastric content into the airways [32]. Consequently, the semi-recumbent body position was proposed as a potential prophylactic maneuver to reduce GER and prevent VAP. More recently, Drakulovik et al. [7] demonstrated that maintaining mechanically ventilated patients in a semi-recumbent

position significantly reduced incidence of VAP, from 34 to 8%. In a subsequent study, however, the semi-recumbent position was not found to fully protect the patient from GER or oropharyngeal colonization of gastric origin [33]. Notably, most of these studies were carried out without enteral nutrition and thus under conditions of low gastric content, which may have resulted in an underestimation of GER.

Clinical implications of serial GER risk factor monitoring

Is the objective assessment of gastric volume clinically relevant?

Gastric volume during intra-gastric feedings is determined by the balance between the amount of fluid emptied from the stomach and the amount of infused formula plus the endogenous secretions of saliva and gastric juice. Because the stomach acts as a reservoir for food and fluids, it is capable of holding large quantities of formula, gastric secretions, and swallowed saliva if gastric emptying is abnormally slowed. For continuously fed patients, GRV is measured every 4 to 6 hours. For intermittently fed patients, GRV is measured immediately before the next scheduled feeding Residual volume measurement is by far the most frequently recommended assessment for gastric emptying [34]. An excessive GRV predisposes one to GER reflux and aspiration; therefore, if a high GRV can be detected early, it may be possible to prevent aspiration. Volumes may be designated as "excessive" at a range from 50 mL to as much as 500 mL, or as a proportion of infused solution (e.g. >20%).

However, the "critical level of GRV" is not known and must be evaluated for each individual. Lin et al. [35] used a software simulation of nasogastric feeding, concluded that the current practice of stopping enteral feedings when GRV exceeds an arbitrarily selected volume threshold might not be physiologically sound, and recommended clinical studies to identify significant volumes. McClave et al. [36] measured GRVs with gastrostomy tubes during the administration of continuous feedings in healthy subjects, critically ill patients, and stable patients. Physical findings of GI dysmotility were associated with a gastric volume >200 mL in patients receiving nasogastric feedings and >100 mL in patients receiving gastrostomy feedings. There is evidence that GRV is greatest in the first few days of tube feedings. Kesek et al. [37] studied 73 critically ill patients from initiating a standard enteral formula via NGT until the patients were discharged from the unit or resumed oral feedings. Interestingly, the investigators concluded that a balanced enteral diet, in itself, has a prokinetic effect.

Some potential limitations with GRV measurement are the variability in pooling of gastric contents due to the patient's position, the positioning of feeding tube ports above the pool of gastric fluid, and use of a small bowel feeding tube only. There is confusion as to how gastric residuals should be handled after they are measured [38]. Only one study has been specifically aimed at assessing outcomes of discarding or returning gastric residuals to the patient [39]. In the absence of adequate research-based data to indicate otherwise, a recent consensus conference statement called for returning GRVs <500 mL to the patient.

Is the objective assessment of gastric emptying clinically relevant?

The primary clinical assessment of gastric emptying consists of measuring GRV. Sophisticated methods for assessing gastric emptying include the acetaminophen absorption test and radionuclide scintigraphy; however, these are limited to research applications, some of them have been questioned [36], and they have not been recommended for regular use [40].

Is the objective assessment of small bowel residual volume clinically relevant?

Small bowel residual volume rarely is measured because it is believed that small bowel feedings generate a negligible residual volume (e.g. <10 mL), presumably because the small bowel propels formula and GI secretions forward quickly. Because of close proximity to the stomach, it is probable that higher residual volumes can be found in the duodenal bulb than in more distal segments of the small bowel. Interestingly, Day et al. [41] found that the small bowel residual volumes did not exceed a mean of 5 mL (SD 7 mL) on any of the 10 days of their study. Similarly, some authors recommend checking residual volumes from small bowel tubes primarily as a method to determine whether the tube may have dislocated upward into the stomach [42].

Is the subjective assessment of abdominal semiology clinically relevant?

Delayed gastric emptying, motility disorders of the small and large intestine, and perhaps intestinal spasms or ischemia may be associated with subjective signs of intolerance of tube feedings, including abdominal fullness, pain, cramping, and nausea [43]. Useful semiological techniques to assess abdominal distension include abdominal girth and abdominal circumference (from iliac crest to iliac crest). Stool pattern (volume, frequency, color, and consistency) is another assessment of GI tolerance of enteral feedings. Nausea and vomiting may be caused by gastric atony or irritation, a rapid infusion rate, or activation of the emetic center by medications, distal obstruction, anxiety, or other disease states. When gastric contents pass from the esophagus into the oropharynx during vomiting, the risk for aspiration is heightened, especially in patients with poor reflexes to protect the airway [44]. Persistent vomiting has been linked to the development of recurrent aspiration in patients with end-stage renal failure who received enteral feedings through nasogastric or gastrostomy tubes. Bowel function is evaluated by listening for bowel sounds in all 4 abdominal quadrants. Normal bowel sounds consist of a series of clicks and gurgles with an estimated frequency of 5 to 34 per minute. The key assessment in critically ill, tube-fed patients is whether bowel sounds are present or absent. There is evidence, as demonstrated by Goldhill et al. [11], that assessment of bowel sounds is of little value in

determining gastric emptying: no correlation was found between bowel sounds and results from the acetaminophen absorption test for gastric emptying in 27 critically ill, tube-fed patients.

Preventive measures aimed at decreasing the risk of GER in patients receiving mechanical ventilation

Several groups find it reasonable and clinically relevant to further investigate new potential preventive measures that are applicable to conventional clinical settings, have little or no impact on selecting resistant microorganisms, and are economically viable. In this regard, several mechanical preventive measures have been evaluated, including intermittent or continuous subglottic aspiration, avoidance of NGT, small-bore NGT, and semi-recumbent body positioning.

Strategies aimed at maintaining esophageal and gastric function

Use of promotility agents (e.g. erythromycin or metoclopramide) improves tolerance of intragastric feedings and reduces the likelihood of gastro-esophageal reflux and pulmonary aspiration [45]. However, despite their usefulness, both erythromycin and metoclopramide can interfere with the pharmacokinetics and metabolism of numerous drugs [46]. Erythromycin may interact with carbamazepine, cyclosporine, theophylline, aminophylline, digoxin, and oral anticoagulants. In addition, side effects of metoclopramide include dystonic and dyskinetic movements and cardiac arrhythmias; erythromycin may contribute to antibiotic resistance [47].

Strategies aimed at decreasing the effect of gravity

Drakulovik et al. [7] demonstrated that maintaining mechanically ventilated patients in a semirecumbent position is able to significantly reduce incidence of VAP from 34 to 8%. In a subsequent study, however, the semirecumbent position was not found to fully protect the patient from GER or oropharyngeal colonization of gastric origin [33].

Strategies aimed at obstructing esophageal lumen.

Orozco-Levi et al. [48] demonstrated that using a NGT with an esophageal balloon is a safe and effective method for reducing the magnitude of GER as well as protecting the airways from aspiration with contaminated gastric contents in patients receiving mechanical ventilation. The study demonstrates that an inflated esophageal balloon significantly delays, and decreases the magnitude of, both GER and bronchial aspiration of gastric contents, compared to the effect of a semi-recumbent position only. These findings imply that the inflated esophageal balloon actually imposed a protective obstructive effect on the GER in patients receiving mechanical ventilation. Arterial perfusion does not substantially diminish because the esophagus, which lacks a serosal layer, is distensible. The pressure of the inflated balloon was controlled and maintained at 30 cmH2O to minimize the possibility of ischemia, necrosis, rupture or fistula of the esophagus. These complications can be found in 15% of patients receiving esophageal tamponade in esophageal variceal bleeding; however, in these cases a higher balloon pressure than that indicated would be applied to the bleeding varix in order to compensate for the intravariceal pressure. This is important when evaluating whether a clinical application of the tube is required for several days, weeks or even months of mechanical ventilation. At present, there is a paucity of such prolonged studies. However, these results highlight the need for further evaluation of the effectiveness of the NGT with an esophageal balloon in preventing nosocomial pneumonia in mechanically ventilated patients. The study suggests that the device could be useful in combination with the semi-recumbent positioning of patients in preventing VAP. The role of the esophageal balloon could be even more relevant in patients requiring mandatory supine position (e.g. shock), receiving paralyzing or sedative agents, or showing decreased abdominal compliance or gastroparesia for various reasons during mechanical ventilation. Before recommending such a technique as a preventive measure for VAP, the long-term impact of the device on GER, along with safety considerations, must be evaluated. Although the method was found to be safe when applied for 8h, longer times (24h) should be considered with caution. The design of future protocols must incorporate two key variables: the minimum level of pressure that decreases or eliminates GER, and the length of time the balloon pressure is applied. Firstly, in addressing the minimum level of pressure, it may become possible to apply pressures below 30 cmH_2O that would also yield favorable results. Secondly, the duration of the applied balloon pressure should initially be <24 h, which may be extended if further studies establish that this can be done safely. Further evaluation may also establish the effectiveness of the NGT with an esophageal balloon in preventing nosocomial pneumonia in mechanically ventilated patients.

Strategies using a small-bore nasogastric tube

An alternative approach to obviate the need for an esophageal balloon is to use a small-bore NGT. However, this technique has been evaluated in two previous studies with contradictory results [49, 50]. Ibáñez et al. [49] demonstrated that a small-bore NGT results in a lower incidence of GER in patients receiving MV. However, Ferrer et al. [50] used two NGT sizes to study their patients, a 6 mm and a 2.85 mm external bore. The authors demonstrated that intubating patients with a smaller-bore NGT does not reduce GER or microaspirations. In fact, no differences were found between the two NGT types and cumulative radioactivity markers in pharyngeal and tracheal samples.

Strategies aimed at decreasing gastric volume

Distal small bowel placement of feeding tube

If prokinetic agents do not work for intragastrically fed patients with slowed gastric emptying, the next step usually is to insert the feeding tube into the distal duodenum or proximal jejunum (preferably past the ligament of Treitz). It has been recommended that patients

who are at greatest risk for aspiration of gastric contents be fed through the jejunum while a NGT is used for concurrent decompression of the stomach [51]. Single tubes with ports in both the stomach and jejunum also exist [52].

Change from bolus or intermittent feedings to continuous feedings

It has been hypothesized that the intermittent feeding method allows gastric pH to decrease between feedings and thus helps to destroy bacteria that could lead to pneumonia after aspiration of regurgitated gastric contents. Although there are no studies that definitively associate continuous feedings with less aspiration than with intermittent feedings, continuous feedings are more commonly used in critically ill patients. When bolus or intermittent gastric feedings are not tolerated, continuous feedings may be tried. In a prospective, randomized study of 41 mechanically ventilated patients, Gowardman et al. [53] compared three methods for delivering enteral nutrition (intermittent or continuous gastric feedings and continual jejunal feedings). The investigators speculated that the probability of gastric colonization over time was significantly lower in the group receiving jejunal feedings than in the two groups receiving gastric feedings and recommended further study to determine the implications for the pathogenesis of ventilator-associated infection.

Discontinuation of enteral feedings

Only rarely, when complicated by both non-occlusive gastric and small bowel necrosis, must enteral feedings be totally suspended in favor of total parenteral nutrition. Gastric tonometry has been proposed for detecting non-occlusive small bowel necrosis because low mucosal pH (<7.30) can reflect gastrointestinal necrosis. Additional clinical signs are usually those from a septic shock, with hypotension, fever, tachycardia, and abnormal white blood cell count. Surgical intervention often is required.

Strategies aimed at suctioning esophageal and oro-pharyngeal contents

Continuous subglottic suction

As is reviewed in a previous chapter of this book, there is evidence demonstrating that continuous subglottic suction helps to prevent or at least delay the development of nosocomial pneumonia in mechanically ventilated patients by removing pooled secretions that may leak around the endotracheal tube cuff [54, 55]. However, whereas continuous aspiration of subglottic secretions can decrease bacterial colonization of the respiratory tract, it may also result in mucosal damage at the level of the suction port [56].

Concluding remarks

Gastro-esophageal reflux is not merely descriptive but a major problem in critically ill patients in the intensive care unit (ICU). Bronchial aspiration is the leading cause of pneumonia in the ICU and the most serious complication of enteral tube feeding. Reflux has been incriminated as an important cause of nosocomial pneumonia [57-59]. Reflux esophagitis is a common finding in critically ill patients, has been reported to be present in 25-30% of ICU patients undergoing upper gastrointestinal endoscopy, and is the most common cause of upper gastrointestinal bleeding [60]. Despite these relevant clinical implications of GER, more research is needed to determine the best delivery methods and feeding sites for specific types of tube-fed patients to prevent, or at least minimize, aspiration [29].

Prospective studies that are sufficiently powered to evaluate the effect of different GRV threshold values on protection against aspiration and on clinical outcomes are also needed. Until more definitive evidence is available, it is helpful to consider the following excerpts from recommendations made at the 2002 North American Summit on Aspiration in the Critically Ill Patient [29]. Traditional clinical monitors of glucose oxidase strips and blue food coloring should no longer be used. A modified approach to use of gastric residual volumes and identification of clinical factors that predispose to aspiration allow for risk stratification and an algorithm approach to the management of the critically ill patient on ETF. Although the patient with confirmed aspiration should be monitored for clinical consequences and receive supportive pulmonary care, ETF may be continued when accompanied by appropriate steps to reduce risk of further aspiration. Management strategies for treating GER are based on degree of diagnostic certainty, time of onset, and host factors.

Conflict of Interest

The authors declare no conflicts of interest.

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