Factors affect how much of an administered dose of aerosol is actually delivered to the airways, it is unlikely that a single dosing regimen is maximally effective in all patients. Accordingly, we have suggested a simple algorithm for titration of aerosolized bronchodilators to physiologic effect in intubated patients.

When optimal techniques are used in a patient who is breathing quietly on the ventilator, 4 to 5 puffs of MDI administered through an in-line spacer are likely to be effective. However, in practice, ideal clinical conditions for maximal aerosol delivery rarely are achieved. Therefore, respiratory therapists must learn effective administration techniques, and respiratory system resistance should be measured before and after treatments to gauge effectiveness. Why take the time to administer a medication if no effect is demonstrated?

The following questions remain unanswered:

1. If MDI use is curtailed due to chlorofluorocarbon emissions, are DPIs effective in intubated patients, or will nebulizers be the only effective option?

2. What is the optimal dosing frequency in critically ill patients? Are the pharmacodynamics of β-agonists and other therapeutic aerosols altered in critically ill patients? If so, one frequency of administration may not be appropriate for all patients. Do patients with severe bronchospasm benefit from continuously aerosolized bronchodilators?

3. Do aerosolized medications improve outcomes, eg, ventilator days and ICU lengths of stay? At many hospitals, a majority of mechanically ventilated patients receive aerosolized medications without clear indications. While it is assumed that aerosolized bronchodilators improve our patients’ outcomes, no studies exist to suggest that these medications are required in all ventilated patients. In patients whose respiratory failure has resulted from bronchospasm, few would argue against the utility of aerosolized bronchodilators. However, when airways resistance is not significantly elevated, the risks of aerosolized therapies may approach or exceed the benefits. Obviously, large numbers of patients would need to be studied to determine the cost-benefit ratio of aerosolized bronchodilators in this cohort. In the absence of such studies, we should circumspect in using these medications in patients with low-to-moderate airways resistance, particularly if they are vulnerable to complications such as hypokalemia and arrhythmias.

Laboratory and clinical investigations of the past 5 years have led to significant advances in our understanding of aerosol delivery in mechanically ventilated patients. It is clear that both nebulized and MDI bronchodilators can reduce airways resistance. Now, physicians and respiratory therapists should utilize the results of these clinical trials to improve patient care. Hopefully, future studies will identify those patients whose outcomes are most likely to improve as a result of aerosolized medications.

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Effects of Selective Digestive Decontamination on Lung Injury and Outcome

The Verdict Is Not Yet In

In this issue of CHEST (see page 491), Sorkine and colleagues report on the effects of selective digestive decontamination (SDD) on serum endotoxin and tumor necrosis factor (TNF) levels, and associated lung injury in a rat model of bowel ischemia and reperfusion. These findings are best interpreted in the context of what is already known about SDD.

Resistance to colonization of the digestive tract is rendered by the integrity of the cellular lining and mucosal function, mucus production and peristalsis, and humoral factors. The presence of endogenous anaerobic microorganisms is also essential in preventing competitive overgrowth by potentially pathogenic bacteria, particularly Gram-negative enteric organisms and enterococci. This natural resistance is undermined by many aspects of critical illness.

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Gut failure and bacterial overgrowth have been implicated in nosocomial infection, in particular, in Gram-negative pneumonia. However, they have also been associated with bacterial translocation of enteric pathogens that may be involved in the pathogenesis of multiorgan dysfunction syndrome (MODS). Occult bacteremia, often with enteric organisms, is frequent in the setting of MODS. A potential source may be translocation of gut pathogens to mesenteric lymph nodes, and hence to the portal circulation, liver, and systemic dissemination. It has been proposed that bacterial translocation is the “motor of MODS,” either by providing a source of continuous infection or by altering the host’s immune response and perpetuating the systemic inflammatory response. The intent of SDD is to rid the gut of pathogens that serve as a reservoir for nosocomial infection, while preserving the normal flora. Toward this end, various combinations of oral and topical enterally nonabsorbable antibiotics have been used, with or without concomitant parenteral antibiotics. The premise of such an approach is that serious infections in compromised patients may be prevented if colonization by pathogenic organisms can be avoided.

SDD was first proposed in a study of trauma patients requiring mechanical ventilation. Oral polymyxin E, tobramycin, and amphotericin B reduced Gram-negative colonization in the oropharynx and rectum; systemic cefotaxime was added to prevent primary Gram-negative pneumonia in the first 48 hours. This corresponded with a reduction in nosocomial infections from 81 to 16% and a decrease in respiratory tract infection from 59 to 8%. However, there was no improvement in mortality despite evidence that the relative risk of death in an ICU population increases 3.5-fold when nosocomial infection is present.

Numerous papers on the subject of SDD have been published. Studies differed in important respects, including design, SDD regimen, patient population, severity of illness, inclusion criteria, primary outcome measures, and criteria used to diagnose pneumonia. Despite this variability, all demonstrated a decrease in Gram-negative colonization of the oropharynx and trachea by 48 hours; decontamination of rectal samples took considerably longer. Reduction in lower respiratory tract infection has also been reported, except in those studies where infection rate was low in the control group. Only three studies documented a decrease in length of ICU stay or mortality. One was a randomized trial where the reduction in mortality was attributable to a decrease in infection-related deaths, which were high in the control group. Meta-analyses of randomized, controlled trials of SDD have been performed, confirming a reduction in respiratory tract infections (relative risk 0.12-0.46) but no decrease in mortality (relative risk 0.7-0.93).

In patients with acute pancreatitis, SDD reduced the incidence of secondary pancreatic infection and, in those with a high expected mortality, improved survival. In an animal model of cirrhosis, SDD decreased the occurrence of spontaneous bacterial peritonitis. Despite evidence that SDD decreases bacterial translocation, a decline in the incidence of MODS has not been shown. In an animal model of zymosan-induced MODS using two regimens of SDD, trimethoprim was superior in eradicating Gram-negative colonization, while streptomycin reduced mortality. These data suggest a possible uncoupling of infection, MODS, and death in critical illness.

While most studies investigating SDD have focused on the reduction in nosocomial pneumonia, the lack of improvement in mortality can likely be extrapolated to bacterial translocation. In trying to understand the absence of survival benefit, several possible explanations can be considered. First, SDD may not truly decrease the incidence of nosocomial pneumonia, but the presence of topical antibiotics may impair the microbiologic diagnosis by inhibiting growth of organisms in culture. Second, studies performed thus far may have lacked statistical power to detect a survival advantage. For example, based on a 30% incidence of nosocomial pneumonia in an ICU setting, with an associated mortality of 35%, along with an expected 60% decrease in pneumonia resulting from SDD and an estimated survival benefit of 10 to 20%, with conventional type I and II errors, 2000 patients would need to be randomized to demonstrate a survival benefit of SDD. Third, a survival advantage may only pertain to specific subsets of patients, such as those with a high risk of infectious complications or those with high predicted ICU mortality. Lastly, nosocomial infection may be a marker of critical illness with no causal relationship between nosocomial infection and mortality.

Sorkine and colleagues document a decrease in serum endotoxin and TNF levels and an attenuation of lung injury in an animal model of intestinal ischemia and reperfusion treated with SDD. This is consistent with endotoxin’s role in neutrophil sequestration and activation in the lung and its role in the stimulation of TNF-α production. Elevated levels of TNF-α have been found in MODS, and persistently elevated levels have predicted poor outcome. Like Sorkine and colleagues, other investigators have evaluated the role of bacterial translocation and gut-derived endotoxin in the pathogenesis of sepsis and the effects of SDD on mortality in a model of rat thermal injury. They demonstrated a reduction in endotoxin levels in portal
and systemic blood of SDD-treated animals, along with a lower incidence of bacterial translocation and improved survival.

Potential downsides of SDD include the fostering of resistant organisms and added ICU cost. Some studies have documented a change in resistance patterns and in the spectrum of nosocomial bacteria in ICUs that use SDD. Although some studies have shown a reduction in cost with the reduced need for systemic antibiotics, others have found an increase in cost due to microbiologic surveillance and the actual cost of SDD.

Accordingly, given the lessons we’ve learned thus far from the sum of these studies, a healthy skepticism is in order as we investigate the cause and effect relationship among gut bacterial overgrowth, gut endotoxin, bacterial translocation, lung injury, MODS, and mortality.

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What’s the Rush? Trust the Process

It is not surprising that the recent controversy surrounding the value of the Swan-Ganz catheter has additionally prompted international remarks. Further commentaries suggest that this balloon flotation catheter may be barely treading water, and that it may be time to pull it, as its swan song is chanted.

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