Dr. Klonoff calls the control skin in the burn victims?

We considered the placement of the catheters when designing the study. The available equipment at the time restricted us to the length of the catheter shaft, as the pump we used had two parallel mounted syringes. To minimize the influence of fluid accumulation and, most important, the effect of blood flow in the tissue, we chose the abdomen or proximal limbs where the lymph flow and blood flow are less generally affected by the tissue edema. We do not have a good answer to this question, as no other skin areas are practically available, especially not in the case of larger burns. We do, however, believe that the changes that we have registered are of global relevance in each subject as there were no deviations from the presented findings in any of the separate patients.

Third, does effective insulin therapy attenuate the disparities between uninjured skin and the controls?

The question is well founded but can only be speculatively answered. At the time of the data collection, Van den Berghe’s work had not been published and tight glucose control was not generally accepted outside of neurointensive care. Assuming that the increase in tissue glucose levels found in our experiment is due to an insulin/receptor/uptake dysfunction, it may be concluded that intensive insulin therapy would improve local tissue glucose levels (5). A shortcoming of this conclusion is that the pathophysiology of trauma-induced insulin resistance is not fully understood.

The author has not disclosed any potential conflicts of interest.

Anders Samuelsson, MD, Professor Folke Sjoberg, Department of Critical Care, University Hospital Linkoping, Sweden

REFERENCES


DOI: 10.1097/01.CCM.0000262532.26296.F8

Erythromycin as a prokinetic: Is the overall benefit corroborated?

To the Editor:

The original work by Dr. Nguyen and colleagues (1) was read with much interest, and I must compliment the authors for the efforts put into conducting the study. On the topic of use of erythromycin as a prokinetic agent, I wonder if the authors share my and other healthcare providers’ (2) misgivings over this proposed role of the drug. There is strong evidence that interventions directed at prudent use of antibiotics can reduce the incidence of antimicrobial drug resistance and healthcare-associated infections. In light of these and other concerns, the role of erythromycin as a prokinetic agent should be acceded to cautiously because of the potential to increase spread of antibiotic resistance, the potential to increase Clostridium difficile-associated diarrhea, marginal proven efficacy over conventional prokinetic agents, lack of sufficient data on appropriate dosage, and patient selection criteria. In addition, the reported adverse effects of erythromycin such as arrhythmias, hepatotoxicity, diarrhea, myasthenia, and increased warfarin and theophylline levels through enzyme inhibition should be paid attention to, especially in a critically ill patient. Also, at present it is difficult to comment on the mortality (by virtue of preventing aspiration) and symptomatic benefits gained from erythromycin use, as the studies reported are limited and have wide disparities. It seems wise to use erythromycin in the lowest effective dose, 70 mg as shown in one study (2), and only when more conservative measures (head-end elevation, control of pain and other contributing factors like hypotension and sepsis, avoidance of opiates, conventional prokinetic agents) have failed (3, 4).

The author has not disclosed any potential conflicts of interest.

Nishith K. Singh, MD, All India Institute of Medical Sciences, New Delhi, India

REFERENCES


DOI: 10.1097/01.CCM.0000262543.59187.36

The authors reply:

We would like to thank Dr. Singh for his insightful comments about the widespread use of erythromycin as a prokinetic in critically ill patients, with regard to the potential development of antibiotic resistance and the adverse effects, particularly Clostridium-associated diarrhea and drug interactions.

Although it is well recognized that “sublethal” concentrations of antibiotics exert selective pressure on bacteria and can contribute to the development of bacterial resistance (1), there are no direct data in the current literature to support this hypothesis regarding the use of a short course of low-dose erythromycin (2). However, if one believes that this hypothesis is true, the use of erythromycin should be strictly avoided rather than modifying the dose from 200 mg to 70 mg, as the “sublethal” concentrations have not been defined (1). Furthermore, the impact of 70-mg erythromycin dosage on either the success of feeding or the occurrence of adverse effects in feed-intolerant critically ill patients has not been evaluated.

Similarly, data on the impact of erythromycin, at prokinetic doses, on the development of Clostridium-associated diarrhoea are limited. In our recent analysis (3), although 40% of 143 feed-intolerant patients who received low-dose erythromycin developed diarrhoea, none was related to Clostridium difficile or bacterial infection in general. In this study, the development of diarrhoea was similar between patients who received erythromycin vs. metoclopramide. Although the other potential adverse effects of erythromycin may be common at full antibiotic dosage, they were not observed when erythromycin was given at prokinetic dosage (4). We believe
that most critical care units are adopting the "conservative" measures mentioned by Dr. Singh, yet >50% of the patients are reported to have feed intolerance.

Given the magnitude of feed intolerance and its adverse impact on both morbidity and mortality of critically ill patients (5), treatment should be instituted promptly. In view of the relatively poor efficacy of metoclopramide, avoiding erythromycin without the availability of other new but safe and effective prokinetic agents may compromise patients' outcomes from the complications of feed intolerance. Furthermore, several potential adverse effects are associated with the use of metoclopramide. Although postpyloric feeding and total parenteral nutrition are alternatives, each has its own problems and is not suitable as the first-line therapy (5).

In view of these limitations, we therefore believe that the benefits of a short course of low-dose erythromycin for feed intolerance in critically ill patients outweigh the unproven concerns raised by Dr. Singh. “Prophylactic” use of low-dose erythromycin outside the context of feed intolerance, however, should be avoided.

Nam Q. Nguyen, MBBS (Hons), FRACP, Richard H. Holloway, MBBS, MD, FRACP, Department of Gastroenterology and Hepatology, Royal Adelaide Hospital, South Australia

REFERENCES

7. Downar J, Mehta S: Bench-to-bedside review: High-frequency oscillatory ventilation in adults with acute respiratory distress syndrome (2), a release of cytokines due to conventional ventilation with high tidal volumes and low positive end-expiratory pressure (PEEP) in patients with normal lungs is mostly related to preexisting damage of lung tissue and systemic inflammatory state (3). This issue was not addressed appropriately by the authors in the study’s title, objectives, or conclusions.

Second, gas exchange was worse during both protective strategies compared with controls. Indeed, lung-protective ventilation strategies are primarily purposed to limit alveolar overdistension and repeat alveolar collapse with the use of small tidal volumes. A key issue in this respect is the choice of an adequate PEEP level (2) that may largely differ from the high PEEP of 10 cm H2O, as it has been used in the present study. Application of high PEEP in healthy subjects has already been shown to result in worse oxygenation (4), as high PEEP prevents atelectasis but also impairs ventilation/perfusion ratio and subsequently increases intrapulmonary shunt (5). Furthermore, high PEEP in normal lungs has also been suggested to cause severe hypercapnia due to alveolar overdistension and decreased respiratory system compliance, an adverse effect also reflected by the authors’ data.

Finally, the observed reduction in cardiac output, systemic oxygenation, and oxygen delivery may have compromised tissue perfusion and metabolism in the periphery. Unfortunately, all variables were measured only once 30 mins after switching to a new ventilation strategy. Changes of hemodynamic variables, however, are most pronounced straight after an increment of mean airway pressure, whereas these variables adapt to increased PEEP level thereafter (6). Therefore, it is particularly important to investigate variables of individual organ perfusion, tissue oxygenation, and biochemistry. Furthermore, brain and cardiac tissue are extremely susceptible to ischemia, and even a few minutes of compromised perfusion can affect metabolic rate of oxygen and tissue integrity. To elucidate the impact of mechanical ventilation on these tissues, the authors should have analyzed regional blood flow or established biomarkers of tissue ischemia.

Patrick Meybohm, MD, Jens Scholz, MD, Norbert Weiler, MD, Berthold Bein, MD, University Hospital Schleswig-Holstein, Campus Kiel, Department of Anaesthesiology and Intensive Care Medicine, Kiel, Germany

REFERENCES

2. Downar J, Mehta S: Bench-to-bedside review: High-frequency oscillatory ventilation in adults with acute respiratory distress syndrome (2), a release of cytokines due to conventional ventilation with high tidal volumes and low positive end-expiratory pressure (PEEP) in patients with normal lungs is mostly related to preexisting damage of lung tissue and systemic inflammatory state (3). This issue was not addressed appropriately by the authors in the study’s title, objectives, or conclusions.

Second, gas exchange was worse during both protective strategies compared with controls. Indeed, lung-protective ventilation strategies are primarily purposed to limit alveolar overdistension and repeat alveolar collapse with the use of small tidal volumes. A key issue in this respect is the choice of an adequate PEEP level (2) that may largely differ from the high PEEP of 10 cm H2O, as it has been used in the present study. Application of high PEEP in healthy subjects has already been shown to result in worse oxygenation (4), as high PEEP prevents atelectasis but also impairs ventilation/perfusion ratio and subsequently increases intrapulmonary shunt (5). Furthermore, high PEEP in normal lungs has also been suggested to cause severe hypercapnia due to alveolar overdistension and decreased respiratory system compliance, an adverse effect also reflected by the authors’ data.

Finally, the observed reduction in cardiac output, systemic oxygenation, and oxygen delivery may have compromised tissue perfusion and metabolism in the periphery. Unfortunately, all variables were measured only once 30 mins after switching to a new ventilation strategy. Changes of hemodynamic variables, however, are most pronounced straight after an increment of mean airway pressure, whereas these variables adapt to increased PEEP level thereafter (6). Therefore, it is particularly important to investigate variables of individual organ perfusion, tissue oxygenation, and biochemistry. Furthermore, brain and cardiac tissue are extremely susceptible to ischemia, and even a few minutes of compromised perfusion can affect metabolic rate of oxygen and tissue integrity. To elucidate the impact of mechanical ventilation on these tissues, the authors should have analyzed regional blood flow or established biomarkers of tissue ischemia.

Patrick Meybohm, MD, Jens Scholz, MD, Norbert Weiler, MD, Berthold Bein, MD, University Hospital Schleswig-Holstein, Campus Kiel, Department of Anaesthesiology and Intensive Care Medicine, Kiel, Germany

REFERENCES

2. Downar J, Mehta S: Bench-to-bedside review: High-frequency oscillatory ventilation in adults with acute respiratory distress syndrome (2), a release of cytokines due to conventional ventilation with high tidal volumes and low positive end-expiratory pressure (PEEP) in patients with normal lungs is mostly related to preexisting damage of lung tissue and systemic inflammatory state (3). This issue was not addressed appropriately by the authors in the study’s title, objectives, or conclusions.

Second, gas exchange was worse during both protective strategies compared with controls. Indeed, lung-protective ventilation strategies are primarily purposed to limit alveolar overdistension and repeat alveolar collapse with the use of small tidal volumes. A key issue in this respect is the choice of an adequate PEEP level (2) that may largely differ from the high PEEP of 10 cm H2O, as it has been used in the present study. Application of high PEEP in healthy subjects has already been shown to result in worse oxygenation (4), as high PEEP prevents atelectasis but also impairs ventilation/perfusion ratio and subsequently increases intrapulmonary shunt (5). Furthermore, high PEEP in normal lungs has also been suggested to cause severe hypercapnia due to alveolar overdistension and decreased respiratory system compliance, an adverse effect also reflected by the authors’ data.

Finally, the observed reduction in cardiac output, systemic oxygenation, and oxygen delivery may have compromised tissue perfusion and metabolism in the periphery. Unfortunately, all variables were measured only once 30 mins after switching to a new ventilation strategy. Changes of hemodynamic variables, however, are most pronounced straight after an increment of mean airway pressure, whereas these variables adapt to increased PEEP level thereafter (6). Therefore, it is particularly important to investigate variables of individual organ perfusion, tissue oxygenation, and biochemistry. Furthermore, brain and cardiac tissue are extremely susceptible to ischemia, and even a few minutes of compromised perfusion can affect metabolic rate of oxygen and tissue integrity. To elucidate the impact of mechanical ventilation on these tissues, the authors should have analyzed regional blood flow or established biomarkers of tissue ischemia.

Patrick Meybohm, MD, Jens Scholz, MD, Norbert Weiler, MD, Berthold Bein, MD, University Hospital Schleswig-Holstein, Campus Kiel, Department of Anaesthesiology and Intensive Care Medicine, Kiel, Germany

REFERENCES

2. Downar J, Mehta S: Bench-to-bedside review: High-frequency oscillatory ventilation in adults with acute respiratory distress syndrome (2), a release of cytokines due to conventional ventilation with high tidal volumes and low positive end-expiratory pressure (PEEP) in patients with normal lungs is mostly related to preexisting damage of lung tissue and systemic inflammatory state (3). This issue was not addressed appropriately by the authors in the study’s title, objectives, or conclusions.

Second, gas exchange was worse during both protective strategies compared with controls. Indeed, lung-protective ventilation strategies are primarily purposed to limit alveolar overdistension and repeat alveolar collapse with the use of small tidal volumes. A key issue in this respect is the choice of an adequate PEEP level (2) that may largely differ from the high PEEP of 10 cm H2O, as it has been used in the present study. Application of high PEEP in healthy subjects has already been shown to result in worse oxygenation (4), as high PEEP prevents atelectasis but also impairs ventilation/perfusion ratio and subsequently increases intrapulmonary shunt (5). Furthermore, high PEEP in normal lungs has also been suggested to cause severe hypercapnia due to alveolar overdistension and decreased respiratory system compliance, an adverse effect also reflected by the authors’ data.

Finally, the observed reduction in cardiac output, systemic oxygenation, and oxygen delivery may have compromised tissue perfusion and metabolism in the periphery. Unfortunately, all variables were measured only once 30 mins after switching to a new ventilation strategy. Changes of hemodynamic variables, however, are most pronounced straight after an increment of mean airway pressure, whereas these variables adapt to increased PEEP level thereafter (6). Therefore, it is particularly important to investigate variables of individual organ perfusion, tissue oxygenation, and biochemistry. Furthermore, brain and cardiac tissue are extremely susceptible to ischemia, and even a few minutes of compromised perfusion can affect metabolic rate of oxygen and tissue integrity. To elucidate the impact of mechanical ventilation on these tissues, the authors should have analyzed regional blood flow or established biomarkers of tissue ischemia.

Patrick Meybohm, MD, Jens Scholz, MD, Norbert Weiler, MD, Berthold Bein, MD, University Hospital Schleswig-Holstein, Campus Kiel, Department of Anaesthesiology and Intensive Care Medicine, Kiel, Germany

REFERENCES