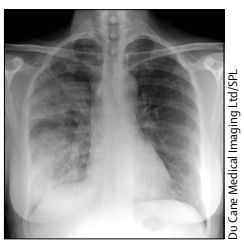
Ventilator-associated tracheobronchitis and pneumonia



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The diagnosis and treatment of respiratory tract infections in mechanically ventilated patients have become increasingly controversial. In addition to the clinical importance of prevention and treatment of ventilator-associated infections, there are now political and economical pressures to reduce the incidence of ventilator-associated pneumonia. However, as long as endotracheal intubation remains the gold standard method of providing ventilator support to critically ill patients, pathogenic bacteria will migrate to and, in some cases, flourish in the airway in the milieu of damaged mucosa and impaired host defences. Respiratory infection is an important clinical infection in the intensive care unit (ICU) and is responsible for 50% of the systemic antibiotics needed for critically ill patients.[1]

The latest quandary in clinical decision-making for the intensivist is whether to treat both ventilator-associated tracheobronchitis and ventilator-associated pneumonia. The diagnosis of tracheobronchitis seems to be associated with the same difficulties as ventilator-associated pneumonia, but a whole new series of questions arise for this disorder. Should both fever and raised white blood cell count be present for a diagnosis of ventilator-associated tracheobronchitis? What is the best way to distinguish between colonisation and proximal airway infection? Should ventilator-associated tracheobronchitis be treated differently from ventilator-associated pneumonia? What are the disadvantages of treating ventilator-associated tracheobronchitis? Will such treatment merely increase the amount of antibiotics used in the ICU and create even more bacterial resistance?

A study by Ignacio Martín-Loeches and colleagues (TAVEM)[2] published in the *Lancet Respiratory Medicine* does not answer these questions, but it was not designed to do so. Their investigation does, however, present the largest collection of data for ventilator-associated infections and their treatment, including both ventilator-associated tracheobronchitis and ventilator-associated pneumonia. This was a prospective, multicentre study done in 114 ICUs in eight countries. The diagnostic criteria for ventilator-associated lower respiratory tract infections (ventilator-associated tracheobronchitis or ventilator-associated pneumonia) included fulfilling two of the following three criteria: a body temperature of more than 38·5°C or less than 36·5°C, a leucocyte count greater than 12 000 cells per μL or less than 4000 cells per μL, or purulent endotracheal aspirate (ETA). Additionally, all occurrences of infection had to have a positive microbiological isolation in the ETA (of ≥10^5 colony-forming units [CFU] per mL) or with bronchoalveolar lavage [BAL] of ≥10^4 CFU per mL). Radiographic criteria for ventilator-associated pneumonia included signs of new or progressive infiltrate on chest radiograph, and no radiographical signs of new pneumonia for ventilator-associated tracheobronchitis.

Of 2960 eligible patients, 689 (23%) had ventilator-associated lower respiratory tract infections: 320 (11%) had ventilator-associated tracheobronchitis and 369 (12%) had ventilator-associated pneumonia. A substantial overlap of these diagnoses cannot be excluded because of the non-specificity of radiographical findings; however, these results show that patients with no visible evidence of radiographical progression on a chest radiograph who met the other diagnostic criteria for ventilator-associated tracheobronchitis had less progression to pneumonia when the tracheobronchitis was treated with appropriate systemic antibiotics. Additionally, patients with ventilator-associated tracheobronchitis had similar mortality to patients without infection, and ventilator-associated pneumonia was associated with a higher mortality consistent with a different outcome than ventilator-associated tracheobronchitis. The increased mortality did not seem to be related to the severity of illness in patients with ventilator-associated pneumonia because that was controlled for in the investigator's statistical design. Both ventilator-associated tracheobronchitis and pneumonia were associated with similar durations of mechanical ventilation, which in both groups of patients were longer than for patients without respiratory infection. Similarly, the length of stay in the ICU was longer for patients with ventilator-associated tracheobronchitis or ventilator-associated pneumonia compared with those patients without respiratory infection. These findings are similar to previous data[3-6] except for the findings from one study[3] that showed increased mortality in patients with ventilator-associated tracheobronchitis compared with patients without infection. However, this result might have been due to overlap between the diagnosis of ventilator-associated tracheobronchitis and pneumonia.

The findings from Martín-Loeches and colleagues' study[2] suggest that ventilator-associated tracheobronchitis, as defined earlier, is associated with subtantial morbidity and that treatment could be beneficial.

So where does this latest study fit in the murky investigational territory of ventilator-associated lower respiratory tract infections? Although most other studies have used the same diagnostic criteria, other investigators have viewed ventilator-associated tracheobronchitis as a geographical diagnosis that should be made independently from ventilator-associated pneumonia and should not require signs of systemic inflammation such as fever and a raised white blood cell count.[7,8] Diagnostic criteria in these other investigations included the presence of purulent secretions with a volume of at least 2 mL per 4 h with pathogens present as shown with a Gram stain. These investigators[7,8] view the proximal airway as a unique compartment with different characteristics from the deep lung. The airways have less vascular supply than the lungs and therefore less surface area exposed to thick purulent secretions, compared with the alveolar space and its abundant capillary bed. In airways with thick purulent secretions, the concentrations of antibiotics needed might need to be 10–25 times the minimum inhibitory concentration for effective treatment.[9] The success of the treatment of ventilator-associated tracheobronchitis in Martín-Loeches and colleagues' study raises the questions whether the secretions of these patients differed from the thick purulent ones described above, or contained organisms that were highly sensitive to antibiotics.

Finally, are there disadvantages associated with the treatment of ventilator-associated tracheobronchitis? Concerns exist that additional systemic antibiotics could add to increasing bacterial resistance. Additionally, no data were presented for post-treatment cultures in Martín-Loeches and colleagues' study, and the effect of antibiotic treatment on resistance over time on pathogens in the ICU is unknown. The findings from two small, randomised controlled studies[7,8] have shown that use of aerosolised antibiotics for ventilator-associated tracheobronchitis can prevent its progression to ventilator-associated pneumonia, and that when patients with ventilator-associated pneumonia are given adjunctive inhaled antibiotics therapy for tracheobronchitis, the need for additional systemic antibiotics decreased. Furthermore, patients given aerosolised antibiotics and systemic antibiotics did not develop resistance after treatment, whereas the patients who received placebo and systemic antibiotics had increased bacterial resistance after treatment.[7,8]

In conclusion, the data from Martín-Loeches and colleagues' study[2] add to the accumulating evidence that proximal airway infection is associated with substantial morbidity, and that treating it might prevent its progression to deep-lung infection. Large, well designed, multicentre randomised trials are needed to suggest improvements for the treatment of both proximal and distal respiratory infections, and to closely monitor the effects of antibiotics (inhaled or systemic) on bacterial resistance.

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