The development of ventilator-associated pneumonia does not change aspects of mechanical ventilation

Abstract Objective: To evaluate whether the development of ventilator-associated pneumonia (VAP) is associated with changes in ventilation parameters.

Design: Matched case-control study.

Setting: Mixed intensive care unit of a university hospital.

Patients: From a large database we selected 33 patients with VAP, diagnosed with quantitative cultures of bronchoscopically obtained specimens. In addition, 33 other mechanically ventilated patients who did not develop VAP were selected (controls). Patients with VAP and controls were matched on seven variables representing severity of illness: duration of ventilation until matching, diagnosis on admission, renal function, liver function, preceding infection, preceding surgery and immunosuppressive therapy. Each patient with VAP was matched to a single control. Variables regarding type and mode of ventilation and interpretation of chest radiographs were not included in the matching procedure.

Measurements and results: Characteristics of mechanical ventilation (mode of ventilation, tidal volume, expired minute ventilation, peak airway pressures, mean airway pressures, level of positive end-expiratory pressure, arterial oxygen tension(PaO₂)/fractional inspired oxygen (FIO₂) ratio), were compared on the day of diagnosis of VAP (or matching for controls) and 2 and 4 days before. Although there was a significant difference in PaO₂/FIO₂ ratios between cases and controls on the day of diagnosis of VAP, the change in PaO₂/FIO₂ ratios during the days of study were not statistically different between patients developing VAP and controls. No significant differences were found for any of the other variables of ventilation at any of the three time points studied, nor were there significant differences in changes of these parameters within individual patients.

Conclusions: Characteristics and parameters of mechanical ventilation are not influenced by the development of VAP. It is, therefore, unlikely that these variables are useful in the diagnostic work-up of VAP.

Keywords Tidal volume · Positive end-expiratory pressure · Arterial oxygen tension(PaO₂)/fractional inspired oxygen (FIO₂) ratio · Ventilator-associated pneumonia

Introduction

Ventilator-associated pneumonia (VAP) is the most prevalent nosocomial infection in intensive care units [1] and most episodes occur during the first 10 days of ventilation [2]. The pathogenesis of this infection is complex and is influenced by colonization of the respiratory and digestive tract, aspiration of oropharyngeal
fluid, severity of underlying illness and duration of ventilation [2, 3]. Diagnosing VAP is problematic, because a clinically useful gold standard is not available [4]. Usually, the diagnosis is established on a combination of clinical, radiographic and microbiological criteria. Body temperature and the number and differential count of peripheral leukocytes are most frequently used as clinical parameters. However, these parameters may change for many other reasons than pneumonia. As a result, the specificity for these clinical parameters for VAP is low. Furthermore, abnormalities on chest radiographs may be caused by many other causes than pneumonia and the presence of pathogens in tracheal aspirates does in no way differentiate between colonisation and infection. Therefore, the specificity of each of the individual criteria for VAP is low.

Although the combination of these criteria increases specificity, its use has been associated with a false positive rate for the incidence of VAP of up to 50% as compared to incidences based on bronchoscopic techniques [5, 6]. In a recent postmortem study the combination of infiltrates on the chest radiographs and at least two of three clinical criteria (leukocytosis, purulent secretions, fever) had a sensitivity of 69% and a specificity of 75% for diagnosing VAP [7]. Variables and changes in mechanical ventilation are usually not included in the diagnostic work-up of VAP. Only Pugin and co-workers used the PaO₂/FI immediately ratio as one of six parameters in their Clinical Pulmonary Infection Score [8].

The relationship between the development of VAP and changes in mechanical ventilation has not been studied extensively. If these variables were predictive for the diagnosis of VAP, their use might increase specificity of the combination of clinical, radiographic and microbiological criteria and, thereby, reduce the need of more invasive and expensive techniques such as bronchoscopy. In order to determine whether blood gas exchange and the mechanics of ventilation change during the development of VAP, we used data from patients that had been included in a previously published matched-cohort analysis, determining the systemic inflammatory response in patients developing VAP and those not developing VAP [9]. In that study, patients had been carefully matched on the duration of ventilation and aspects of the severity of the underlying disease. Blood gas exchange and mechanics of ventilation were not included in the matching process. We therefore used this database to compare these parameters in patients developing, and not developing, VAP.

**Materials and methods**

**Study location and patients**

The study was conducted in the ICU of the University Hospital, Maastricht, The Netherlands. The ICU is a 16-bed ward with patients from the departments of surgery, internal medicine, trauma, pulmonology, neurology and neurosurgery. The study period extended from January 1, 1992 until January 1, 1994. All mechanically ventilated patients admitted to this ward were enrolled. The study was reviewed and approved by our institutional review board, which deemed that informed consent was not required.

**Study design and data collection**

Demographic data were obtained on admission and clinical data were recorded on a daily basis from admission until death or discharge. On admission, the APACHE II score was assessed as described by Knaus et al. [10]. The following data were recorded: age; sex; dates of admission and discharge from ICU; period of hospitalization prior to admission to the ICU; list of medical history; surgical procedures performed; body temperature; number of leukocytes in peripheral blood; levels of blood urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin; use of and indication for antibiotics; and administration of immunosuppressive therapy. With these data a matched-cohort analysis was performed as described in detail previously [9]. Importantly, cases and controls were carefully matched for the duration of ventilation at the moment of matching. Characteristics of mechanical ventilation were not included, in any form, in the matching procedure. Day 0 (D0) was defined as the day of diagnosis of VAP for cases and the day of matching controls. Relative to D0, data were recorded for days −2 (D−2) and −4 (D−4).

The diagnosis of VAP was based on a combination of clinical and radiographic criteria in combination with positive quantitative cultures of samples obtained by protected specimen brush and/or bronchoalveolar lavage (Table 1).

For the present analysis, the following data were recorded from the patients charts: the type of ventilator (Servo 300 or Evita) and the mode of ventilation (pressure-regulated volume-controlled (PRVC), intermittent positive pressure ventilation (IPPV), synchronized intermittent mandatory ventilation with assisted spontaneous breathing or pressure support ventilation (SIMV/ASB or PSV)), Peak inspiratory pressure (Peak), mean airway pressure (Pmean), positive end-expiratory pressure (PEEP), tidal volume (VT), expired minute ventilation (VE) and the arterial oxygen tension (Pao₂)/fractional inspired oxygen (FIO₂) ratio were also recorded. In addition, the acute lung injury (ALI) as described by Murray et al.[11] was calculated. When variables changed during the day, values recorded at 06.00 a.m. were used. PRVC and IPPV were considered modes of controlled ventilation, whereas SIMV/ASB or PSV were considered ‘weaning’ modes. The duration of controlled ventilation on D0 was calculated by dividing the number of days with either PRVC or IPPV by the total number of days from the start of ventilation until day of matching. Characteristics of patients developing VAP were compared to patients not developing VAP on the day of diagnosis (or matching for controls) (D0), and 2 and 4 days before (D−2 and D−4).

**Mortality**

Mortality rates were calculated 10 and 28 days after the day of matching.