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ORIGINAL ARTICLE

The impact of cytomegalovirus infection on mechanically ventilated patients in the respiratory and geriatric intensive care units

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KEYWORDS

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Critically ill

Abstract *Background:* Reactivation of cytomegalovirus (CMV) has been reported in critically ill patients (especially elderly) lying in the intensive care units. So identifying such patients to treat is important.

The aim of this study: To detect the frequency of CMV infection in mechanically ventilated patients, and its correlation with patients' risk factors, and outcomes.

Subjects and methods: The present study was carried out on 51 mechanically ventilated patients admitted to the Respiratory (20) and Geriatric ICU (31) of the Ain Shams University hospitals over a 3 month period. Serum CMV load was measured by real-time PCR.

Results: The overall rate of active CMV infection by RT-PCR among the studied populations was (68.6%), (77.4%) in patients of geriatric ICU versus (55%) in respiratory ICU patients. Comparison between CMV positive and negative cases showed a significant difference in the duration of mechanical ventilation and mortality rate. A statistically higher CMV load was recorded in respiratory ICU patients admitted due to exacerbation of chronic respiratory disease or stroke and developing ventilator associated pneumonia (VAP) or septic shock. Also there was a significant direct correlation between CMV load and age of the patient, duration of mechanical ventilation and duration of ICU stay.

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Conclusion: CMV infection is frequent in mechanically ventilated critically ill patients especially the elderly. It is associated with poor outcomes, leads to increased mortality and morbidity in terms of increased ICU stay, longer duration of mechanical ventilation, and higher rates of nosocomial infections.

Introduction

Cytomegalovirus (CMV) is a major β herpes virus, latently persisting in the majority of the adult human population worldwide. Infection is common with seroprevalence rates increasing steadily from 65% among 40–49 year olds to 91% in those aged 80 years or over [1]. It has been suggested that chronic CMV infection is a driving force in age related T cell immunosenescence [2]. It has increasingly come to be recognized that critically ill patients who are traditionally considered immunocompetent may also be at risk for CMV infection. Reactivation from the latency rather than primary infection is believed to be the cause of CMV infection [3]. CMV serology is not useful for the diagnosis of active infections and its culture is impractical for clinical purposes. Real-time PCR is a sensitive, specific and reliable marker to monitor the clearance of viremia [4].

The presence of CMV infection in critically ill patients was associated with a significant increase in morbidity and mortality, although this infection might be self-limited with spontaneous resolution within 2–3 weeks after reactivation [5]. Several studies showed that a CMV infection in this population was associated with prolonged ventilator support, high rates of nosocomial infections and prolonged hospital and/or ICU stay. However, the impact of CMV infection on the outcome of those patients is still debated [4].

The aim of the current study was to detect the frequency of CMV infection in mechanical ventilated patients, and its correlation with patients' risk factors, and outcomes, aiming to evaluate the need for screening for CMV infection.

Subjects and methods: This prospective study was performed in the Respiratory and Geriatric ICU of the Ain Shams University hospitals. Over a 3 month period, 20 patients were admitted to the Respiratory ICU and 31 patients were admitted to Geriatric ICU. All consecutive patients (18 years or older) were included in this study if they were mechanically ventilated.

Exclusion criteria: Patients were not included if they were pregnant, HIV positive, had solid organ or bone marrow transplantation, had received immunosuppressive agents or, long-term treatment with corticosteroids (□ 3 months), had solid cancer or hematologic malignancy with previous anticancer radiotherapy or chemotherapy.

Baseline assessment and data collection

Informed consent was taken either from patients' relatives or their guardians before the start of this study. Each patient's hospital chart was prospectively implemented, and the following data were recorded during admission to the ICU: age, sex, presence of co-morbidities {diabetes mellitus (DM) and/or renal diseases}, Main cause of ICU admission; the time spent on a mechanical ventilator, and duration of ICU admission. Other relevant clinical characteristics and outcomes complicating the ICU stay as {adult respiratory distress syndrome (ARDS), ventilator-associated pneumonia (VAP), septic shock, and mortality} were also recorded throughout the ICU stay. Peripheral venous blood samples were collected; serum was separated and stored at −80 °C till use in PCR analysis.

Identification of CMV by real time PCR

The presence of CMV was tested with a quantitative real-time PCR. DNA was extracted from serum samples using a Qiagen kit (Qiagen, Valencia, CA, USA) and quantified using the standard laboratory protocol recommended by the manufacturer's instructions. Quantitative real for CMV was performed using a light Cycler H Instrument (Roche Diagnostics, Meylan, France) with the QuantiTect Probe PCR Kit (Qiagen). The presence of CMV was tested with forward primer (5′GCAGCCACGGGATCGTACT-3′) and the reverse primer (5′GGCTTTTACCTCACACGAGCATT-3′), and the specific TaqMan probe (6FAM-CGCGAGACCGTGGAACTGCG-TAMRA) according to Coisel et al. [6]. The reaction was carried out in 20 mL, in a final volume containing 10 mL of QuantiTect master mix, 0.2 mM of probe, 0.2 mM of each primer, and 4 mL of DNA. The PCR was initiated by an enzyme-activation incubation at 95 °C for 15 min to activate DNA Polymerase, followed by 40 cycles of denaturation at 95 °C for 10 s and an annealing-extension step at 60 °C for 1 min. Serial dilutions, ranging from 10^2 to 10^5 copies/ml of synthesized sequences that correspond to the targeted viral genes, were used as positive controls. These dilutions were also used to determine the viral load in positive samples. A CMV negative specimen was used as a negative control sample was considered positive by real-time PCR if it crossed the threshold.

Data management and statistical analysis

Quantitative data are presented as mean and SD for parametric data or median for non-parametric data and categorical data are presented as numbers of cases and percentages. Student *T* and Mann Whitney tests were used to assess the statistical significance of the difference between the two groups regarding Quantitative data. Chi square and Fisher's exact tests were used to examine the relationship between Categorical variables. Spearman's correlation coefficient was used to assess the correlation between quantitative variables. A significance level of $P < 0.05$ was used in all tests. All statistical procedures were carried out using SPSS version 15 for Windows (SPSS Inc, Chicago, IL, USA).