Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Journal of Clinical Virology 40 Suppl. 1 (2007) S55–S57

www.elsevier.com/locate/jcv

Value of RVP in clinical settings: intensive care

Tony Mazzulli*

Department of Microbiology, Mount Sinai Hospital, Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

Keywords: Rapid diagnostics; Molecular; Respiratory viruses; Intensive care unit

Infections, particularly pneumonia, in patients in the Intensive Care Unit (ICU) are common and are associated with significant mortality (Alberti et al., 2002; Heyland et al., 1999a). Patients with different types of lower respiratory tract infections may be managed in the ICU, including those with severe community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), healthcare-associated pneumonia (HCAP) and ventilator-associated pneumonia (VAP) and thus the range of pathogens that may be associated with these infections is vast (El-Solh et al., 2001; Heyland et al., 1999a,b; Reimer and Carroll, 1998; Rello et al., 2003). In most ICUs, much effort is placed on the diagnosis and treatment of bacterial agents causing pneumonia with very little effort being placed on the detection and management of viral agents except in specialized situations (ATS/IDSA, 2005). In fact, recent guidelines have suggested that the incidence of HAP and VAP due to viruses is low in immunocompetent hosts although outbreaks of HAP, VAP and HCAP due to viruses have been reported (ATS/IDSA, 2005). Thus little emphasis has been placed on trying to make a viral diagnosis. To some extent the perception that viruses are uncommon in this setting is due to the difficulty in detecting such agents in the clinical microbiology lab and the lack of available treatment for most viruses causing infections of the respiratory tract (Holladay and Campbell, 1995). However, the development of molecular diagnostic techniques such as the polymerase chain reaction (PCR), particularly when it can be multiplexed to detect multiple different viruses in a single reaction, has the potential to provide new insights into the epidemiology and management of patients with pneumonia in the ICU setting (Mahony et al., 2007). As many as 30% of bronchoalveolar lavage (BAL) specimens and 63% of bacteria-negative BALs collected from adult patients with acute pneumonia in an intensive care unit may be positive for respiratory viruses (Legoff et al., 2005). The rates may be even higher in children (Straliotto et al., 2004). Others have suggested that despite finding a respiratory virus in 25% of the tracheobronchial aspirates collected from patients ventilated for more than 48 hours, nosocomial viral VAP is likely to be rare in the ICU (Daubin et al., 2005).

Because of their greater sensitivity over traditional laboratory techniques, these assays can detect viruses that previously would have been missed and can thus help re-define the spectrum of disease and contribution these agents have to the morbidity and mortality of patients in the ICU. Traditional viral techniques such as culture, antigen detection and immunofluorescence staining have the capability of detecting agents such as influenza viruses A and B, respiratory syncytial virus, parainfluenza viruses, and adenovirus. Molecular techniques have expanded the range of viruses that can be rapidly detected in the laboratory including many newly identified agents such as human metapneumovirus, bocavirus, coronaviruses and others (Mahony et al., 2007). Molecular techniques may also aid in preventing nosocomial spread of these viruses within the ICU by allowing for the appropriate infection control measures to be implemented quickly once an agent is identified. Some molecular assays can also subtype viruses which can help in determining the relatedness of strains during an epidemiological outbreak investigation.

Although these assays have the potential for reducing unnecessary antibiotic use and overall costs associated with managing patients, this was not the case in a recent study of patients admitted to hospital for the management of their lower respiratory tract infection (Oosterheert et al., 2005). In this study, Osterheert et al. showed that although the use of real-time PCR for the detection of viral and atypical bacterial pathogens in patients with lower respiratory tract infections increased the diagnostic yield considerably, it did not reduce the number of diagnostic procedures, antibiotic use, length of hospital stay or costs (Oosterheert et al., 2005). This likely reflected the fact that clinicians were reluctant to change their clinical management based on the results of the PCR test and preferred to continue antibiotics because of concerns of missing a bacterial agent. The increased use of molecular diagnostic techniques may actually result in increased costs, not only because these

* Correspondence: Tony Mazzulli MD. Tel.: +1 416 586 4695.
E-mail address: tmazzulli@mtsinai.on.ca (T. Mazzulli).

1590-8658/ $ – see front matter © 2007 Elsevier B.V. All rights reserved.

tests are relatively expensive, but also because a positive result (e.g. influenza virus) may lead to the addition of an antiviral agent such as oseltamivir, rather than a replacement of a patient's current antibiotic regimen. This is based on the well-recognized association of co-infection with bacteria and viruses in the respiratory tract (de Roux et al., 2004). If this can be shown to improve clinical outcomes, then the added cost may well be worth it.

Studies using rapid, but less sensitive tests such as direct immunofluorescence assays (DFA) and antigen detection assays for the diagnosis of respiratory viruses have suggested that these tests can have significant impact on decision-making, antibiotic use and overall costs (Barenfanger et al., 2000; Bonner et al., 2003; Byington et al., 2002; Sharma et al., 2002). Most of these studies, however, have been done in infants and children in the emergency department, outpatient setting or hospital ward. Similar studies are needed using the newer multiplex molecular assays in the ICU setting to determine if the same potential benefits can be achieved in this sicker and more complex patient population.

Another issue with the use of multiplex assays for the detection of respiratory viruses in the ICU is the seasonality of these agents. Studies looking at the optimal time when these assays should be performed are needed. It will take some time and more research before clinicians are comfortable in using the results of these assays to modify their decision-making and management strategies in the ICU. At the moment, guidelines for the management of CAP, HAP, HCAP and VAP have not recommended the routine use of molecular techniques for the detection of viruses because of the lack of information on their clinical utility (ATS/IDSA, 2005; Mandell et al., 2007). This could change if well conducted studies can demonstrate the benefits of these assays in the ICU setting and clinicians are educated regarding their use.

Conflict of interest statement

None declared.

Acknowledgement

Research support from Tm BioScience.

Alberti C, Brun-Buisson C, Burchardi H, Martin C, Goodman S, Artigas A, et al. Epidemiology of sepsis and infection in ICU patients from an international multicentre cohort study. Intensive Care Med 2002;28: 108–21.

ATS/IDSA. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med 2005;171:388–416.

Barenfanger J, Drake C, Leon N, Mueller T, Troutt T. Clinical and financial benefits of rapid detection of respiratory viruses: an outcomes study. J Clin Microbiol 2000;38:2824–8.

Bonner AB, Monroe KW, Talley LI, Klasner AE, Kimberlin DW. Impact of the rapid diagnosis of influenza on physician decision-making and patient management in the pediatric emergency department: results of a randomized, prospective, controlled trial. Pediatrics 2003; 112:363–7.

Byington CL, Castillo H, Gerber K, Daly JA, Brimley LA, Adams S, et al. The effect of rapid respiratory viral diagnostic testing on antibiotic use in a children's hospital. Arch Pediatr Adolesc Med 2002;156:1230–4.

Daubin C, Vincent S, Vabret A, du Cheyron D, Parienti JJ, Ramakers M, et al. Nosocomial viral ventilator-associated pneumonia in the intensive care unit: a prospective cohort study. Intensive Care Med 2005;31: 1116–22.

de Roux A, Marcos MA, Garcia E, Mensa J, Ewig S, Lode H, et al. Viral community-acquired pneumonia in non-immunocompromised adults. Chest 2004;125:1343–51.

El-Solh AA, Sikka P, Ramadan F, Davies J. Etiology of severe pneumonia in the very elderly. Am J Respir Crit Care Med 2001;163:645–51.

Heyland DK, Cook DJ, Griffith L, Keenan SP, Brun-Buisson C. The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient. The Canadian Critical Trials Group. Am J Respir Crit Care Med 1999a;159:1249–56.

Heyland DK, Cook DJ, Marshall J, Heule M, Guslits B, Lang J, et al. The clinical utility of invasive diagnostic techniques in the setting of ventilator-associated pneumonia. Canadian Critical Care Trials Group. Chest 1999b;115:1076–84.

Holladay RC, Campbell Jr GD. Nosocomial viral pneumonia in the intensive care unit. Clin Chest Med 1995;16:121–33.

Legoff J, Guerot E, Ndjoyi-Mbiguino A, Matta M, Si-Mohamed A, Gutmann L, et al. High prevalence of respiratory viral infections in patients hospitalized in an intensive care unit for acute respiratory infections as detected by nucleic acid-based assays. J Clin Microbiol 2005;43:455–7.

Mahony J, Chong S, Merante F, Yaghoubian S, Sinha T, Lisle C, et al. Development of a Respiratory Virus Panel (RVP) test for the detection of twenty human respiratory viruses using multiplex PCR and a fluid microbead-based assay. J Clin Microbiol 2007;45:2965–70.

Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(Suppl 2): S27–72.

Oosterheert JJ, van Loon AM, Schuurman R, Hoepelman AI, Hak E, Thijsen S, et al. Impact of rapid detection of viral and atypical bacterial pathogens by real-time polymerase chain reaction for patients with

lower respiratory tract infection. Clin Infect Dis 2005;41: 1438–44.
Reimer LG, Carroll KC. Role of the microbiology laboratory in the diagnosis of lower respiratory tract infections. Clin Infect Dis 1998;26:742–8.
Rello J, Bodi M, Mariscal D, Navarro M, Diaz E, Gallego M, et al. Microbiological testing and outcome of patients with severe community-acquired pneumonia. Chest 2003; 123:174–80.
Sharma V, Dowd MD, Slaughter AJ, Simon SD. Effect of rapid diagnosis of influenza virus type A on the emergency department management of febrile infants and toddlers. Arch Pediatr Adolesc Med 2002;156:41–3.
Straliotto SM, Siqueira MM, Machado V, Maia TM. Respiratory viruses in the pediatric intensive care unit: prevalence and clinical aspects. Mem Inst Oswaldo Cruz 2004;99:883–7.