Maastricht University

In search of new diagnostic modalities and techniques in ventilator-associated pneumonia

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Valorisation addendum

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Relevance

Ventilator-associated pneumonia (VAP) is a nosocomial infection affecting the lungs. It is responsible for substantial healthcare costs and additional hospital mortality. The present thesis addresses new aspects with regard to causative microorganisms, diagnostic algorithms and novel non-invasive diagnostic techniques.

The knowledge of the pathogenic potency of a microorganism is essential to understand the infectious disease process, to develop a diagnostic strategy and therapy. This can benefit patient outcome. It is of interest to identify pathogenic microorganisms. In this thesis the potential role of Acanthamoeba polyphaga mimivirus (APMV) has been investigated. It has been demonstrated that APMV is not present in BAL lavage fluid and not a cause of VAP. Furthermore, the role of *Candida* as a causative microorganism of ICU pneumonia was investigated. Although rarely occurring, certain clinical circumstances were defined in which Candida pneumonia should be considered and treated.

Diagnostic algorithms give guidance to physicians in a complex decision making process stratifying the likelihood of diagnoses and the invasiveness of necessary diagnostic techniques. These must hold to the old Hippocratic paradigm not to harm patients in the first place. If it concerns invasive diagnostic techniques the expected benefits ought to outweigh the risks to justify application. In the present thesis the diagnostic tool fibreoptic bronchoalveolar lavage (BAL) in critical ill mechanically ventilated patients was investigated. BAL has been routinely performed in patients with clinical suspicion of VAP to confirm the diagnosis. In all patients with a negative BAL for bacterial growth possible alternative diagnoses accountable for their clinical symptoms were analysed. Other infectious causes like viral infections or *Pneumocystis jirovecii* infections, but also non-infectious causes like heart-failure or malignancies, were frequently found. With this information, therapy can be adequately adjusted. Next to the utility of BAL the clinical course and complications of the procedure in critical ill mechanically ventilated patients were analysed. It could be demonstrated in the present thesis that BAL is frequently followed by haemodynamic and respiratory instability and should be conducted under careful supervision by experienced physicians.

Exhaled breath analysis is a new diagnostic modality in respiratory medicine. It carries no procedural risks even in critical ill mechanically ventilated patients. In the studies of the present thesis exhaled breath was directly analysed in order to identify patients with VAP. Two different techniques were applied. Gas chromatography-mass spectrometry (GC-MS) directly analyses the presence of volatile organic compounds (VOCs) in breath and changes related to disease state. GC-MS is a complex and expensive technology. The advantage is the possibility to develop certain VOC profiles as markers of infectious diseases. Electronic noses (e-nose) indirectly analyse patterns

of VOCs. The advantage of e-nose is their smaller size, portability and usability with potentials for point-of-care applications.

Target groups

The results from the studies are of interest for clinicians in intensive care - and respiratory medicine. A broad spectrum of professionals is involved in the development of exhaled breath analysis devices and their clinical application such as biologists, biochemist, physicians, physiologists and engineers.

Innovation and implementation

Point-of-care devices examining exhaled breath could be used for the diagnosis of respiratory disease and infections. It could support the discrimination of a bacterial lung infection from other respiratory conditions and the decision making on the necessity of antibiotic treatment. This could contribute to the reduction of antibiotic use. Exhaled breath analysis could be used for a fast discrimination of different forms of pneumonia as pneumococcal pneumonia, legionella or pneumonia caused by *Pneumocystis jiroveci* to initiate the right antimicrobial therapy. Devices that analyse exhaled breath could be integrated in respirators to detect a developing VAP early and subsequently to monitor the efficacy of antibiotic treatment.