Laboratory analysis workflows within the ASPIRE-ICU study

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*Advanced understanding of Staphylococcus aureus and Pseudomonas aeruginosa infections in EU FP8 – Intensive Care Units

Facts & Figures

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<th>-MAGNET</th>
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Challenge

The epidemiology and potential routes and reservoirs leading to the development of pneumonia by Staphylococcus aureus or Pseudomonas aeruginosa in mechanically ventilated patients are not well-elucidated. These data are, however, urgently needed to support the development of effective interventions.1,2

Approach & Methodology

The objective of the ASPIRE-ICU study is to estimate the incidence of S. aureus and P. aeruginosa ICU pneumonia and to assess its association with patient-related and contextual risk factors, e.g., colonization status, serum antibody levels against S. aureus alpha toxin (AT) and the P. aeruginosa PcrV/Psv virulence factors and others.

The study is a prospective, observational, multi-centre cohort study nested within routine surveillance among ICU patients in Europe. Two thousand study cohort subjects are being enrolled (50% S. aureus colonized) from whom specimens and data are collected. Microbiological study samples (lower respiratory samples (LRS), nasal swabs (NS) and per-anal swabs (PS)) are being shipped to the central laboratory at the University of Antwerp to undergo uniform procedures (Figures 1 and 2).

Because of the centralised analysis, uniformly generated data will be obtained from around 4500 LRS, 2500 NS, 3500 PS, 2500 S. aureus isolates and 250 P. aeruginosa isolates by the end of ASPIRE-ICU.

Results

To determine if the S. aureus and P. aeruginosa colonization loads in LRS are predictive of S. aureus and P. aeruginosa pneumonia development, these are measured and compared between patients developing and not developing infection. Also, the temporal evolution of the S. aureus and P. aeruginosa loads in LRS are investigated. In addition, the association of NS/LRS and PS/LRS colonization status at ICU admission with the incidence of ICU pneumonia caused by S. aureus or P. aeruginosa, respectively, is being determined.

The spectrum of S. aureus / P. aeruginosa clonal types associated with colonization and infection is investigated. AT variants in S. aureus are identified and their expression characterized. The proportion of P. aeruginosa in which pcrV and the psl loci are present and expressed, along with variations in these and associated genes is assessed. Finally, antibiotic resistance profile of all strains is determined.

Value of IMI collaboration

IMI provides an unique framework to engage academic and industry experts in a mutually enriching collaboration, which aligns with fulfilling the primary goals of the project also allows capacity building. The provided framework also allows to run consecutive studies from observational to phase II and phase III trials where experiences and knowledge obtained from each study facilitates the subsequent trials.

Impact & take home message

By investigating one of the most deadly nosocomial infections, this epidemiological cohort study will provide new insights on predictors of S. aureus and P. aeruginosa ICU pneumonia. Outcomes of this observational study will also allow to refine the design of phase II and III follow-up trials on S. aureus and P. aeruginosa ICU pneumonia. Finally, the large expanse of clinical, bacteriological and immunological knowledge generated from a large number of patients in ASPIRE-ICU is also likely to facilitate further development of early diagnostic or prognostic disease markers and of therapeutic targets, possibly non-antibiotic based.

Abbreviations: AT: alpha toxin; LRS: Lower Respiratory Samples; NS: Nasal Swabs; PS: Per-anal swabs

References:

1 Paling et al. Pseudomonas aeruginosa colonization at ICU admission as a risk factor for developing P. aeruginosa ICU pneumonia, Antimicrob Resistant Infect Control. 2017 Apr 20;6:38.
2 Paling et al. Staphylococcus aureus colonization at ICU admission as a risk factor for developing S. aureus ICU pneumonia, Clin Microbiol Infect. 2017 Jan; 23(1).

Figure 1: ASPIRE-ICU S. aureus workflow at the Central laboratory UAntwerp

Figure 2: ASPIRE-ICU P. aeruginosa workflow at the Central laboratory UAntwerp