Chapter 4

Sepsis: beyond mortality.

PUBLISHED AS

Quinten VM, van Meurs M, Ligtenberg JJ, ter Maaten JC. Prehospital antibiotics for sepsis: beyond mortality? Lancet Respir Med 2018; 6: 168–70.

In the Lancet Respiratory Medicine, Nadia Alam and colleagues assessed prehospital administration of intravenous ceftriaxone 2000 mg in addition to usual care (fluid resuscitation and supplementary oxygen) in the ambulance for patients with suspected sepsis in the randomized controlled PHANTASi trial[1].Unfortunately, this early intervention did not lead to improved sepsis survival compared with patients receiving usual care alone. Fewer patients died in the study (8% across both arms) than was predicted (40%) based on epidemiological studies at the time of the trial design. As is commonly known, mortality from sepsis has substantially decreased in recent decades, and in fact, the low mortality rate of PHANTASi exceeds that from our previous cohort study (4%) in our emergency department[2].

In an accompanying comment, Jean-Louis Vincent argued that the low severity of illness of the patients included in PHANTASi made it difficult to show an effect of prehospital antibiotics on mortality[3]. Although we agree with this argument, the patients included in this well designed trial matched the mix of sepsis severity and percentage of admissions to intensive care in our emergency department cohort. Therefore, we disagree with Vincent that only patients with signs of organ dysfunction–i.e., with sepsis according to the Sepsis-3 definitions –might benefit from early antibiotics[4]. Furthermore, we disagree that the PHANTASi trial reinforces the fact that timing of antibiotics is not very important in patients with infection. In a separate study, investigators showed that 22% of patients presenting at an emergency department with suspected sepsis without signs of organ dysfunction developed organ dysfunction within 48 h of admission despite antibiotic and supportive treatment[5]. Previously, we noted that 4% of patients with uncomplicated sepsis needed to be admitted to an intensive-care unit, and such patients would probably benefit from early administration of antibiotics[2]. Alam and colleagues showed that the number of patients readmitted to hospital after 28 days was significantly lower in the intervention group with prehospital antibiotics, but could not explain the reason for this difference[1]. We speculate that early antibiotics might attenuate the development of organ failure during a patient's hospital stay, and suggest that the time has come to make a shift from mortality towards (early) signs of organ failure as a marker and endpoint for future emergency department-based sepsis research. There is more to life than death alone.

REFERENCES

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3 Vincent JL. Antibiotic administration in the ambulance? Lancet Respir Med 2018; 6: 5–6.

4 Singer M, Deutschman CS, Seymour C, *et al*. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA - J Am Med Assoc 2016; 315: 801–10.

5 Glickman SW, Cairns CB, Otero RM, *et al*. Disease progression in hemodynamically stable patients presenting to the emergency department with sepsis. Acad Emerg Med 2010; 17: 383–90.