CHAPTER 6

TIME FOR A RANDOMIZED CONTROLLED TRIAL TO INVESTIGATE OPTIMAL TIME TO ANTIBIOTICS FOR PATIENTS WITH SEPSIS

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TO THE EDITOR

In a recent issue of Critical Care Medicine, we read with great interest the study by Sterling et al (1) in which they investigated the association between timing of antibiotics and mortality in severe sepsis and septic shock. Previous studies investigating the effects of time to antibiotics on outcomes had inconsistent results, some suggesting that delay in antibiotic administration leads to a dramatic rise in mortality, whereas others found no difference. The research group carried out a robust systematic review in which they give a comprehensive overview of available data, concluding that in patients with severe sepsis and septic shock, antibiotic administration within 3 hours of emergency department (ED) triage and/or within 1 hour of shock recognition is not associated with significant improvement in mortality. Timely administration of antibiotics is seen as a cornerstone of treatment for patients with sepsis; however, a definite answer to the question what the best timing of antibiotic administration is can only be obtained by a prospective randomized controlled trial that avoids selection bias. However, as authors mentioned, it may be unethical to randomize patients and delay initiation of antibiotic therapy at the ED. An alternative option is to perform a prospective randomized trial in the prehospital setting, that is, in the ambulances. In current practice, initiation of antibiotic therapy starts at the ED and not in the ambulances. Prehospital antibiotic administration may be a solution to avoid delays in treatment at the ED and a way to finally perform a prospective randomized trial to examine the effects of timing of antibiotics on clinical endpoints, such as improved survival. Emergency medical services (EMS) personnel have made significant contributions in improving care for patients with critical, time-dependent illnesses, such as acute coronary syndrome, multiple trauma, and stroke (2,3). In parallel, patients with severe sepsis could also benefit greatly from timely prehospital care (4), as it can accelerate and improve care in the hospital setting (5,6). Therefore, we designed a study with the aim of investigating whether prehospital administration of antibiotics after training EMS personnel to recognize suspected (severe) sepsis or septic shock leads to improvement in-patient outcomes, such as a reduction in 28-day mortality compared with usual care. In summary, the Prehospital Antibiotics against Sepsis (PHANTASi) trial (Clinicaltrials.gov; identifier: NCT01988428) is the first prospective, investigator-initiated, randomized controlled, multicenter trial, which will compare the effects of early prehospital antibiotic treatment for sepsis patients with usual care, nested within a step wedge design to evaluate the effect of the training of EMS personnel in early recognition and initiating treatment. The PHANTASi trial started in June 2014 in the Netherlands; a total of 36 hospitals and 10 ambulance regions are participating, and more than 1,000 EMS personnel have already been trained. This large multicenter trial will not only help healthcare providers gain better insight in providing optimal care for patients with sepsis but also strengthen the whole acute care chain, as well as increase awareness for sepsis.
REFERENCES


