EDITORIAL

Early Goal Directed Therapy: Do We Reach the End of Road?

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Rivers et al in their study in 2001 randomly assigned 263 patients admitted to emergency department with severe sepsis or septic shock to receive either six hours of early goal-directed therapy (EGDT) or standard therapy before admission to the intensive care. 130 were randomly assigned to EGDT and 133 to standard therapy. Demographic characteristic of patients were the same, but in hospital mortality in EGDT group was 30.5% versus 46.5 % in patients with standard treatment (P=0.009). Also there was a significant difference between groups regarding lactate level and organ dysfunction during first 72 hours [1].

EGDT is designed to balance tissue oxygen demand and oxygen delivery in patients with severe sepsis or septic shock. Goal Directed Therapy (GDT) uses mean arterial pressure, central venous pressure and central venous O2 saturation parameters for hemodynamic management of septic patients. There are some studies that reported beneficial effect of EGDT in septic patients during its application [2-4]. Surviving Sepsis Campaign guidelines [5] have endorsed EGDT for initial resuscitation of septic patients but there were some barriers to uptake which include concerns regarding the generalisability of the original EGDT trial findings outside of a single US centre, the infrastructure and resource requirements needed to implement EGDT and the potential risks associated with individual elements of the protocol [6]. The results of The ARISE Investigators [7], ProCESS [8] and ProMISe [9] studies showed that EGDT, as compared with usual resuscitation practice, did not decrease mortality among patients presenting to the emergency department with early septic shock meaning that patients in whom sepsis was managed without a protocol had an outcome as good as those in patients in whom the sepsis was managed with the use of a protocol. Recently published meta-analysis which analysed the results of EGDT in 11 RCTs (more than 5000 patients with septic shock) showed that EGDT did not decrease mortality but was associated with increased ICU admission [6]. Yu H et al. [10] in their meta-analysis showed the data from five RCTs and found no survival benefit of EGDT in patients with sepsis but they emphasized on the heterogeneity of these negative trials that might bias the results and diminish the treatment effect of EGDT.

So based on mentioned negative trials, considering on early recognition [11], antibiotics and fluid resuscitation during 3 hours is more important than EGDT targets [12-13]. But we should notice that in developing countries antibiotic resistance is rapidly increasing and there are so many problems in early recognition of sepsis however, more invasive medical procedures are performed in these situations by physicians. Also there are some concerns with these published trials like: different methods for reporting mortality (different primary and secondary outcomes), high risk of bias in RCTs (only there was low risk for bias in two RCTs) and differences in local healthcare services where in EGDT was delivered. The last parameter could be an important confounding factor especially in developing countries. So, we could not generalize the results of these high quality trials which were performed in countries with high level of monitoring, diagnostic tests and managements, to all situations especially in resource limited or developing countries as physicians of these countries need simple and easy protocols for rapid management of critically ill patients regardless of resources not based on their judgment. Finally, further well-designed studies should eliminate all potential source of bias to determine if EGDT has a mortality benefit.

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