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The impact of timing of antibiotic administration on clinical outcomes in patients with community-onset severe sepsis and septic shock: a multicentre observational study

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Background: Early appropriate antibiotic therapy is a cornerstone of sepsis care. However, timing of antibiotic therapy used as a quality measure to evaluate the hospitals has caused concern over the antibiotic overuse and misuse. The purpose of this study was to evaluate the effects of timing of antibiotic therapy on mortality in patients with community-onset severe sepsis and septic shock.

Material/methods: This multi-center observational study was conducted using the prospective data collected from 12 teaching hospitals in the Republic of Korea. Community-onset severe sepsis patients were registered in the Korean Sepsis Registry System (KSRS) from May 2005 to December 2008. Prospectively collected data from KSRS included demographic data, underlying diseases, source of infection, severity of sepsis, hospital stay and mortality, and antibiotic therapy. The impact of incremental time to antibiotics as markers of quality of care was evaluated by a generalized estimating equation (GEE) population averaged logistic regression model.

Results: During the study period, a total of 1,192 cases were compromised as community-onset severe sepsis or septic shock. Among them, 585 patients identified the definitive pathogens and documented the precise timing of antibiotic administration, were subsequently included this study. Of 585 cases, 394 (67.4%) septic shock patients and 325 (55.6%) bacteremia patients were included. All cause in-hospital mortality and 28-day mortality rates were 30.1% and 24.3%, respectively. The most common primary site of infection was pneumonia (30.9%), followed by the urinary tract infection (26.8%) and intra-abdominal infection (24.1%). Patients aged ≥ 70 yrs (*P*=0.04) or those with septic shock (*P*=0.07) were observed a tendency of earlier antibiotic administration than those who were not. In the logistic regression model, the significant impact of incremental time to antibiotics on 28-day mortality was not found (Table). Particularly, there was no significant 28-day mortality benefit from administering antibiotics within 3 hours of severe sepsis or septic shock recognition [odds ratio (OR) 1.18; 95% confidence interval (CI) 0.89-1.56; *P*=0.253] or within 1 hour of septic shock recognition (OR 0.88; 95% CI 0.45-1.71; *P*=0.704). Even regarding the appropriate antibiotic administration, the increase in the risk of mortality for each hour delay was not detected.

Conclusions: Our analysis suggests that inconsiderate use of broad spectrum-antibiotics without reasonable benefit, to achieve compliance with metrics of quality of care, should be discouraged, to avoid potential detrimental effects on antibiotic stewardship.

Time to antibiotics (hr)	No. (%)	OR	95% CI	*P* value	Probability of mortality (%)
≤ 1	65 (11.1)	1			0.251
1-2	84 (14.1)	0.96	(0.49-1.88)	0.895	0.243
2-3	127 (21.7)	1.18	(0.58-2.40)	0.652	0.283
3-4	70 (12.0)	0.98	(0.35-2.69)	0.962	0.246
4-5	49 (8.4)	0.88	(0.26-3.01)	0.838	0.228
5-6	30 (5.1)	0.89	(0.35-2.27)	0.807	0.230
> 6	160 (27.4)	0.95	(0.52-1.74)	0.879	0.242