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LETTER

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Antimicrobial de-escalation in septic cancer patients: is it safe to back down?

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Dear Editor,

Antimicrobial stewardship programs (ASP) aim for de-escalation of initial broad-spectrum antibiotics to reduce selective pressure, toxicity, and costs. The literature on antimicrobial de-escalation in septic cancer patients is scarce. We retrospectively examined the frequency and outcomes of antimicrobial de-escalation in 105 adult cancer patients admitted to a 20-bed intensive care unit (ICU) with severe sepsis from the Urgent Care Center (UCC) at Memorial Sloan Kettering Cancer Center, New York, NY between January 2008 and March 2013 (eSupplement Fig. 1). The hospital has an active ASP that developed local sepsis guidelines with the UCC and ICU. De-escalation was defined as discontinuing or narrowing of the regimen by ICU day 5 [1]. Primary outcomes were length of stay (LOS) (ICU, hospital) and all-cause mortality (ICU, hospital, 28-day).

Nearly all study patients (96 %) were on empiric combination therapy on ICU admission; 61 (58 %) of 105 patients had therapy de-escalated. The mean number of antibiotics per patient was 3 ± 0.8 in both groups on ICU admission. By ICU day 5, the mean number of antibiotics remained at 3 ± 0.9 in the non de-escalation group, while the mean number of antibiotics dropped to 1.5 ± 0.8 in the de-escalation group. While the average duration of antibiotic therapy was the same for both groups (Table 1), durations of certain antibiotics (e.g., resistant gram-positive agents, anti-pseudomonal beta-lactams, quinolones, metronidazole) were significantly shorter for de-escalated patients (eSupplement Table 1). Initial therapy was appropriate in 58 (97 %) of 60 microbiologically confirmed infections (eSupplement Table 2).

The de-escalation group had a lower mean lactate on ICU admission (2.4 ± 2.1 vs 3.2 ± 2.3 mmol/L, $P = 0.03$), a lower mean SOFA score on ICU day 5 (5.1 ± 3.9 vs 7 ± 3.5, $P = 0.002$), less history of resistant organisms (3 vs 16 %, $P = 0.03$), and fewer concomitant multiple infections (16 vs 36 %, $P = 0.02$) compared to the non de-escalation group. There were no differences in ICU, hospital, or 28-day mortality between the two groups (Table 1). The de-escalation group had shorter ICU (8.1 vs 11.2 days, $P = 0.006$) and hospital (17.1 vs 23.4 days, $P = 0.04$) LOS after adjusting for known prognostic factors in a multivariate analysis (eSupplement Table 3).

Our frequency of de-escalation (58 %) was higher than that of Mokart et al. (44 %), the only other de-escalation study in septic cancer patients [2]. The dissimilarities in study populations may account for the difference in de-escalation rates between our two cancer centers.

In our study, by ICU day 5, the non de-escalation group had a higher mean SOFA score compared to the de-escalated patients, implying slower clinical resolution. One factor that may be influencing the decision to de-escalate is the physician's perception of the clinical progress of the septic patient, and following serial SOFA scores, or other severity-of-illness measures as suggested by Joung et al. [3], may be useful to de-escalate patients safely.

In conclusion, de-escalating antimicrobial therapy in septic cancer patients admitted to the ICU from the UCC was associated with shorter ICU and hospital LOS. No adverse effect of de-escalation on mortality was found. Future sepsis studies should focus on investigating whether de-escalation can definitively improve patient outcomes and/or slow emerging antimicrobial resistance.

Compliance with ethical standards

Conflicts of interest None of the authors have any financial disclosures or conflicts of interest.

Table 1 Baseline characteristics and outcomes of de-escalation and non de-escalation groups

Variable	De-escalation ($N = 61$)	Non de-escalation ($N = 44$)	P value
Age (years)	62.5 (±13.2)	61.7 (±12.8)	0.7
Gender (male)	39 (64 %)	28 (64 %)	1
Cancer type			
Hematologic	24 (39 %)	17 (39 %)	1
Solid	37 (61 %)	27 (61 %)	
Neutropenia on ICU admission	13 (21 %)	11 (26 %)	0.64
History of antibiotic allergy	15 (25 %)	8 (18 %)	0.48
Prior history of resistant organism	2 (3 %)	7 (16 %)	0.03
Lactate level (mmol/L) on ICU admission	2.4 (±2.1)	3.2 (±2.3)	0.03
Blood culture on ICU admission that turned positive	15 (25 %)	7 (16 %)	0.34
Time to first antibiotic administration from initial blood culture collection (hours)	1.1 (±3)	1 (±3)	0.86
Concomitant multiple infections	10 (16 %)	16 (36 %)	0.02
Use of MV during ICU stay	29 (48 %)	22 (50 %)	0.84
Use of MV on day 5	20 (33 %)	18 (41 %)	0.42
Total MV duration (days) (for those on MV)	7.1 (±3.4)	10.1 (±6.6)	0.18
Use of VP during ICU stay	42 (69 %)	35 (80 %)	0.27
MPM II score on ICU admission	0.5 (±0.2)	0.5 (±0.3)	0.96
SOFA score on ICU admission	7.2 (±3.3)	8 (±3.4)	0.18
SOFA score on ICU day 5	5.1 (±3.9)	7 (±3.5)	0.002
Difference between SOFA on day 5 and SOFA on ICU admission	−2.1 (±3.5)	−1 (±3.5)	0.05
Duration of therapy	13.3 (±7.2)	15.5 (±11.1)	0.6
ICU mortality	11 (18 %)	10 (23 %)	0.62
Hospital mortality	21 (34 %)	15 (34 %)	1
28-day mortality	24 (39 %)	15 (34 %)	0.68
ICU LOS	8.1 (±4.6)	11.2 (±7.4)	0.001
Hospital LOS	17.1 (±22.9)	23.4 (±17.6)	0.005

Data are expressed as number (percentage) or mean (±standard deviation). $P < 0.05$ was considered significant

ICU intensive care unit, *LOS* length of stay, *MV* mechanical ventilation, *MPM* mortality probability model, *SOFA* sequential organ failure assessment, *VP* vasopressors

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