1334. Performance of C-Reactive Protein and Procalcitonin in Immunocompromised Children with SIRS

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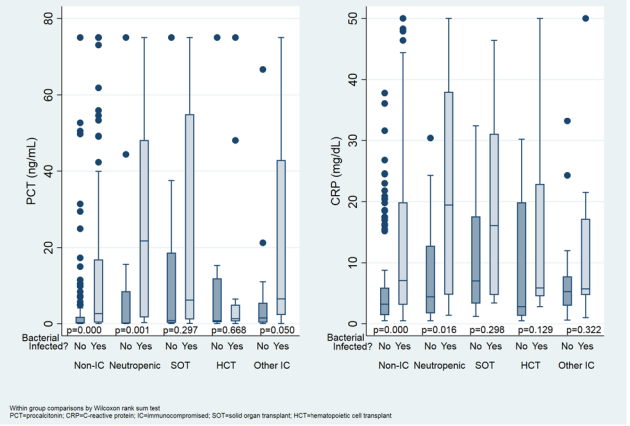
Background. Biomarkers (C-reactive protein [CRP], procalcitonin [PCT]) have been used in patients with systemic inflammatory response syndrome (SIRS) to identify those with and without bacterial infection. However, their performance in immunocompromised (IC) children is not well studied.

Methods. Retrospective chart review of episodes of SIRS in IC children <19 years old admitted to the PICU August 2012–June 2016 with: (a) blood culture, PCT, and CRP obtained within 6 hours of SIRS, (b) no recent SIRS episodes (> 30 days), and (c) no positive blood culture in 2 days preceding SIRS. We defined IC as neutropenia (ANC< 500), solid-organ transplant (SOT), hematopoietic cell transplant (HCT), and other (immunosuppressive medications or primary immunodeficiency). To identify a comparator group, we additionally reviewed a previously published cohort of non-IC children with SIRS (Downes, et al, JPIDS 2018), applying the same inclusion criteria. For each episode (first 48 hours after SIRS), we determined the presence of bacterial infection using NHSN definitions and viral infection as symptoms with positive PCR. We compared biomarkers in IC children with and without bacterial infection, and in IC and non-IC children, using Wilcoxon rank-sum tests.

Results. We identified 108 SIRS episodes in 94 IC children (neutropenia = 35, SOT = 18, HCT = 22, other = 33) and 278 episodes in 250 non-IC children. Age (P = 0.15) and gender (P = 0.70) were similar among IC and non-IC groups. 41% of episodes in both IC and non-IC children had bacterial infections (P = 0.96). PCT and CRP were significantly higher in IC children with bacterial infection than those without (Figure 1). Biomarkers did not differ significantly among episodes in IC and non-IC children with bacterial infection; however, among episodes without bacterial infection, biomarkers were higher in IC than non-IC children (Table 1). Detection of a viral infection did not affect biomarker values in IC or non-IC children when bacterial infection was absent (Table 2).

Conclusion. In IC children with SIRS, PCT and CRP were higher when bacterial infection was present. Meanwhile, in the subset of non-bacterial SIRS episodes, biomarkers were higher in IC compared with non-IC children. PCT and CRP may be valuable markers to discriminate bacterial from non-bacterial causes of SIRS in IC children.

Figure 1: Box Plots of PCT and CRP for Bacterial Infected vs Uninfected by Group



Within group comparisons by Wilcoxon rank sum test
PCT=procalcitonin; CRP=C-reactive protein; IC=immunocompromised; SOT=solid organ transplant; HCT=hematopoietic cell transplant

Table 1: Biomarkers in IC vs Non-IC Patients Based on the Presence of Bacterial Infection

Group	PCT (ng/mL), median (IQR)			CRP (mg/dL), median (IQR)		
	Bacterial infection present	Bacterial infection absent	p-value[a]	Bacterial infection present	Bacterial infection absent	p-value[a]
Non-IC (n=278)	2.67 (0.32-16.91)	0.32 (0.09-1.83)	0.000	7.05 (3.10-19.90)	3.20 (1.40-5.90)	0.000
All IC (n=108)	4.85 (1.02-43.16)	0.79 (0.20-7.74)	0.001	7.85 (4.70-25.70)	4.95 (2.20-12.40)	0.002
p-value[b]	0.063	0.008	--	0.086	0.006	--

All biomarker values reported as median (IQR). PCT=procalcitonin, CRP=C-reactive protein, IC=immunocompromised
[a]Wilcoxon rank sum tests used for comparison of within group biomarkers based on presence or absence of bacterial infection
[b]Wilcoxon rank sum tests used for comparison of biomarkers between IC and non-IC groups with same bacterial infection status

Table 2: Biomarkers in the Subset of Patients Without Bacterial Infection Based on Presence of Viral Infection

Group	PCT (ng/mL), median (IQR)			CRP (mg/dL), median (IQR)		
	Viral infection detected	Viral infection not detected	p-value[a]	Viral infection detected	Viral infection not detected	p-value[a]
Non-IC (n=164)	0.30 (0.08-2.90)	0.33 (0.11-1.47)	0.765	2.90 (1.65-4.80)	3.50 (0.95-8.20)	0.277
All IC (n=64)	0.77 (0.20-15.33)	0.80 (0.20-7.52)	0.881	5.10 (2.10-8.70)	4.80 (2.30-12.80)	0.953
p-value[b]	0.233	0.019	--	0.111	0.089	--

All biomarker values reported as median (IQR). PCT=procalcitonin, CRP=C-reactive protein, IC=immunocompromised
[a]Wilcoxon rank sum tests used for comparison of within group biomarkers based on presence or absence of viral infection
[b]Wilcoxon rank sum tests used for comparison of biomarkers between IC and non-IC groups with same viral infection status

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1335. A Translational Nephrotoxicity Model to Probe Acute Kidney Injury with Vancomycin and Piperacillin–Tazobactam

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Background. Vancomycin and piperacillin–tazobactam (VAN+TZP) are two of the most commonly utilized antibiotics in the hospital setting and are reported in clinical studies to increase acute kidney injury (AKI). However, no clinical study has demonstrated that synergistic AKI occurs, only that serum creatinine increases with VAN+TZP. Previous preclinical work demonstrated that novel urinary biomarkers and histopathologic scores were not increased in the VAN+TZP group compared with VAN alone. The purpose of this study was to assess changes in urinary output and plasma creatinine between VAN, TZP, and VAN+TZP treatments.

Methods. Male Sprague–Dawley rats (n = 32) received either saline, VAN 150 mg/kg/day intravenously, TZP 1,400 mg/kg/day intraperitoneally, or VAN+TZP for 3 days. Animals were placed in metabolic cages pre-study and on drug dosing days 1–3. Urinary output, plasma creatinine, urinary biomarkers were compared daily and kidney histopathology was compared at the end of therapy between the groups. Mixed-effects, repeated-measures models were employed to assess differences between the groups.

Results. In the VAN-treated rats, urinary output was increased on days 1, 2 and 3 compared with baseline and saline ($P < 0.01$ for all), whereas it increased later for VAN+TZP (i.e., day 2 and 3 compared with saline, $P < 0.001$). No changes in urinary output were observed with saline and TZP alone. Plasma creatinine rose for VAN on days 1, 2, and 3 from baseline and VAN+TZP on day 3 ($P < 0.02$ for all), but no treatment group was different from saline. In the VAN-treated rats, urinary KIM-1 and clusterin were increased on days 1, 2, and 3 compared with controls ($P < 0.001$). Elevations were seen only after 3 days of treatment with VAN+TZP ($P < 0.001$ KIM-1, $P < 0.05$ clusterin). No changes in urinary biomarkers output were observed with saline and TZP alone. Histopathology was only elevated in the VAN group compared with saline ($P < 0.002$). No histopathology changes were noted with VAN+TZP.

Conclusion. All groups with VAN demonstrated kidney injury; however, VAN+TZP did not cause more kidney injury than VAN alone in a rat model of VIKI when using plasma creatinine, urinary output, or urinary biomarkers as outcomes. Histopathology data suggest that adding TZP did not worsen VAN-induced AKI and may even be protective.

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1336. Impact of Procalcitonin-Guided Antibiotic Management in Chronic Obstructive Pulmonary Disease Exacerbation and Community-Acquired Pneumonia

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