Outcomes of Colistin Weight-Based Dosing Versus The Non-Weight-Based Dosing

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Background

Colistin is considered a salvage therapy for several multi-drug resistant organisms (MDROs). New guidelines were recently published recommending non-weight-based (NWB) dosing of colistin. There is limited data on outcomes with this new dosing strategy.[1,2]

Objective

To investigate the outcomes of the new NWB dosing strategy in comparison to the previously used weight-based (WB) dosing strategy.

Methods

A retrospective study was conducted at our quaternary care hospital between January 2016 and April 2020. Adults (≥18 years), who received intravenous colistin for ≥72 hours were included. Documented clinical cure was the primary endpoint, defined as having at least two of the following:

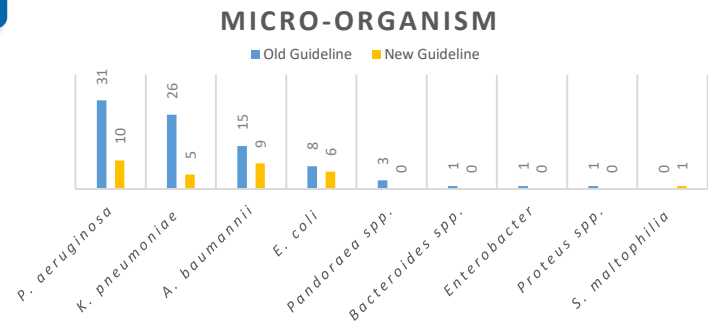
- Normalization of white blood cell count or ≥25% reduction,
- Defervescence,
- Hemodynamic stability,
- Normalization of inflammatory markers (C-reactive protein and procalcitonin values) or ≥25% reduction, or
- Resolution of signs and symptoms of infection by the end of the therapy.

Secondary outcomes were:

- Microbiological cure,
- Incidence of acute kidney injury (AKI),
- Time to AKI,
- Outcomes of AKI,
- Time to AKI recovery,
- New infection while on IV colistin,
- Recurrence of infection, and
- All-cause mortality.

Table 2: Primary and Secondary Outcomes

Parameters	Total (n=104) Mean ± SD or n (%)	WB dosing (n=74) Mean ± SD or n (%)	NWB Dosing (n=30) Mean ± SD or n (%)	P-value
Primary Endpoint				
Clinical cure	82 (78.85)	57 (77.03)	25 (83.33)	0.48
Secondary Endpoints				
Microbiological Cure	27 (56.25)	19 (51.35)	8 (72.73)	0.22
AKI	**40 (62.50)**	**24 (53.33)**	**16 (84.21)**	**0.02**
Time to AKI	3.64 ± 2.86	4.23 ± 3.31	2.85 ± 1.91	0.13
AKI recovery	**16 (29.63)**	**7 (17.95)**	**9 (60.00)**	**0.00**
Time to AKI recovery	34.14 ± 54.32	40.19 ± 60.67	24.45 ± 43.49	0.48
New infection while on colistin	30 (28.85)	23 (31.08)	7 (23.33)	0.43
New infection resolved	17 (73.91)	15 (75.00)	2 (66.67)	0.77
Recurrent infection	41 (52.56)	23 (69.26)	9 (37.50)	0.08
All-Cause-Mortality	**50 (48.08)**	**41 (55.41)**	**9 (20.00)**	**0.02**
Mortality during colistin	**22 (44.00)**	**15 (36.59)**	**7 (77.78)**	**0.02**
Time to Mortality	105.59 ± 249.65	125.61 ± 272.12	14.38 ± 9.62	0.23



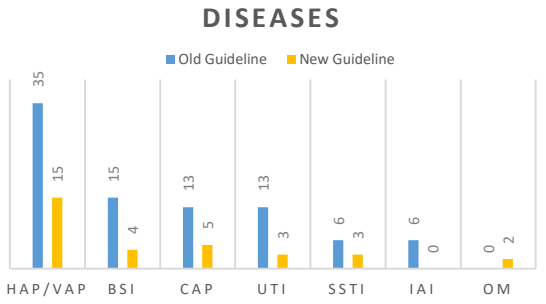
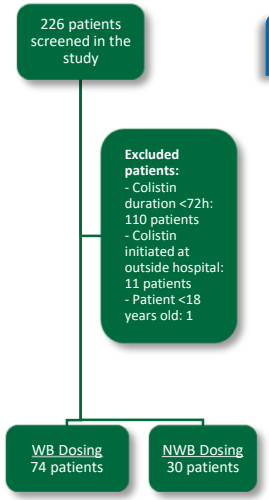


Table 1: Hospital's Dosing Guideline

WB Dosing LD: 170,000 units/kg		NWB Dosing LD: 9 million units	
CrCl ≥ 50	50,000 units/kg q8h	CrCl ≥ 80	5 million units IV q12h
CrCl 30 – 49	60,000 units/kg q12h	CrCl 50 – 79	4 million units IV q12h
CrCl 10 – 29	40,000 units/kg q12h	CrCl 30 – 49	3 million units IV q12h
CrCl <10	50,000 units/kg q24h	CrCl <30	2.5 million units IV q12h
Hemodialysis/ Peritoneal Dialysis	50,000 units/kg q24h	Continuous Renal Replacement Hemodialysis	5 million units IV q12h 4 million units IV q24h

Table 3: Abbreviations

Acronym	Meaning	Acronym	Meaning
A. baumannii	*Acinetobacter baumannii*	BSI	Bloodstream infection
CAP	Community-acquired pneumonia	E. coli	*Escherichia coli*
HAP/VAP	Hospital-acquired/ Ventilator-acquired pneumonia	IAI	Intra-abdominal infection
K. pneumoniae	*Klebsiella pneumoniae*	OM	Osteomyelitis
P. aeruginosa	*Pseudomonas aeruginosa*	S. maltophilia	*Stenotrophomonas maltophilia*
SSTI	Skin and Soft-tissue infection	UTI	Urinary tract infection



Results

A total of 104 primarily male (57.7%) patients with a mean age of 63 ± 20.23 years and weight of 70.24 ± 19.46 kg met the inclusion criteria. The estimated creatinine clearance was 74.23 ± 70.86 mL/min and renal replacement therapy was observed in 34.62% at baseline for total study population. There was no statistically significant difference observed in clinical cure rate between the two groups (WB 77.03% vs. NWB 83.33%; p-value 0.48). However, a higher rate of AKI was observed in NWB (84.21%) vs. the WB (53.33%) (p-value 0.02). Amongst those who had AKI, NWB had better AKI recovery status (60%) compared to the WB group (17.95%) (p-value 0.00). A higher all-cause mortality rate was observed in the WB versus the NWB group (55.41% vs. 20%, respectively; p-value 0.02).

Conclusion

The study showed no statistical difference in the primary outcome between the two groups, however, higher AKI rates, AKI recovery, and mortality during colistin therapy was observed in NWB dosing when compared to the WB dosing. All-cause mortality was higher in WB dosing. Our data needs to be validated in a larger study.

References

1. Tsuji, B. et al. (2019). International Consensus Guidelines for the Optimal Use of the Polymyxins: Endorsed by the American College of Clinical Pharmacy (ACCP), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Infectious Diseases Society of America (IDSA), International Society for Anti-infective Pharmacology (ISAP), Society of Critical Care Medicine (SCCM), and Society of Infectious Diseases Pharmacists (SIDP). Pharmacotherapy: The Journal Of Human Pharmacology And Drug Therapy, 39(1), 10-39. doi: 10.1002/phar.2209
2. T. Loho and A. Dharmayanti, "Colistin: an antibiotic and its role in multiresistant Gram-negative infections.," Acta Medica Indonesiana, vol. 47, no. 2, pp. 157-68, 2015.