HIGH-DOSE COLISTIN COMBINED WITH CVVH FOR TREATMENT OF MULTIDRUG-RESISTANT GRAM-NEGATIVE INFECTION IN CRITICALLY ILL PATIENTS.

Universitair Ziekenhuis Brussel

Verdoodt A¹, Honoré PM², Hubloue I¹, Spapen H².
Departments of Emergency¹ and Intensive Care² Medicine, Universitair Ziekenhuis Brussel, Brussels, Belgium.

No conflict of interest

Introduction

Gram-negative (GN) infections susceptible only to colistin (COL) are emerging in critically ill patients. Pharmacological studies suggest that a higher COL dose is needed to ensure microbiological and clinical cure. High doses may enhance COL-related renal toxicity. COL is effectively removed from the blood by continuous veno-venous hemofiltration (CVVH). This technique may allow to administer high COL doses without inducing or enhancing nephrotoxicity.

Objective and Methods

To assess safety and clinical/microbiological efficacy of high-dose COL treatment under “prophylactic” CVVH.

Methods:

- Adult ICU patients.
- GN infections only susceptible to Colistin: COL (colistimethate sodium, Colistineb™) as monotherapy or in combination with meropenem ± amikacin.
- Dose of Colistin: 9 MIU loading dose followed by 3 x 4.5 MIU daily.
- CVVH: citrate anticoagulation at a dose of 35mL/kg/h, a highly adsorptive AN69 ST filter with 1.5m² surface area.
- Evaluation of Clinical and Microbiological efficacy at the end of the therapy.

Age (year)	Male / female	Weight (kg)	Length (cm)	Apache II score
47	female	70	168	34
65	male	65	160	43
66	male	89	176	17
46	female	43	146	18
74	female	81	159	29
58	male	80	180	37
76	male	80	170	16
34	male	75	187	22
53	male	55	176	10
54	male	100	180	40
71	female	63	163	23
61	male	62,2	173	31
73	male	84	167	37
58	female	90	157	13
72	male	88	184	21
32	female	76	165	14
31	male	75	180	16

Table: Characteristics of patients treated with high-dose Colistin and protective CVVH.

Results

- Population: 16 patients: 10 males, age 57 ± 15 years, Apache II score: 26 ± 10 . Pneumonia: n = 14, Urosepsis: n = 2
 - Colistin MICs (for 14 pathogens) ranged from 0.03 to 3 mg/L.
 - Colistin + CVVH therapy: 13 (6–27) days.
 - Length of ICU stay: 48 (13–128) days.
 - A favourable clinical response: 14 (88%) patients
 - Microbiological eradication: 10, presumed in 4 and absent in 2 subjects.
 - 7 (45%) patients survived.
 - Serum creatinine (n=6) at the predefined time points was 2.12 ± 1.52 ; 1.59 ± 0.96 ; and 0.91 ± 0.29 mg/dL, respectively.
- One patient required intermittent dialysis at ICU discharge.

Site of infection	MDR pathogen	MDR pathogen	MIC (mg/l)	Mechanism of resistance
lung and feaces	Klebsiella pneumoniae complex		0,125	unknown
lung	Pseudomona's aeruginosa		0,125	MBL
lung	Pseudomona's aeruginosa		0,38	unknown
lung	Klebsiella pneumoniae complex		0,094	unknown
lung	Klebsiella pneumpniae complex		0,047	unknown
lung	Pseudomona's aeruginosa		0,38	unknown
urine	Pseudomona's aeruginosa		unknown	unknown
lung	Pseudomona's aeruginosa		0,032	KPC (carbapenemase)
lung	Pseudomona's aeruginosa		0,38	VIM
lung	Enterobacter aerogenes		0,38	MBL
lung	Pseudomona's aeruginosa		2	VIM
lung, Graft versus host	Stenotrophomona's maltophilia	Aspergillosis	3	unknown
lung	Enterobacter cloacae		0,125	OXA 48
lung	Klebsiella pneumoniae complex		3	unknown
lung	Pseudomona's aeruginosa		0,38	CPE
lung	Klebsiella pneumoniae complex		unknown	unknown
urine	Klebsiella pneumoniae complex		0,125	KPC carbapenemase

Table: Characteristics of infection treated with high-dose Colistineb and protective CVVH

Conclusion

- Emerging multiresistant Gram-negative infections necessitate administration of toxic dosages of antibiotics.
- Using the proof of concept by the group of Tascone for amikacin, we implemented a new scheme of high dosage Colistin therapy.
- 16 patients were included, 10 microbiological responders, 7 hospital survivors, preserved renal function in 6 survivors.
- High dosage of Colistin using protective CVVH with a highly adsorptive membrane may represent a valuable option to enable safe and effective high-dose Colistin treatment to protect against neuro- and nephrotoxicity.