STABILITY AND COMPATIBILITY OF VANCOMYCIN FOR ADMINISTRATION BY CONTINUOUS INFUSION.

Violeta Raverdi[1], Els Ampe[1], Jean-Daniel Hecq[2], and Paul M. Tulkens[1],
[1] Pharmacologie cellulaire et moléculaire et Centre de pharmacie clinique, Louvain Drug Research Institute, Université catholique de Louvain, Brussels, Belgium;
[2] Département de pharmacie, CHU Mont-Godinne, Yvoir, Belgium;

tulkens@facm.ucl.ac.be

Background

- Vancomycin is increasingly used by continuous infusion but few specific data is available about stability under practical conditions of preparation and use and compatibility with other intravenous drugs commonly used in routine hospital setting.

Methods

- Vancomycin stability (defined as recovery ≥ 93% of the original content [validated HPLC assay]) was examined for the whole process of centralized preparation, storage, and use in the ward by infusion for up to 48 h, with allowances for deviations of recommended practice (exposure to high temperature; use of concentrated solutions [up to 83 g/L]).

- Compatibility was assessed by mimicking co-administration in a single line via Y-shaped connectors with contact of 30 min at 25°C, followed by visual inspection in professional viewer, detection of particulate matter (particle analyzer), and HPLC assay of vancomycin.

Results

- Vancomycin was stable during the whole process and also during 72 h exposure of concentrated solutions at temperatures up to 37°C.

- Major incompatibilities were seen with -lactams (temocillin, piperacillin/tazobactam, ceftazidime, imipenem, cefepime, flucloxacillin) and moxifloxacin but not with ciprofloxacin, aminoglycosides and macrolides.

- Propofol, valproic acid, phenytoin, theophyllin, methyprednisolone, and furosemide were also incompatible,

- Ketamine, sufentanil, midazolam, morphine, piritramide, nicardipine, uradipil, dopamine, dobutamine, and adrenaline were compatible.

- No effect of N-acetyl-cystein or aminoacid solutions was detected.

Table 1: Compatibility of vancomycin with other drugs under conditions mimicking their co-administration through the same infusion line[a]

Drug	Dose (mg) [b]	Volume per administration (ml)	Time of infusion (h)	drug: vancomycin weight ratio[c]	Results [d]
Antiinfectives					
temocillin	2000	20	0.33	12.63	i (phys)
piperacillin/tazobactam	4000	20	0.33		i (phys)
ceftazidime	6000	48	24		i (phys)
imipenem	1000	40	0.5		i (phys)
	1000	200	0.5		i (phys)
cefepime	4000	48	24		c [f]
	2000	10	0.33		i (chem)
flucloxacillin	1000	4	0.33	6.31	i (phys)
amikacin [e]	1500	100	0.25	25.25	c
tobramycin [e]	600	100	0.25	10.1	c
gentamicin [e]	600	100	0.25	10.1	c
ciprofloxacin	400	200	1		c
moxifloxacin	400	250	1		i (chem)
erythromycin	100	20	0.33		c
clarithromycin	500	10	0.33	6.31	c
fluconazole	200	100	0.5		c
Sedatives / Anticonvulsivants / Analgesics					
ketamine	480	48	24		c
sufentanil	0.12	24	24	2.1×10^{-5}	c
midazolam	600	120	24	0.11	c
morphine	5	5	1	0.02	c
piritramide	10	5	1	0.04	c
propofol	300	300	24		i (phys) [g]
valproic acid	1200	12	24	0.21	i (phys)
phenytoin	750	15	0.25	12	i (phys)
Bronchodilatators					
theophylline	200	10	0.33	2.39	i (phys)
Antihypertensives, vasodilatators and drugs acting on the sympathic nervous system					
nicardipine	120	120	24	0.02	c
uradipil	2400	480	24	0.42	c
isosorbide dinitrate	6	30	1	0.02	c
furosemide	960	96	24	0.17	i (phys)
dopamine	0.4	1	0.016	0.1	c
dobutamine	0.84	0.84	0.016	0.21	c
adrenaline	0.5	10	0.33	0.0063	c
Hormones					
insulin	60 UI	0.6	3	0.08 UI/mg	c
methylprednisolone	500	10	0.5	4.0	i (phys)
Miscellaneous					
N-acetylcystein	10000	100	24	1.74	c
amino acid solution [h]	18000	1000	24	3.16	c

[a] see ref. 14 for a general description of the methods
[b] calculated (when appropriate) for a 70 kg male subject
[c] in final infusate
[d] key : c, chemically and physically compatible; i, incompatible; phys, physically incompatible (precipitate, flocculation and/or presence of particles as evidenced by passing solutions through a particle analyzer); chem, chemically incompatible less than 90% recovery (> 10% loss of antibiotic compared to nominal content).
[e] assuming a once-a-day schedule (30 min infusion)
[f] physically and chemically compatible, but degradation of cefepime limits its stability to 24h at 25°C, 14h at 30°C, and <10h at 37°C (see reference 15)
[g] trapping in emulsion
[h] VAMIN® (standard amino acid solution for parenteral nutrition; 18 g aminoacid nitrogen/L).

Conclusion

- Centralized preparation of vancomycin and its use by continuous infusion in wards is safe concerning stability,

- Careful attention must be paid for incompatibilities with several drugs (including all -lactams), requiring distinct intravenous lines or appropriate procedures to avoid undue contact.

25ème Journée de l'AFPHB, 02/03/2013, Bruxelles

Possible conflict of interest :
nothing to disclose.

Acknowledgments
We thank Dr K. Berthoin for help in the HPLC analyses of vancomycin.

Funding
This work was supported by Belgian Fonds de la Recherche Scientifique Médicale (F.R.S.M.; grants no. 3.4.597.06 and 3.4530.12), the Belgian Fonds de la Recherche scientifique (F.R.S-FNRS; grant no. 1.5118.11).