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Short Communication

Compatibility of the cephalosporin, cefamandole nafate with injections

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Cefamandole and its formyl ester, cefamandole nafate, are cephalosporin antibiotics with activity against Gram-positive and Gram-negative bacteria (Wick and Preston, 1972; Neu, 1974; Wold et al., 1978). This communication reports the findings of a study designed to investigate the compatibility of cefamandole nafate with a wide range of injections of potential clinical use with the antibiotic.

Compatibility of cefamandole nafate with 46 injections was determined at concentrations of 2, 20 and 100 mg/ml on storage at 5 and 25°C. Chemical stability of the antibiotic was determined polarographically (Hall, 1973) and physical compatibility assessed according to colour, clarity, pH and, where appropriate, microscopical appearance. An injection was considered compatible when: (a) more than 90% of original activity remained; (b) no change occurred in physical appearance; and (c) no gross pH change occurred over 24 h (25°C) and 72 h (5°C). Table 1 lists the compatibility profile for cefamandole nafate with the series of injections, data being presented for 2 mg/100 ml injections stored at 25°C for 24 h.

Chemical potency. Polarographic assay showed the antibiotic to be chemically compatible with 41 of the 46 injections tested. In only a few cases did chemical interaction occur which was not shown by gross change in appearance.

Physical appearance. Few changes occurred in injection appearance on the addition of cefamandole nafate. Calcium gluconate showed gross incompatibility in producing a viscous gel. Hazing visible under ambient light was absent in each injection. However, hazing was observed under polarized light with 3 proprietary preparations. It should be noted, however, that absence of haze, per se, is not an index of compatibility.

Effect of pH. In the range of injections studied, pH varied from 3.2 to 10.3. On constitution, no gross changes in injection pH were found and only those injections with pH above 8.0 and containing Tris (hydroxymethylaminomethane) were found unstable. The use of certain injections with cefamandole has not been recommended although the antibiotic was stable in these combinations. This reflects difficulties in monitoring the constituents of multi-component injections and also current good clinical practice.

TABLE 1

CEFAMANDOLE NAFATE INJECTION COMPATIBILITY PROFILE

Injection	pH injection	pH Reconstituted cefamandole injection	Percentage cefamandole remaining 25°C/24 h	Suitability for use with cefamandole
Non-electrolytes				
Amino acid sources				
Aminoplex	7.4	7.3	98.5	not recommended
Aminosol	5.2	5.1	100.0	not recommended
Aminosol–fructose–ethanol	5.1	5.2	98.4 [a,b]	no
Vamin–fructose	5.1	5.1	99.8	not recommended
Calorie sources:				
Glucose 5%	4.2	6.8	98.9	yes
Glucose 10%	3.9	6.8	97.7	yes
Glucose–saline	4.1	6.4	103.0	yes
Intralipid	7.3	7.2	97.7	not recommended
Laevulose	3.2	4.8	100.0	yes
Sorbitol 30%	5.2	6.6	96.9	yes
Plasma expanders:				
Dextran 40/dextrose	4.3	6.5	100.0	yes
Dextran 70/dextrose	4.2	6.3	94.0	yes
Dextran 110/dextrose	4.2	6.4	97.2	yes
Dextran 40/saline	4.7	6.2	102.0	yes
Dextran 70/saline	4.8	6.2	95.9	yes
Dextran 110/saline	6.1	6.3	102.0	yes
Dextran 150/saline	6.5	6.3	97.5	yes
Haemocoel	7.4	7.0	96.1	yes
Electrolytes				
Calcium gluconate	6.1	gross incompatibility		no
Compound sodium lactate	6.0	6.5	98.9	yes
Ionosteril	6.2	6.4	106.0	yes
Ionosteril bas	5.5	5.8	99.4	yes
Ionosteril HL5	4.5	5.0	101.0	yes
Ionosteril st	6.2	6.3	100.7	yes
Normal saline		6.6	100.0	yes
Normofundin	7.2	6.8	102.0 [a]	no
Normofundin MD	5.4	5.4	103.0 [a]	no
Potassium chloride	5.6	6.8	98.1	yes
Potassium chloride/saline	4.9	6.8	90.7	yes
Ringer saline	4.8	6.3	99.0	yes
Sterofundin	5.8	6.8	97.1	yes
Sterofundin B	5.3	5.8	99.1	yes
Sterofundin HL5	4.8	5.4	97.8	yes
Sterofundin L10	4.7	4.7	96.5	yes
Sterofundin Tris	10.1	gross incompatibility		no
Tris steril	10.3	gross incompatibility		no
Tutofusin Az	8.0	6.5	96.3	yes
Tutofusin B	5.7	5.8	102.0	yes
Tutofusin IK5	6.8	5.8	99.5	yes

TABLE 1 (continued)

Injection	pH injection	pH Reconstituted cefamandole injection	Percentage cefamandole remaining 25°C/24 h	Suitability for use with cefamandole
Tutofusin K10	6.3	6.3	<90	no
Tutofusin LC	4.5	4.6	93.0	yes
Tutofusin Pad	6.3	5.7	102.0	yes
Tutofusin Tris	10.1	gross incompatibility		no
Miscellaneous				
Mannitol 10%	5.5	6.7	100.0	not recommended
Mannitol 20%	6.1	6.1	98.7	not recommended
Water for injection	6.0	6.5	96.5	yes

[a] Hazing visible under polarized light.
[b] Hazing visible under polarized light at cefamandole concentrations of 20 and 100 mg/ml.

REFERENCES

Hall, D.A., Polarography of cephalosporin-C derivatives. I. 3-(5-methyl-1,3,4 thiadiazol-2-ylthiomethyl)-7-[2-(3-sydnone)-acetamido]-3-cephem-4-carboxylic acid, sodium salt. J. Pharm. Sci., 62 (1973) 980–983.

Neu, H.C., Cefamandole, a cephalosporin antibiotic with an unusually wide spectrum of activity. Antimicrob. Agents Chemother., 6 (1974) 177–182.

Wick, W.E. and Preston, D.A., Biological properties of three 3-heterocyclic-thiomethyl cephalosporin antibiotics. Antimicrob. Agents Chemother., 1 (1972) 221–234.

Wold, J.S., Joost, R.R., Black, N.R. and Griffiths, R.S., Hydrolysis of cefamandole nafate to cefamandole in vivo. J. Infect. Dis., 137 (Suppl.) (1978) 17–24.