Technical method

In vivo and in vitro interference due to cefotaxime on the assay of creatinine

MW MCKENDRICK AND EF LEGG *From the Departments of Communicable and Tropical Diseases and Clinical Chemistry, East Birmingham Hospital, Birmingham, UK*

Swain and Briggs¹ have shown that a number of cephalosporin antibiotics interfere in the Jaffé (alkaline picrate) reaction for the analysis of creatinine, while Durham *et al.*² recently reported interference by cefoxitin. Difficulties may therefore arise in the interpretation of the creatinine clearance test, which is usually used as the means of monitoring glomerular filtration rate. One of us (MM) was involved in a clinical trial of a new cephalosporin (cefotaxime, HR 756 Roussel Laboratories),³ in which the monitoring of kidney function formed an integral part of the study. Since cefotaxime is partially metabolised *in vivo* to desacetyl cefotaxime it was important to investigate the influence of both these compounds on the Jaffé reaction.

Methods

IN VITRO STUDY

Creatinine in serum and urine was measured by the Jaffé reaction with a continuous-flow technique

(Technicon method N 11B).

Cefotaxime was measured by microbiological assay.

Stock solutions of cefotaxime and its desacetyl derivative were prepared in 10 mmol/l phosphate buffer, pH 7.4, and added to serum and urine in order to effect concentrations of up to 100 mg/l in serum and 5000 mg/l in urine.

IN VIVO STUDY

Serum creatinine was estimated on samples taken at 10 minutes, 2 hours, and 5 hours after intravenous administration of 1 g cefotaxime in four healthy volunteers. Two-hourly collections of urine were also obtained from each volunteer for creatinine analysis.

Results and discussion

In this study, drug concentrations of up to 100 mg/l and 5000 mg/l in serum and urine, respectively, showed no significant interference with creatinine assay. This was true for both cefotaxime and desacetyl cefotaxime.

The results of the *in vivo* work are shown in the Table. Serum levels up to 98 mg/l at 10 minutes after intravenous administration of 1.0 g cefotaxime were achieved. In each volunteer, the serum creatinine at 10 minutes and 2 hours remained constant, despite a substantial fall in serum cefotaxime.

Since the serum creatinine showed no alteration in relation to serum cefotaxime concentrations in any of the volunteers, there is no need to relate the timing of blood or urine sampling for creatinine assay to dosage.

Accepted for publication 13 August 1980

Demonstrating the effect of cefotaxime on creatinine clearance

Subject	Time after dose	Serum creatinine (μmol/l)	Serum cefotaxime (mg/l)	Urinary creatinine (μmol/l)	Urine vol (ml)	Creatinine clearance (ml/min)	Urine cefotaxime (mg/l)
1	10 min	120	IS				
	2 h	120	3.4	8400	255*	149	3063
	5 h	90		3400	445†	140	100
2	10 min	130	80				
	2 h	130	6.7	1800	700*	81	1020
	5 h	90		9500	125†	110	100
3	10 min	90	98				
	2 h	90	9.2	3800	440*	155	750
	5 h	85		4000	345†	135	100
4	10 min	100	87				
	2 h	100	6.1	11000	170*	156	1850
	5 h	65		4200	390†	210	100

*Volume of urine collected from 0-2 hours after cefotaxime dose.

†Volume of urine collected from 4-6 hours after cefotaxime dose.

IS = insufficient specimen.

References

¹ Swain RW, Briggs SL. Positive interference with the Jaffé reaction by cephalosporin antibiotics. *Clin Chem* 1977; **23**:1340-2.
² Durham SR, Bignell AHC, Wise R. Interference by cefoxitin in the creatinine estimation and its clinical relevance. *J Clin Pathol* 1979;**32**:1148-51.

³ McKendrick MW, Geddes AM, Wise R, Andrews JA. *J Antimicrob Chemother* in press.

Requests for reprints to: Dr EF Legg, Department of Clinical Chemistry, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST.

Letters to the Editor

Assay of chloramphenicol in clinical specimens

We welcome the paper by De Louvois and colleagues (June issue, page 575) and feel strongly that all children receiving chloramphenicol should have levels monitored.

In their comparison of methods for assaying chloramphenicol they dismiss several techniques which were not as sensitive as originally claimed. The methods they recommend, while being simple, have disadvantages in that they are slow and, in the use of relatively large volumes of blood, unsuitable if repeated tests are to be performed on small babies.

The lack of sensitivity they have demonstrated with both *Escherichia coli* and *Clostridium perfringens* can be overcome by the use of more sensitive strains. We have used strains of both of these organisms which are capable of detecting 2.5 mg/l.

We agree that the *Cl. perfringens* assay is tedious, but this can be reduced by using a 21 cm square glass assay plate sealed in a plastic bag with catalyst and Gas-paks. This technique in our hands has given results within 3 to 4 hours using 40 µl of serum per well, thus enabling the use of capillary samples. Interference by metronidazole is seldom a problem in the child with meningitis.

For routine use, however, we favour a strain of *E. coli* which is also capable of detecting 2.5 mg/l although, except for CSF, we use standards ranging from 5 mg/l upwards. An overnight broth culture of the organism is diluted appropriately and surface-seeded on DST agar (Oxoid) and the plate is incubated at 40°C. Capillary samples are collected and wells are filled with 60 µl of serum. Zone diameters can be determined on a 'zone reader'. However, we find that an overhead projector gives clearer margins but zones should be centred around a cross marked on the projector stage to eliminate errors due to

misalignment of projector and screen (the wall). As results are routinely available within 4 hours the dose can be adjusted in the light of samples taken 1 hour after the previous dose. On one occasion it also enabled us to detect excessive levels resulting from the accidental administration of 10 times the prescribed dose.

We feel that other laboratories wishing to assay chloramphenicol should look for a sufficiently sensitive strain of either of these species if, like us, they require a rapid diagnostic method, which is also suitable for use on small volumes of serum.

RH GEORGE
DE HEALING
ME OULD

Department of Microbiology,
Birmingham Children's Hospital,
Birmingham B16 8ET

Transfusion of patients with leucocyte antibodies using cotton wool filtered blood

We report our preliminary findings in the use of cotton wool filters in the preparation of leucocyte free blood. Techniques used to eliminate leucocytes include Dextran sedimentation, inverted centrifugation, and freezing-thawing-washing red cells. We have most experience with the latter method, which is very effective and can eliminate reactions in transfusions. It is, however, an expensive and time-consuming process. As an alternative we have tested cotton wool filters, which have recently become commercially available.¹ Blood 5 to 9 days old was processed using

the filters. After filtration the blood was packed by centrifugation, and the plasma plus buffy coat was removed. The following results were obtained (Table).

It is important that the small but definite buffy coat be removed to obtain platelet removal figures of this order. These results compare very favourably with those obtained by the frozen, thawed, washed cell technique.

We have now transfused eight patients who have multispecific white cell antibodies and severe transfusion reactions to unprocessed blood. No untoward symptoms or pyrexia have developed during the transfusion of a total of 132 units of filtered blood. We have found the use of cotton wool filters to be easier, less time-consuming, and more economical than any other technique of providing leucocyte-depleted blood.

KENNETH E MAJOR
J ANTHONY CHILD
BRYON E ROBERTS
Department of Haematology and
Blood Transfusion,
The General Infirmary,
Great George Street,
Leeds LS1 3EX

Reference

¹ Terumo Corporation, Tokyo, Japan.

Addendum

Since this letter was written, 12 patients have now received a total of 260 units of filtered blood with similar results to those shown. No untoward reactions have been seen.

No. of units filtered	Mean removal of:		Mean time for processing 4 units of blood
	White cells %	Platelets %	
132	98	89.2	1 hour