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Pharmacokinetics of cyclophosphamide in Kenyan African children with lymphoma

The pharmacokinetics of cyclophosphamide have been extensively studied in adult man (Grochow *et al.*, 1979). A few studies have been done to compare the pharmacokinetics of this important anticancer agent in children and adults of a comparable population. The present study was designed to investigate the possible differences in the pharmacokinetics of cyclophosphamide that may arise due to age using a specific gas liquid chromatographic method of Juma *et al.* (1978). The accuracy and convenience of this method have been highlighted by van des Bosch & Vos (1980).

The parents of eight (four female and four male) children between 1 and 4 years in age with lymphoma who had been admitted under the care of the Oncology Unit of Kenyatta National Hospital gave consent for the study. The children weighed between 10–18 kg, and had normal renal and liver functions as verified by standard clinical tests. The children were all receiving cyclophosphamide for the first time and the five patients with Burkitt's lymphoma received cyclophosphamide alone while the rest who had stage II Hodgkins disease received in addition vincristine and prednisone on the second day of

treatment. Cyclophosphamide was administered as a bolus dose (5 mg/kg) intravenous via a cannula inserted in the cubital vein. The collection of samples, estimation of cyclophosphamide in biological fluid and data analysis was similar to that reported earlier (Juma & Ogada, 1983).

The pharmacokinetic data derived from the study of eight Kenyan African children with lymphoma appears in Table 1. The mean $\pm$ s.d. elimination half-life ($t_{1/2}$) was 4.10 ± 0.05 h. This was significantly shorter than that we have reported in Kenyan Africans which was 7.58 ± 1.3 h (Student's *t*-test) (Juma & Ogada, 1983). This was also significantly shorter than that we have reported in Caucasians (Juma *et al.*, 1979), and to that reported by other workers (Bagley *et al.*, 1973). The mean volume of the central compartment was 0.38 ± 0.18 l/kg and the apparent volume of distribution was 0.61 ± 0.17 l/kg. These later two parameters were not significantly different from what we have reported in adults. The total body clearance was 94.47 ± 5.04 (ml kg⁻¹ h⁻¹). This was significantly larger than that in adults suggesting that cyclophosphamide is eliminated faster in children.

De Vita & Adamson (1970) studied the depos-

Table 1 Pharmacokinetic parameters determined following administration of cyclophosphamide to eight children of Kenyan African origin.

Subject	β (h ⁻¹)	$t_{1/2}$ (h)	V_1 (l/kg)	V (l/kg)	CL (ml kg ⁻¹ h ⁻¹)
1	0.15	4.62	0.80	0.97	119.6
2	0.16	4.33	0.40	0.68	108.8
3	0.20	3.46	0.25	0.50	99.7
4	0.14	4.95	0.35	0.72	100.7
5	0.16	4.33	0.39	0.68	109.0
6	0.18	3.85	0.25	0.49	88.7
7	0.71	4.08	0.23	0.47	79.8
8	0.19	3.64	0.27	0.52	99.7
Mean	0.17	4.16	0.38	0.61	94.47
s.d.	0.02	0.05	0.18	0.17	5.04

ition of radiolabelled cyclophosphamide in African and American children. Sladek *et al.* (1980) estimated cyclophosphamide in urine of children with malignant disease. Both of these studies agree with our finding that the elimination half-life ($t_{1/2}$) of cyclophosphamide is shorter in children than in adults. However, in these earlier studies no mention was made of any other pharmacokinetic parameters other than the $t_{1/2}$ and no direct comparison was made with an adult population.

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Plasma levels and pharmacokinetics of sulphinpyrazone in renal impairment during chronic treatment: a case report

A 59-year old man has been examined regularly for a proteinuria lasting for 10 years. The proteinuria, which ranged from 4 to 6 g/24 h, was not associated with haematuria or leucocyturia. This patient presented a congenital absence of the left kidney. In 1972, a surgical renal biopsy was performed. The examination of twelve glomeruli indicated that some of them presented no abnormalities whereas others exhibited a simple mesangial thickening. No tubular, interstitial or vascular alterations were observed. At this time, no evaluation by immuno-florescence or electronic microscopy was performed. The observations indicated a nephrotic syndrome with only minor glomerular lesions. No treatment was proposed.

He was admitted to the hospital in 1979 for a left hemiplegia. Normal EEG and cranial scan were recorded. At this time, the nephrotic syn-

drome still existed. A creatinine clearance of 28 ml/min was indicative of renal impairment.

This patient was re-admitted in May 1980, for checking his renal function. At this time, side-effects due to cardiovascular drugs were recorded: digestive troubles and diarrhoea associated with dipyridamole, pruritus with cutaneous rash tentatively attributed to ticlopidine. This therapy was abandoned and long-term treatment with sulphinpyrazone alone (SP) was started in June 1980, with a daily dose of 400 to 600 mg. The influence of this chronic treatment on the pharmacokinetics of the parent drug as well as on renal function was studied. For this purpose, the plasma levels of SP and its sulphide metabolite following a 2 min intravenous infusion of 16.6 μmol (6.7 mg)/kg were determined by h.p.l.c. (Lecaillon & Soupart, 1976; Godbillon *et al.*, 1982) before the treatment and after 120 and 340