Fucidin in patients on haemodialysis

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SYNOPSIS Fucidin is useful against 'antibiotic-resistant staphylococci' which are a major problem in causing shunt site infections in patients on chronic intermittent haemodialysis for end-stage renal failure. A new form of intravenous fucidin has been used *in vivo* in three patients on haemodialysis, and also in experiments *in vitro* in order to assess its dialysing properties. The experiments *in vitro* show that some fucidin does cross the dialyser membrane but, in the patients studied, adequate serum levels were maintained throughout a 10-hour haemodialysis. A single intravenous dose of Fucidin is, therefore, adequate for treating 'antibiotic-resistant' staphylococcal infections in patients during haemodialysis.

Chronic intermittent haemodialysis is now an established form of treatment for end-stage renal failure and it is therefore of clinical importance to determine the dialysis properties of as many antibiotics as possible. In patients maintained by regular haemodialysis infections of the arteriovenous shunt site are a major problem. These infections are frequently due to 'antibiotic-resistant staphylococci', and Fucidin has been shown to be a useful antibiotic in the treatment of infections due to such organisms (Porter and Wilson, 1963).

In normal individuals Fucidin is excreted almost entirely by the liver, very little appearing in the urine (Godtfredsen, Roholt, and Tybring, 1962). Its excretion should therefore not be impaired in patients with chronic renal failure. In patients undergoing haemodialysis, however, antibiotic may be lost across the dialyser membrane and dosage may have to be adjusted accordingly. To determine whether a significant amount of Fucidin is lost during the course of dialysis we have investigated the fate of a single intravenous dose in three patients on chronic intermittent haemodialysis.

Patients and Methods

The three patients had all been on twice-weekly dialysis for more than two months. They were virtually anuric and had normal liver function. Dialysis was carried out for 10 hours using the Capon Heaton twin minicoil (Simpson, Blainey, Dawson-Edwards, Hilton, and Williams, 1967) in conjunction with the Lucas haemodialysis machine (Simpson, Blainey, Dawson-Edwards, Hilton, and Wilson, 1967).

A single dose of 500 mg of Fucidin in 250 ml of saline was administered intravenously over a period of two hours on two separate occasions: (1) at the onset of a 10-hour dialysis and (2) one day between dialyses. Samples of blood were obtained 10 minutes after the end of the infusion and thereafter at three, six, nine, and 10 hours (at the end of dialysis). The serum was separated, frozen, and subsequently assayed for Fucidin. For antibiotic assay 150 ml of medium pre-seeded with *Staphylococcus aureus* (NCTC 6571) was poured in levelled 10 in. square glass plates. Holes were cut with a 6 mm cork borer and standards and samples added using a quasi latin square random distribution. The method gives satisfactory results down to levels of approx-

Fig. 1

Fig. 2

Fig. 3

Figs. 1, 2, and 3 The variation of serum level of Fucidin with time following a single intravenous dose in patient T.M. (Fig. 1), in patient P.S. (Fig. 2) and in patient M.W. (Fig. 3).

O-O—patient on haemodialysis, X-X—repeat experiment on a day between dialysis.

imately 1 µg/ml in serum and much lower levels in buffer. Serum levels were plotted against time and the results are shown in Figures 1, 2, and 3.

As our results suggested that dialysis had no effect on the rate of fall of the serum Fucidin levels, an experiment was performed *in vitro*. Two solutions, one containing 6,200 µg Fucidin in 10 ml of distilled water, and the other containing 6,200 µg Fucidin in 10 ml of pooled human serum, were dialysed against 100 ml of dialysate for 18 hours. The level of antibiotic in the original solution was assayed in parallel with the level in the same solution after dialysis and the level in the dialysate after dialysis. The results are shown in the Table. It can be seen that while equilibrium was obtained in the non-protein-containing dialysis fluid, far less Fucidin dialysed from the protein-containing solution. Fucidin is known to be 97.2% protein bound in

	Antibiotic inside Dialysis Tubing				Antibiotic in Dialysate after 18 Hours	
	At Start		After 18 Hours		Total (µg)	Concentration (µg/ml)
	Total (µg)	Concentration (µg/ml)	Total (µg)	Concentration (µg/ml)		
Fucidin in human serum	6,200	620	5,600	560	540	5.4
Fucidin in water	6,200	620	640	64	5,500	45

Table Comparative results in vivo and in vitro.

serum (Rolinson and Sutherland, 1965), and presumably protein binding is the reason for the low levels in the dialysate and also for the finding *in vivo* that dialysis does not alter the rate of fall of serum Fucidin levels.

Comment

Although the studies *in vitro* showed that some Fucidin does cross the dialyser membrane, dialysis had no effect on the rate of fall of serum Fucidin levels in our three patients. The rate of fall after a dose of 500 mg intravenously is such that therapeutic levels are maintained for at least 10 hours (Barber and Waterworth, 1962; Godtfredsen *et al*, 1962) and no modification of the dosage schedule is required during dialysis.

Both oral and intravenous Fucidin are available for use, but in the treatment of shunt infections intravenous antibiotic therapy is preferable because of the need to produce therapeutic levels

at the site of infection as quickly as possible to preserve the shunt and prevent septicaemic complications. In addition we have found the severe gastrointestinal side effects of oral Fucidin to be a limiting factor in its use, and these do not occur using the intravenous route. Venospasm and subsequent thrombosis have been reported following injection of Fucidin into a peripheral vein (personal communication), and for this reason the manufacturers advise the above method of administration. However, this should not be a problem when Fucidin is given into an arteriovenous shunt where the blood flows fast

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