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LETTER TO EDITOR

After liver transplantation, there are marked variations in the enteral absorption of cyclosporine, as judged by whole-blood cyclosporine concentrations measured with radioimmunoassay (*1*, *2*). The absorption is influenced by the presence or absence of external bile drainage, a clinically significant factor that can be demonstrated by describing a few cases of the many that have been encountered.

Case No. 1. A 36-year-old woman who had an orthotopic liver transplantation for cholangiocarcinoma, returned more than a year later with a rising serum bilirubin. A percutaneous cholangiocatheter was inserted, which drained significant amounts of bile. Without changing her oral cyclosporine dosage, the blood cyclosporine level fell over 48 hr from 991 ng/ml, to 362 ng/ml. The blood cyclosporine level remained in the 300–500 ng/ml range until the tube was clamped, at which time it increased from 676 ng/ml to 1,126 ng/ml, again without changing the oral cyclosporine dose. (Fig. 1).

Case No. 2. A 38-year-old man who underwent an orthotopic liver transplantation 8 months earlier was admitted because of recurrent fevers and a rising serum bilirubin. Ultrasound examination showed common bile duct dilatation; a percutaneous biliary catheter was inserted. The blood cyclosporine level before percutaneous tube insertion was 1,023 ng/ml. Twenty-four hours after biliary drainage, the cyclosporine concentration fell to 459 ng/ml. The level remained between 200 and 500 ng/ml despite increasing his daily oral dose from 480 mg to 1,200 mg (Fig. 1). Dilatation of a biliary stricture was performed under radiographic control, and eventually the drainage tube was clamped and removed. After the tube was clamped, the cyclosporine concentration increased from 247 ng/ml to 1,441 ng/ml over 48 hr, necessitating a major downward revision in the daily oral dosage.

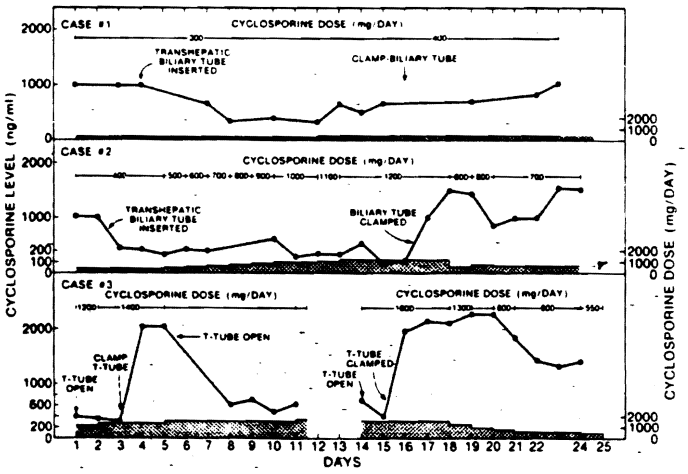

FIGURE 1. The influence of biliary tube insertion, opening, or clamping in three patients.

Case No. 3. A 56-year-old man had his T tube clamped 3½ days after orthotopic liver transplantation. He had already begun cyclosporine by the oral route, and had resumed a diet. The blood level of cyclosporine rose over the next 24 hr to the toxic level of 2,251 ng/ml (Fig. 1). His serum transaminases and BUN increased, and he developed malaise and upper extremity tremors. His T tube was unclamped and his blood cyclosporine level fell precipitously over the next 3 days. Later his T tube was clamped again before its removal, with a prompt tripling of the cyclosporine blood level (Fig. 1).

The correlation between cutaneous bile diversion and whole-blood cyclosporine levels is well shown in these 3 examples, and can be demonstrated quite clearly in virtually every similar case. Because cyclosporine is fat-soluble, its efficient absorption presumably is dependent on the bile salts that are removed with bile diversion.

At one time, it was thought that cyclosporine had a significant enterohepatic circulation (*3*). If so, interruption of this cycle could be a factor. However, recent studies by Venkataramanan et al. (*2*) have shown the enterohepatic circulation of cyclosporine to be too minor to account for the major effect of bile diversion herein described.

Whatever the explanation, adjustments in cyclosporine dosage must be considered whenever external bile diversion is instituted or discontinued. The changes are best guided by pharmacologic monitoring.

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