Cyclosporine Slide/Lecture Guide

Slide 11

Cyclosporine metabolism and excretion.

Nearly all (>99%) cyclosporine is metabolized by the liver (8). Unchanged cyclosporine (0.1%) and its metabolites are eliminated via the biliary and urinary routes. At least 15 metabolites have been found in urine, and 9 have been isolated and identified (17). The terminal half-life of cyclosporine in humans ranges from four to 60 hours. Drug clearance is impaired by liver disease, while hemodialysis and renal failure do not significantly alter cyclosporine clearance.

Slide 12

Cyclosporine indications.

Cyclosporine is indicated for the prophylaxis of organ rejection in kidney, liver, and heart transplants. It is always to be given with adrenal corticosteroids. Cyclosporine also may be used in the treatment of chronic rejection in patients previously treated with other immunosuppressive agents. Many studies have shown that the results of cyclosporine therapy generally are as good as or better than those achieved with conventional immunosuppression in terms of patient and graft survival. When considering the length of hospitalization and rehabilitation, the results usually are superior to those achieved with conventional immunosuppression.

Slide 13

Cyclosporine/steroids vs historic experience in renal transplants (University of Pittsburgh).

In a University of Pittsburgh randomized study of 41 primary renal allografts treated with cyclosporine and steroids (n=20) (18), patient survival in both groups was 100%. There was, however, a 90% one-year graft survival rate for the cyclosporine group, compared with a 55% rate for the azathioprine group. In addition, five rejection episodes occurred in the cyclosporine group and were reversed, while 31 occurred with azathioprine, of which seven were not reversible.

Slide 14

Cyclosporine/steroids vs historic experience in secondary renal transplants (University of Pittsburgh).

In a University of Pittsburgh study (35), all 42 patients undergoing repeat cadaver kidney transplants in a one-year period were managed with cyclosporine and low doses of steroids. At one year, patient survival was 100% and graft survival was 83%. This was a marked improvement over the 36% one-year graft survival rate for historic controls treated with azathioprine and steroids at the same institution. During followup, 6 patients in the cyclosporine group lost the kidney because of rejection. Three of these were complete HLA mismatches, and the other 3 had reactive antibodies against 99% lymphocyte donors (preformed reactive antibodies). Humoral factors may have been involved in the rejections, as 4 of the 6 were accelerated, occurring one week after transplantation. Nephrotoxicity was not a recognized cause of graft loss in any of the patients (19).

Slide 15

Three-year survival rates in renal allograft patients (University of Minnesota).

Recipients of renal allografts from cadaver or mismatched related donors were randomized to receive one of two immunosuppressive regimens. One group was treated with cyclosporine and prednisone, and the other with azathioprine and prednisone, plus antilymphocyte globulin (ALG). After three years there was no significant difference between patient survival or graft survival in the two treatment groups. The same was true for those receiving a second graft. In the subgroup of diabetic patients receiving cadaver grafts, the graft survival rate was significantly higher in cyclosporine than in azathioprine-treated recipients (20).

Slide 16

Incidence of rejection episodes in renal allograft patients (University of Minnesota).

The cumulative incidence of rejection episodes in patients receiving renal transplants and randomly assigned to cyclosporine or azathioprine treatment was significantly less (about one-half) in the cyclosporine-treated recipients than in the azathioprine-treated recipients. The incidence of chronic or irreversible rejection also was less in the cyclosporine group (20).

Slide 17

Comparison of renal function in allograft patients (University of Minnesota).

Based on serum creatinine levels as a measure of

renal function, graft recipients treated with cyclosporine had lower renal function than did those treated with azathioprine. The differences between the two groups were significant at all time points up to the second year. Graft functional deterioration attributed to cyclosporine nephrotoxicity occurred in 109 of the 131 cyclosporine-treated patients (83%). Graft biopsies confirmed the nephrotoxicity in 44 instances (20).

Slide 18

Length of hospitalization in renal allograft patients (University of Minnesota).

In the admission surrounding the transplant, patients on cyclosporine immunosuppression spent about 80% as long in the hospital as did those in on conventional therapy. They were also readmitted for a total of 70% fewer days during the period of 3 to 42 months following transplant. Both differences are statistically significant (34).