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CMV prophylaxis after renal transplantation with immunoglobulin or CMV-hyperimmunoglobulin – a prospective clinical trial

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Abstract. Three groups of 40 patients each entered this prospective randomized trial. Patients of group A received 2 ml/kg body weight CMV-Polyglobulin, patients of group B 15 g Intraglobin and patients of group C, serving as controls, received no specific anti-CMV prophylaxis. All patients were given the same sequential immunosuppressive therapy. Patient survival and graft function did not show any significant differences at 2 years follow up. The incidence of fever, CMV infections, dialysis and steroid bolus therapy were lower in group A, but without statistical significance. Patients receiving a graft from a CMV–AK-positive donor were at high risk of developing an infection or reactivation of CMV. A study examining this subgroup seems appropriate.

Key words: CMV prophylaxis – Renal transplantation – Immunoglobulin

During the first year post-transplantation CMV infection is a major threat to graft and patient survival. The aim of this study was to examine the effect of prophylactic CMV-hyperimmunoglobulin as compared with immunoglobulin or no CMV prophylaxis.

Materials and methods

During a period of 2 years all recipients of a first or second cadaver renal graft were randomly assigned to one of the three groups ($n = 40$, each). Patients of group A received a CMV-hyperimmunoglobulin (CMV-Polyglobin, 2 ml/kg body weight) immediately after surgery. Patients of group B received an immunoglobulin (Intraglobin F, 15 g) immediately after surgery. Patients of group C received no specific CMV prophylaxis.

The immunosuppressive regimen was standardized, starting with prophylactic antilymphocyte globulin for 8–10 days, azathioprine and steroids being switched to long-term immunosuppression with steroids and cyclosporine (whole blood levels of 300 ng/ml).

CMV-KBR titres and CMV-IgM titres (ELISA) were determined prior to surgery and on days 1, 21, 42, 63, 84 and 105 post-transplantation. A rise of four times the initial KBR or an IgM titre > 1:10 was considered a CMV infection/reactivation. Combination with a fever > 38 °C or a rise in serum creatinine, transaminases, leucocytopenia or thrombocytopenia was considered symptomatic of CMV infection. Primary infection was defined as the above together with a preoperative negative CMV-KBR. Reactivation was defined as the above together with a preoperative positive CMV-KBR.

Results

There were no significant differences between the three groups with respect to age, sex, frequency of HLA-A, HLA-B or HLA-DR mismatches, conservation time, anastomotic time, frequency of first versus second transplant or preoperative CMV status. Donor CMV status was known in 71 out of 120 cases. There were no significant irregularities in the distribution of known CMV-negative

Table 1. Frequency of symptoms and complications after renal transplantation depending on the kind of CMV prophylaxis

Results: III

Symptoms	Group A (CMV-IgG) ($n = 40$) n	Group B (IgG) ($n = 40$) n	Group C (Control) ($n = 40$) n
Fever	10	16	14
Pneumonia	1	5	1
Urinary infection	6	6	6
Herpes infection	9	16	6
CMV infection with CMV-immunoglobulintherapy	2	4	3
CMV infection without CMV-immunoglobulintherapy	9	15	12
Dialysis after transpl.	2	7	5
Steroid bolus injection	8	15	14

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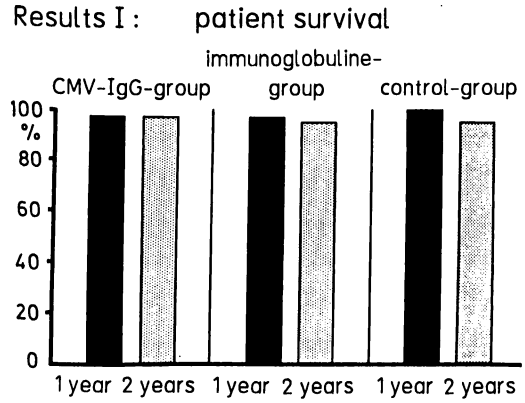

Fig. 1. Patient survival after 1 and 2 years depending on the kind of CMV prophylaxis

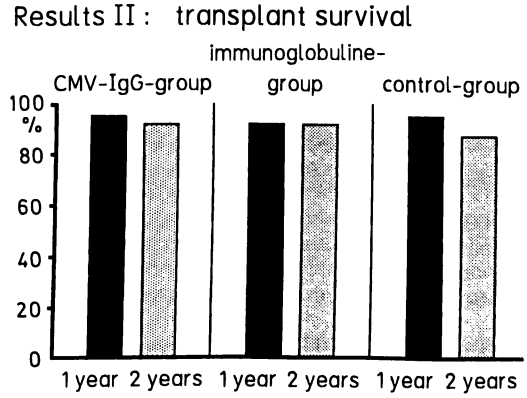

Fig. 2. Graft survival after 1 and 2 years depending on the kind of CMV prophylaxis

donors, but group B was at a slight disadvantage with four negative donors out of 24 with known status compared with 11 out of 23 in group A and 9 out 24 in group C.

There were no significant differences in either patient or transplant survival (Figs. 1 and 2). There were 22 CMV primary infections, and 72 CMV reactivations, the frequency within the three groups being as follows: primary infections: group A 12.5%, group B 27.5%, group C 15%; reactivation: group A 60%, group B 57.5%, group C 62.5% (differences without statistical significance).

Table 1 shows the distribution of various complications between the groups. Group A had the lowest frequency of fever, pneumonia, urinary tract infection, dialysis, and rejection episodes; none of the differences were significant.

Discussion

Administration of CMV-hyperimmunoglobulin or immunoglobulin did not result in a significant improvement in patient or transplant survival. Injection or reactivation developed in 27.5% of patients receiving CMV-hyperimmunoglobulin, 47.5% of patients receiving immunoglobulin and 37.5% of patients of the control group. The number of symptomatic CMV infections leading to therapeutic use of CMV-hyperimmunoglobulin was not significantly different between the groups. There was a tendency towards a lower rate of complications in the CMV-hyperimmunoglobulin group. Considering that there is a subgroup at higher risk (donor CMV-IgG-positive/recipient CMV-IgG-negative) a study examining this subgroup seems appropriate.