

INTRAVENOUS METHYLPREDNISOLONE AT THE TIME OF RENAL TRANSPLANTATION

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Summary

Ninety-five consecutive transplants performed prior to the introduction of methylprednisolone bolus at transplantation were compared to 136 consecutive transplants performed after the policy change. No difference was found in the incidence of reversible or irreversible rejection in the two groups. The treated group were exposed to a higher total dose of steroid than the non-treated group. Routine bolus methylprednisolone therapy at transplantation is not recommended.

Introduction

Large intravenous pulses of methylprednisolone have been shown to effectively reverse a high proportion of episodes of acute rejection following renal transplantation and this treatment is used in many renal units [1-3]. It has been claimed that similar doses administered directly into the renal artery [4], or given intravenously immediately following transplantation [5] have a beneficial effect on subsequent graft survival. A prospective double-blind trial of bolus methylprednisolone given at the time of renal transplantation failed to show any benefit to the treated group, although numbers were rather small [6]. In an attempt to improve graft survival routine intravenous methylprednisolone therapy given at the time of transplantation was introduced for all transplant recipients in Newcastle from early 1978. In view of conflicting evidence of benefit from this treatment, we have analysed our results retrospectively to try and determine the effect of this policy change.

Patients and methods

Two hundred and thirty-one consecutive transplants performed between January 1976 and December, 1980 were analysed. Ninety-five were performed before

routine early steroid bolus treatment was introduced (Group A) and 136 after the policy change (Group B). Acute rejection was usually diagnosed on the basis of clinical features and a change in urine output and plasma creatinine, more recently with the additional aid of serial technetium-99 DTPA gamma-camera scans, and less commonly renal biopsy. Treatment for rejection was with a daily bolus of intravenous methylprednisolone 1,000mg on three consecutive days.

Policy in Newcastle

From February, 1978, all patients received routine intravenous methylprednisolone 1,000mg at vascular anastomosis during transplantation, and a further dose of 1,000mg 24 hours later. Background initial oral prednisone dose was reduced from 40mg to 30mg daily in two divided doses in September 1979. Azathioprine 1.5–2.5mg/kg daily was given to all patients with an initial intravenous dose of 1mg/kg up to February 1978, and 5mg/kg subsequently. A positive transfusion policy and attempt to increase the proportion of HLA-B antigen matches was formally introduced in early 1978 [7] although awareness of the importance of both these factors had already had some effect prior to 1978. Single dose prophylactic antibiotic treatment was introduced in November 1978.

Results

The two groups were virtually identical in respect of age, primary renal disease and time on dialysis prior to transplantation. Immunological data are shown in Table I.

TABLE I. Immunological data in patients who did (Group B) and did not (Group A) receive methylprednisolone at transplantation

Group	A (no early bolus)	B (early bolus given)
Mean age	36.9	37.3
Follow up	4–6 years	1.5–4 years
Pre-transplant blood transfusion	87%	97%
Living donor	10.5%	17.5%
B-locus match	48%	59%
Mean number of mismatches at HLA A and B	1.6/patient	1.2/patient
Pre-existing cytotoxic antibodies detected	32%	17.5%
2nd or 3rd transplant	16%	19%

Acute rejection

Within the first 40 days after transplantation 112 episodes of acute rejection were observed in Group A (1.18 episodes/patient) and 153 episodes in Group B (1.13 episodes/patient) (NS). The distribution of acute rejection with respect to time after transplantation was not substantially altered (Figure 1) with a peak at day six in both groups, although the diagnosis of acute rejection within 48 hours of transplantation was rarely made after routine early steroid bolus. Hyperacute rejection did not occur in either group.

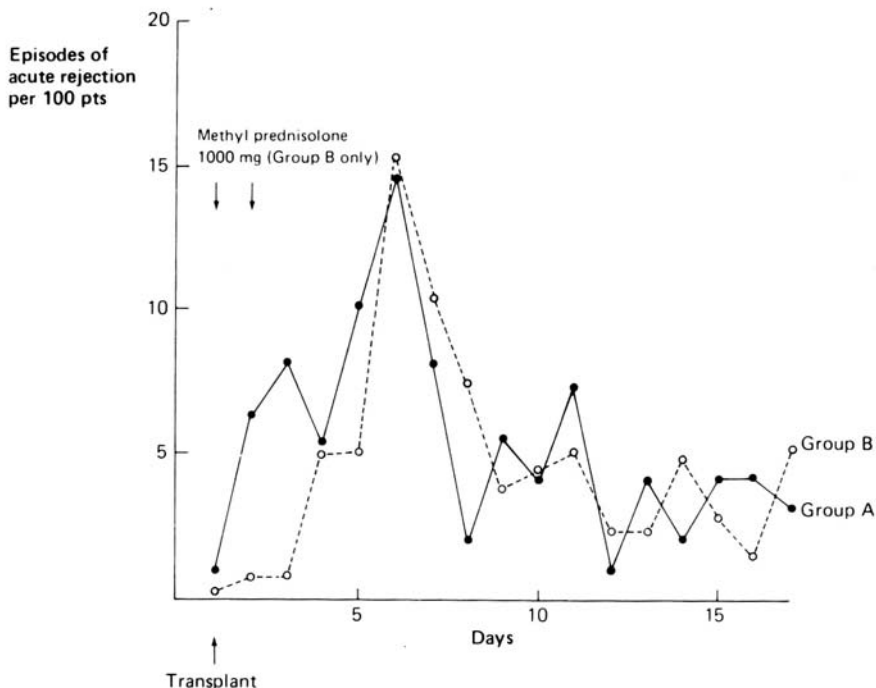


Figure 1. Incidence of acute rejection per 100 patients with and without methyl-prednisolone at transplantation

Survival

Actuarial survival was analysed according to the method of Barnes [8], both including and excluding non-immunological failures. There were 28 non-immunological failures in Group A as compared to 12 in Group B within three months of transplantation. This is reflected in Figure 2a, which shows significantly better survival in the treated group. If non-immunological failures are excluded from the analysis (Figure 2b), survival is identical in the two groups.

Steroid dose

Mean dose of methylprednisolone within 40 days of transplantation was significantly lower in Group A (4440mg) than Group B (5690mg) ($p < 0.05$). Over twice

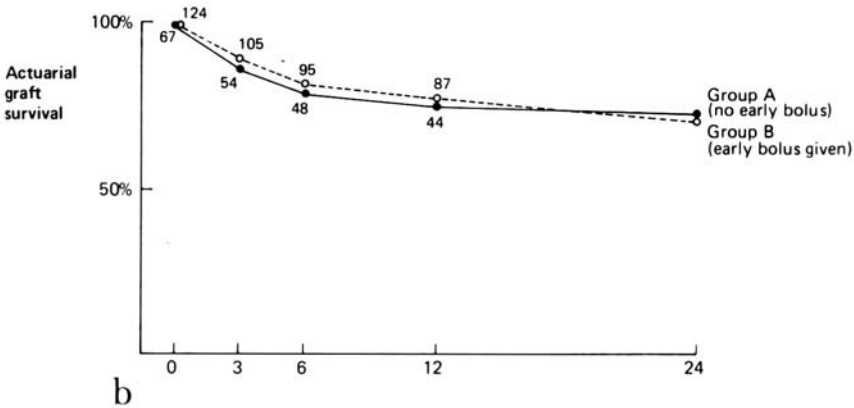
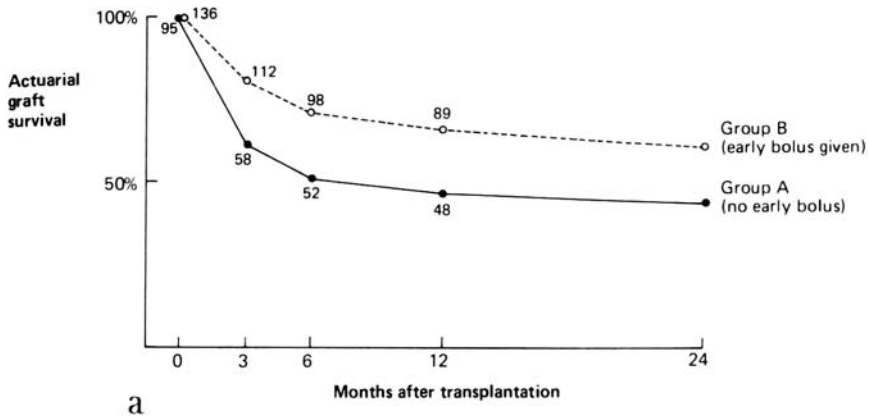


Figure 2. Actuarial graft survival in patients with and without methylprednisolone at transplantation
 a) Non-immunological failure included; b) Non-immunological failure excluded

as many patients in Group B received a total dose in excess of 6,000mg methylprednisolone (Figure 3).

Steroid-related complications

The introduction of routine pre-operative antibiotic cover in November 1978, markedly reduced the incidence of infective complications (Table II). There was no difference in the incidence of other steroid-related complications.

Discussion

We have demonstrated no benefit in terms of reducing the incidence of acute rejection, or of irreversible rejection by routine intravenous methylprednisolone

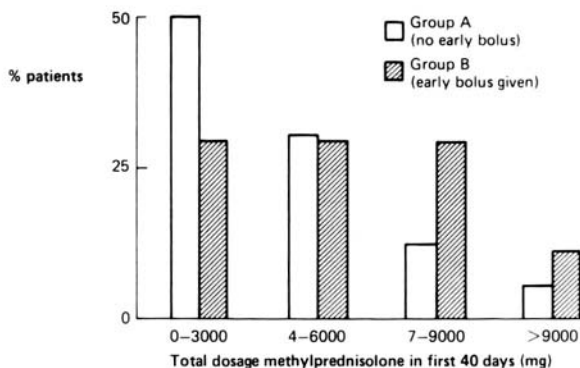


Figure 3. Total dose of methylprednisolone in the two groups in the first 40 days after transplantation

TABLE II. Steroid related complications in patients who did (Group B) and did not (Group A) receive methylprednisolone at transplantation

Group	A	B
Wound infection	19%	6.5%
Other serious infection	23%	17%
Other, e.g. avascular necrosis, psychosis	3%	2%

given at the time of renal transplantation. Other changes in clinical management have led to improved survival since 1978 and interpretation of the data is therefore limited by the large difference in the incidence of non-immunological failure in the two groups. It could be argued that the analysis excluding non-immunological failure could flatter survival in the untreated group by excluding failures due to immunosuppression given for rejection, but this is unlikely as the treated group received more steroids than the untreated group, and when rejection contributed substantially to a failure it was not excluded.

A number of studies have reported complications related to the use of large doses of methylprednisolone [9-11]. In one report the complications rate increased substantially when the total dose was above 5,000mg methylprednisolone [11]. This study shows that routine early boluses of methylprednisolone will lead to a higher mean total dose of steroid and expose patients to an increased risk of such complications, although we have failed to demonstrate such an effect.

This study supports the view that routine early boluses of methylprednisolone are ineffective, potentially harmful and cannot be recommended.

Acknowledgments

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