Free radical injury in human renal allograft rejection


Departments of Nephrology & *Gastrointestinal Sciences, Christian Medical College & Hospital, Vellore

Accepted May 13, 1994

Plasma and renal tissue levels of lipid peroxide and plasma vitamin E were estimated as measures of free radical injury in five renal allograft recipients with untreated and four with unsuccessfully treated acute cellular rejection and compared with 11 control patients with minimal change disease. Plasma lipid peroxide was significantly higher in patients studied before antirejection therapy (13.2 ± 3.5 nmol/ml; P < 0.01) as well as in those after unsuccessful antirejection treatment (11.7 ± 0.7 nmol/ml; P < 0.01), compared to controls (5.7 ± 2.8 nmol/ml). Levels of plasma vitamin E and renal tissue lipid peroxide were similar in both groups, however the latter was significantly raised in patients evaluated prior to antirejection therapy than in those after unsuccessful antirejection therapy (5.1 ± 1.7 and 3.0 ± 0.8 nmol/mg protein; P < 0.05). These findings suggest possible free radical mediated injury during renal allograft rejection.

Key words Free radical-kidney transplantation-rejection-steroids

Free radicals are implicated in the pathophysiology of organ transplant rejection1. Infiltrating inflammatory cells in renal disease2 and piglet cardiac allograft rejections3 are thought to be the source of free radicals. Cyclosporine and steroids have been shown to attenuate free radical generation4,4. We report our observations on the role of free radical injury in human renal allograft rejection.

Material & Methods

Nine male patients (mean age of 26.9 ± 10.6 yr), who received renal allografts (8 haplomatched and 1 fullmatched) from live related donors 2 to 11 months earlier with biopsy acute cellular rejection were included in the study. All had smooth contracted native kidneys. Cyclosporine, azathioprine and prednisolone were used in five patients; cyclosporine and prednisolone in four. Five patients were biopsied and studied within 48 h of rejection, before antirejection therapy was instituted (group 1A) and in four after unsuccessful antirejection therapy, 5-6 days after the rejection episode (group 1B).

The 11 control patients (group 2) who included four women (mean age of 16 ± 12.6 yr) had histologically proven idiopathic minimal change disease with normal renal function. They had not received steroids for 15 days prior to renal biopsy.

Renal allograft recipients and controls were comparable in age, free from infections and were non-smokers. The patients were not on any drugs which would modify free radical generation, other than immunosuppressants.

The renal tissue and plasma samples were stored at -70°C for approximately 2 wk till estimation. Tissue and plasma lipid peroxide were measured by thiobarbituric acid reactions47 and plasma vitamin E by HPLC4.
The statistical analysis was done using Mann Whitney U test.

**Results & Discussion**

Plasma lipid peroxide was significantly higher in patients with acute cellular rejection studied before antirejection therapy (group 1A; 13.2 ± 3.5 nmol/ml; P < 0.01) and among those after unsuccessful antirejection therapy (group 1B; 11.7 ± 0.7 nmol/ml; P < 0.01), compared to controls (group 2; 5.7 ± 2.8 nmol/ml). Renal tissue lipid peroxide and plasma vitamin E levels were not significantly different between patients with rejection and controls (Table). The tissue lipid peroxide levels in renal allograft recipients studied before starting antirejection therapy were significantly higher than those studied after failed antirejection therapy (5.1 ± 1.7 and 3.0 ± 0.8 nmol/mg protein; P < 0.05). The levels of plasma lipid peroxide or of vitamin E were not significantly different in the two transplant patient groups (Table).

Free radical injury is mediated through lipid peroxidation of cellular membranes. Therefore, evaluation of free radical injury was done, as in most studies, using lipid peroxide in the tissue and plasma. Patients with idiopathic minimal change disease were selected as controls since there was no evidence of significant tissue inflammation in this condition.

There was a significant rise of lipid peroxide in the plasma and not in the renal tissue of patients when compared with the controls. Lipid peroxide possibly diffuses into the plasma where high levels were detected. The tissue lipid peroxide levels were significantly higher in patients with acute cellular rejection evaluated prior to steroid therapy than in those with steroid resistant cellular rejections indicating that, in the latter, steroids attenuated free radical injury.

The levels of vitamin E were similar in both groups probably due to adequate tocopherol regeneration and sufficient dietary intake, compensating its consumption as an antioxidant during free radical injury. Thus the increased levels of tissue and plasma lipid peroxide in patients with renal allograft rejection suggest a possible free radical mediated injury. High doses of steroids appear to attenuate the free radical injury by increasing the antioxidant activity.

**Acknowledgment**

Authors thank Dr Jayaseelan, for statistical analysis.

**References**


---

**Table. Lipid peroxide (in tissue and plasma) and plasma vitamin E in patients and controls**

(Data are mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1A</td>
<td>Group 1B</td>
</tr>
<tr>
<td>(n=5)</td>
<td>(n=1)</td>
<td>(n=9)</td>
</tr>
<tr>
<td>Tissue lipid peroxide (nmol/mg protein)</td>
<td>5.1±1.7</td>
<td>3.0±0.5*</td>
</tr>
<tr>
<td>Plasma lipid peroxide (nmol/l)</td>
<td>13.2±3.5**</td>
<td>11.7±0.7**</td>
</tr>
<tr>
<td>Plasma vitamin E (mg/l)</td>
<td>6.7±2.8</td>
<td>4.5±1.9</td>
</tr>
</tbody>
</table>

*P < 0.05 as compared to group 1A
**P < 0.01 as compared to group 2


*Reprint requests*: Dr J.C.M. Shastry, Professor of Nephrology, Christian Medical College and Hospital, Vellore 632004