High incidence of bacteriuria following renal transplantation in children

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Abstract

Background. Bacteriuria is common post-transplant. However, most studies are in adults with a short follow-up. We have assessed the incidence of bacteriuria, predisposing causes and its effect on short and long-term graft function in children.

Methods. The notes of 142 children (67% male) who received 168 kidney transplants (138 cadaveric) between 1987 and 1994 were studied. The mean age at transplantation was 9.0 ± 4.5 years, and 32 children were transplanted pre-emptively. Diagnoses reflected those found in any children’s renal failure programme.

Results. Two hundred and thirty one episodes of bacteriuria were detected in 66 patients (46%): a rate of one episode per 23 patient months of follow-up. Fifty two percent were during the first year, and 29% of these during the first 4 weeks post-transplant. Forty two children (28%) had recurrences. The incidence was not affected by sex, vesico-ureteric reflux into native kidneys, donor source, circumcision in boys, dialysis pre-transplant or acute rejection. Bacteriuria was significantly more common in patients with a history of bacteriuria before transplant (P < 0.005) and with bladder pathology (P < 0.001). Organisms were predominantly coliforms (41%); 70% were Gram-negative. Sixty percent were resistant to the prescribed antibiotic prophylaxis. There was an associated transient rise in plasma creatinine concentration: mean pre-episode 111 ± 86 μmol/l vs mean post-episode 134 ± 108 μmol/l (P < 0.0001). Seventy two percent of episodes were asymptomatic, but even in this group 81% had an associated rise in plasma creatinine (P < 0.001). Despite this, there was no significant decrease in glomerular filtration rate in patients with bacteriuria compared with patients without at the end of follow-up: 50 vs 56 ml/min/1.73 m² respectively.

Conclusion. Bacteriuria is common post-transplant, occurring most often in those with bladder pathology or with a history of bacteriuria pre-transplant.

Key words: bacteriuria; children; post-transplant

Introduction

Urinary tract infection (UTI) is common following renal transplantation, and is a major cause of Gram-negative bacteremia [1,2]. The incidence has been reported to vary between 20 and 88% [3,4]. One reason for this wide variation is the difficulty in distinguishing between asymptomatic bacteriuria and symptomatic infection in immunosuppressed patients who may be symptomatic for many reasons. UTI is diagnosed most frequently in the first month after transplantation [3]. Factors that have been found to contribute to the incidence and severity of UTI include: routine immunosuppressive therapy and treatment for rejection episodes; urological abnormalities of the native kidneys; or surgical complications after transplantation [3–6].

Bacteria are reported to be similar to those causing UTI in the general population, Escherichia coli; Pseudomonas aeroginosa and Enterococci; Enterobacter cloacae, Streptococcus faecalis and Proteus being the most common [3,7,8].

The majority of studies have been in an adult transplant recipients with a short period of follow-up [3,8,9]. Only a small number are in children [6,10–13]. We have studied retrospectively the incidence and factors predisposing to bacteriuria complicating the post-transplant period, its associated symptoms and its effect on short- and long-term allograft function.

Subjects and methods

Between January 1987 and December 1994, 152 children received 179 allografts. In five patients, the graft failed within 12 days; three patients died within 3 months post-transplant of causes unrelated to UTI; and two patients were transferred to another centre. This left 142 patients, 47 (33% girls), who received 168 grafts, for review. The mean age (years) at transplantation was 9.0 ± 4.5 (median 9.5, range 1.3–17.7) and 36 patients were aged < 5 years. The mean (range) period of follow-up was 37.7 months (0.9–95). Thirty two (23%) patients were transplanted pre-emptively, 103 (72%) were peritoneally dialysed and seven (5%) haemodialysed prior to transplantation. Thirty six (25%) had renal dysplasia, of whom 16 (44%) had no vesico-ureteric reflux (VUR) or obstruction. Twenty one (15%) had a posterior urethral valve (PUV), 15 (71%) with VUR. Six percent had obstruction.
due to other causes. Twenty four (17%) had primary bladder pathology, i.e. neuropathic bladder and prune belly syndrome, 10 (7%) reflux nephropathy and three (2%) hyperoxaluria. Seventy two (51%) had glomerular and miscellaneous diseases that are not known to predispose to UTI.

At the time of transplant, 20 (14%) were anephric and 16 (11%) had a single kidney. Thirty five (25%) had VUR (bilateral in four). Eight (6%) had augmented bladders (two colocystoplasties, two gastrocystoplasties, one ileocystoplasty and three ureterocystoplasties), and six of these had a continent stoma (Mitrofanoff). Eleven (8%) used clean intermittent catheterization. Only 64 (45%) had structurally normal renal tracts. Nineteen (14%) of the boys were circumcised. Three patients with oxalosis received combined liver and kidney transplants and two girls had a splenectomy, one cised. Three patients with oxalosis received combined liver normal renal tracts. Nineteen (14%) of the boys were circum-

Antimicrobials were used in patients receiving their second transplant. Acute rejection episodes were treated for 3 days with methyl prednisolone 600 mg/m2 within 6 weeks post-transplant, and oral prednisolone 3 mg/kg thereafter. ATG (2 mg/kg for 10 days i.v.) was used for steroid-resistant rejection.

Cadaveric transplant recipients received antibiotic prophylaxis using a cephalosporin or ciprofloxacin in standard paediatric doses from the time of pre-medication until a negative culture was obtained from the transplant transport fluid. Prior to a change in protocol, 53 (37%) received prophylaxis for *Pneumocystis carinii* pneumonia with septrin (2 mg/kg as trimethoprim component) for 6 months post-

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Results

Of 142 patients, 66 (46%) had between one and 18 episodes of bacteriuria. A total of 231 episodes were documented: a rate of one episode per 23 patient per months. The prevalence of infection according to primary renal disease and effect of structural abnormality of the urinary tract is shown in Table 1. Bladder pathology was the most important predisposing factor (*P*<0.001), followed by history of bacteriuria before transplantation (*P*<0.005). Among children with bladder pathology, patients with bladder augmentation, especially those with gastrocystoplasty and colorectomy, had the highest rate of UTI: 20% of UTIs in these patients were asymptomatic, and two patients had acquired areas of defective uptake of 99mtechnetium dimercaptosuccinic acid in the transplanted kidney.

Of the 66 patients with bacteriuria, 24 (36%) patients had one; 31 (47%) had 2–5; eight (12%) had 6–10; and three patients had 10–18 infections. Recurrence therefore occurred in 42 (64%) of patients; 10 (24%) of recurrences were relapses, 13 (31%) were re-

Bacteriuria occurred in 57% of girls and 41% of boys, but 60% of the total number of episodes were in males. These differences were not significant. Fifty two percent were in the first year, and of these 29% in the first month post-transplant. Sixty five (28%) were symptomatic: 40 (17%) patients had fever; 13 (6%) dysuria and frequency; five (2%) graft tenderness; 10 (4%) were unwell; and five (2%) had abdominal pain and/or vomiting. One patient had multiple abscesses in the transplant which resolved with antibiotic therapy. In three children, pylonephritis was diagnosed unexpectedly at diagnostic transplant biopsy (two with negative urine culture). Thirty five patients (15% of episodes) required re-hospitalization and i.v. antibiotics, at least at the beginning of treatment.

There was no correlation between the incidence of bacteriuria and circumcision, the use of prophylactic antibiotics, the number of acute rejection episodes and associated treatment, and the use of ATG. There was no difference between cadaveric and living related transplants or pre-emptive transplant and prior dialysis, and no effect from positive transport media culture, previous reconstructive surgery, urologic complications and re-exploration after transplantation. The commonest organism was *E. coli*. Forty eight
percent of bacteria were resistant to ampicillin and only 13% to nitrofurantoin. One hundred and sixty four episodes of bacteriuria occurred during antibiotic prophylaxis. Cephradin or cephalexin were the most used prophylaxis [83 (51%) of the total]. Forty seven (60%) of 78 available results showed organisms that were resistant to prophylaxis. The antibiotics most commonly used for treatment of infection were cephalexin or cephradine, followed by ampicillin and nitrofurantoin.

Mean plasma creatinine (μmol/l) before the episode was 111 ± 86 (range 4–542) and after was 134 ± 108 (range 4–715), P < 0.0001. In asymptomatic patients, creatinine after the episode was higher than before in 81% (P < 0.001). At the end of follow-up, the mean plasma creatinine in patients with and without bacteriuria was 118 ± 58 and 107 ± 50, and mean GFR 50 ± 20 and 56 ± 20 ml/min/1.73 m² respectively (NS).

Discussion

This study confirms previous reports describing a high frequency of bacteriuria post-transplant, the increased incidence in the first month post-surgery and the lack of difference between males and females and between cadaveric and live related donors [1,3,6,15]. Although many children were asymptomatic, there was an associated increase in serum creatinine, suggesting that parenchymal involvement of the transplant may occur even without symptoms, and that such episodes should be treated.

The highest rates of bacteriuria occurred in those with bladder pathology as indicated by abnormal urodynamics and significant residual urine in the bladder post-micturition. Bladder augmentation was the most significant predisposing factor for bacteriuria (P < 0.0001), resulting in scarring of the transplant in 25% of these children. However, unlike most previous studies, we were unable to find a significant difference in the incidence of bacteriuria in patients with and without VUR into native systems. A comparison of 11 patients transplanted following successful surgical correction of VUR in their native systems and 28 transplanted with continuing VUR demonstrated an increased incidence of UTI in those with VUR (42.8 vs 18%), and particularly in those with high-grade (3 and 4) VUR. The authors recommend that high-grade VUR in native kidneys must be operated on before transplantation, even when there is no history of UTI [16]. One explanation for the different findings are that our children with reflux had less severe bladder pathology.

We found, as have others, an increased incidence of bacteriuria in PUV patients, and also a particularly high infection rate (one episode per 11 patients month of follow-up). One boy had 18 episodes of relapse and re-infection. A review of 14 boys with PUV who underwent kidney transplantation [13] found the incidence of UTI to be significantly greater in the PUV group than in the controls: 15 UTIs occurred in five children (36%) with PUV (one per 30 patients-months follow-up) whereas only one of 26 controls (4%) without VUR had UTI (one per 1144 patient-months). The authors suggested the use of antimicrobial prophylaxis in all boys with PUV, at least during the initial months after renal transplantation [6].

Several authors have recommended antibiotic prophylaxis post-transplant [12,17], although others have found it to be of no value, either perioperatively or long-term [18]. Our study confirmed the lack of benefit of prophylaxis, and demonstrated a very high rate of bacterial resistance. The least bacterial resistance occurred with nitrofurantoin. Similar results have been reported by others [19].

Some studies have reported a high incidence of pyelonephritis in patients with VUR into the transplanted kidney, even resulting in graft loss. We have not analysed the incidence of VUR into the transplant in our patients because it is our practice to perform ureteroneocystostomies with an anti-reflux procedure, and micturating cysto-urethrogrammes were not performed routinely. However, serious complications such as graft loss due to infection were not experienced in our patients.

There are increasing data suggesting that circumcision-

Table 1. Effect of structural abnormality of the urinary tract on the incidence and frequency of bacteriuria

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of patients</th>
<th>% of patients with bacteriuria</th>
<th>Rate of bacteriuria episodes/patient month</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No predisposing urological abnormality identified</td>
<td>72</td>
<td>36</td>
<td>1:37</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>PUV</td>
<td>21</td>
<td>57</td>
<td>1:18</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>VUR</td>
<td>35</td>
<td>49</td>
<td>1:15</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>History of bacteriuria before Tx</td>
<td>42</td>
<td>67</td>
<td>1:14</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>PUV + VUR</td>
<td>15</td>
<td>60</td>
<td>1:11</td>
<td>&gt;0.05*</td>
</tr>
<tr>
<td>Significant post-micturition residual volume and/or abnormal urodynamics</td>
<td>17</td>
<td>77</td>
<td>1:8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Bladder augmentation</td>
<td>8</td>
<td>100</td>
<td>1:4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Overall rate</td>
<td>142</td>
<td>46</td>
<td>1:23</td>
<td></td>
</tr>
</tbody>
</table>

*Based on multiple regression analysis and χ².

*P < 0.05 for rate of episodes of bacteriuria.
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Nitrofurantoin had the best sensitivity results for prophylaxis.

References


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