Renal biopsies in children: current practice and audit of outcomes

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Abstract

Background. There is considerable variation in the way that children are prepared for and the techniques employed in a renal biopsy. There was national agreement between UK paediatric renal centres to review current practice and audit outcomes

Methods. An initial questionnaire survey was undertaken and a 12-month prospective audit performed of renal biopsies against agreed standards for the number of needle passes, adequacy of biopsy material and complication rates.

Results. Eleven of 13 centres participated. Information leaflets are sent pre-biopsy in five centres with only one using play preparation. Six of 11 routinely perform biopsies as day-case (DC) procedures and 6 use general anaesthesia (GA). Real-time ultrasound is the favoured method in eight centres. Biopsies are performed by nephrologists only in four centres, nephrologists with radiologists in five and radiology alone in two. Of 531 biopsies (352 native), 31% were performed as a DC with 49% being done under GA.

The standard for the number of passes of native kidneys (≤3 in 80%) was achieved in 86.4%, but the standard of ≤2 passes in 80% was achieved in only 73.4% of transplanted kidneys. Adequate tissue was obtained for diagnosis in 97.5% (standard >95%). The major complication rate was higher than the standard of ≤5% at 10.4%. There was no significant difference in complication rates when the biopsy was performed as a DC or inpatient procedure (P = 0.73) or when GA or sedation was used (P = 0.8).

Conclusions. The audit highlights significant variation in clinical practice with limited use of preparation materials and DC procedures. The results have stimulated constructive debate about preparation and indications for biopsy and training issues. The audit enables centres and individuals to monitor their own performance.

Keywords: audit; day-case procedures; renal biopsy; standards

Introduction

A renal biopsy is more difficult in children than in adults due to size variation and different levels of cooperation. Variation also exists in the techniques employed and indications for a renal biopsy between paediatric renal units.

There are a number of reports about percutaneous renal biopsies being performed as day-case procedures [1–4]. There is also discussion as to whether the biopsy should be performed by a nephrologist and/or interventional radiologist. No nationally or internationally agreed standards of practice and complication rates for renal biopsies in children exist. Such standards would allow outcomes between centres to be compared and permit individual operators to monitor their own performance.

The British Association of Paediatric Nephrology agreed to undertake a comprehensive survey and prospective audit of all renal biopsies performed over a 1-year period with outcomes compared to one unit’s published standards [1].

Methods

A preliminary questionnaire was sent to all 13 UK paediatric nephrology centres. Details were sought regarding organization of biopsies within each centre including use of information and play preparation, duration of admission, use of sedation or general anaesthesia (GA). The routine use of intravenous fluids, type of biopsy needle used, biopsy technique and specialty and grade of operator were also recorded.

Audit forms were also sent to each centre to complete prospectively for every biopsy undertaken between 1 January and 31 December 2005. The forms detailed age and weight of the patient, indication for biopsy, type of sedation used, operator, number of needle passes and the details of any complications and diagnosis. Ultrasound of the kidney post-procedure was not routine. All the audit forms were analysed by the principal authors. The standards applied are shown in Table 1.

Statistics

All data were entered onto a database and analysed using SPSS (Statistical Package for the Social Sciences). Categorical data were analysed with the chi-square test using a significance level of P < 0.05.
Table 1. Standards for renal biopsies [1]

- Number of needle passes to obtain an adequate biopsy material in native kidneys that should be ≤ 3 in 80% of patients
- Number of needle passes to obtain an adequate biopsy material in transplant kidneys that should be ≤ 2 in 80% of patients
- Adequate tissue for histological diagnosis (on review with histopathologists) should be obtained in > 95% of biopsies
- Major complication rates (defined as macroscopic haematuria, requirement for blood transfusion and/or surgical exploration, delay in discharge or readmission for observation) should be < 5% of total biopsies

Results

Eleven of 13 UK centres participated in the survey and audit. Five of 11 centres give families an information sheet or provide them with a booklet about a renal biopsy and only one centre specifically provides play preparation. In six centres, the child is allowed home the same day although three of these do admit the child the night before, if they live a long distance from the centre. The other centres perform the biopsy as an inpatient procedure with two centres routinely admitting the night before, one centre detaining them until the night after and two centres admitting both before and after.

Six centres routinely use GA for biopsies, whereas five centres use intravenous sedation and occasionally nitrous oxide (entonox) by mouthpiece. Two centres vary between sedation and GA. Drugs used for sedation include midazolam, pethidine, alimemazine tartrate (Vallergan), fentanyl, diazemuls, entonox and local anaesthesia.

Intravenous hydration is used in 4 of 11 centres, with 1 using pre-hydration alone, 1 using post-hydration alone and 2 centres using both.

The biopsies are performed under real-time ultrasound in 8 of 11 centres with 2 centres using ultrasound localization to pre-mark the site. In addition, one centre uses ultrasound and also fluoroscopy.

In 2 of 11 centres, the biopsies are performed exclusively by the radiologist, in 4 centres exclusively by a nephrologist and in 5 centres a combination of both nephrologist and radiologist.

Five of 11 centres use a biopsy gun with a 16- to 18-gauge needle and 2 use automated Cook® spring-loaded needles. The four other centres employ other needle types.

Prospective audit

A total of 531 forms were returned from 11 centres. These represented 352 native biopsies and 179 transplant biopsies. The variation in biopsy numbers between the 11 centres is shown in Figure 1.

The median age of patients was 11.8 years (range 0.08 – 18.9 years) with a median weight of 39.3 kg (range 3.4– 125 kg).

A total of 69% (369) of the biopsies were performed by nephrologists [155 (29%) by radiologists and in 7 (2%) it was unclear]. Senior medical staff performed 288 (54%) procedures and trainee staff 206 (39%) (missing data 21, others not specified 16).

Audit against agreed standards

Number of passes. Three units did not achieve the standard of obtaining apparently sufficient kidney tissue from

Fig. 1. Biopsy numbers by centre.
Table 3. Final diagnosis in 346 native kidney biopsies

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Henoch Schönlein purpura nephritis</td>
<td>55</td>
<td>15.9</td>
</tr>
<tr>
<td>Minimal change nephrotic syndrome</td>
<td>44</td>
<td>12.7</td>
</tr>
<tr>
<td>Focal and segmental glomerulosclerosis</td>
<td>32</td>
<td>9.2</td>
</tr>
<tr>
<td>Normal</td>
<td>32</td>
<td>9.2</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>31</td>
<td>9.0</td>
</tr>
<tr>
<td>SLE nephritis</td>
<td>30</td>
<td>8.7</td>
</tr>
<tr>
<td>Membranoproliferative glomerulonephritis</td>
<td>20</td>
<td>5.8</td>
</tr>
<tr>
<td>Acute post infectious glomerulonephritis</td>
<td>10</td>
<td>2.9</td>
</tr>
<tr>
<td>Thin basement membrane disease</td>
<td>9</td>
<td>2.6</td>
</tr>
<tr>
<td>Alport disease</td>
<td>8</td>
<td>2.3</td>
</tr>
<tr>
<td>Vasculitis (other)</td>
<td>8</td>
<td>2.3</td>
</tr>
<tr>
<td>Acute interstitial nephritis</td>
<td>6</td>
<td>1.7</td>
</tr>
<tr>
<td>Acute tubular necrosis</td>
<td>6</td>
<td>1.7</td>
</tr>
<tr>
<td>Chronic tubulo-interstitial nephritis</td>
<td>5</td>
<td>1.4</td>
</tr>
<tr>
<td>Chronic kidney disease (aetiology uncertain)</td>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>Congenital nephrotic syndrome</td>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>Membranous nephropathy</td>
<td>4</td>
<td>1.2</td>
</tr>
<tr>
<td>Crescentic glomerulonephritis</td>
<td>3</td>
<td>0.9</td>
</tr>
<tr>
<td>Drug-induced nephrotoxicity</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>Anti-glomerular basement disease</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>Other</td>
<td>32</td>
<td>9.2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>346</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

*Data available for 346 of 352 native biopsies.

Complications. A total of 55 patients (10.4%) suffered major complications as defined in Table 1. The complication rate varied from 0 to 30% between centres, with only 3 of the 11 centres reaching the specified standard of <5% (Table 4). The rate was 6.7% in 4 centres in which over 50 biopsies were performed.

Of 55 patients with complications, 39 had macroscopic haematuria with 4 requiring a blood transfusion. The latter four patients had acute renal failure due to systemic lupus erythematosus, chronic tubulo-interstitial nephritis, Henoch–Schönlein purpura nephritis and atypical haemolytic uraemic syndrome. One of the four patients requiring transfusion, a 10-year-old child who had a biopsy under GA with four needle passes, developed hypotension and required blood transfusion and coil embolization for an AV fistula. Another, a 5-year-old boy with atypical HUS developed pulmonary oedema after transfusion. There were no fatalities or loss of kidneys, and so severe complications could be summarized as surgical intervention (1), transfusion requirement (4) and severe anaesthetic complication (3).

Nine children were readmitted; five had macroscopic haematuria and four had other indications. In those children who had macroscopic haematuria, 6/175 (3.4%) of day-case biopsies were readmitted or had a delayed discharge versus 7/231 (3%) of elective in-patient biopsies.
There was no significant difference in complication rates between biopsies performed by a trainee or non-trainee ($P = 0.60$). There was also no significant difference between nephrologists and radiologists ($P = 0.74$). There was no difference in complication rate whether the biopsy was performed as a day-case or in-patient procedure ($P = 0.73$), or whether GA or sedation was used ($P = 0.8$).

**Discussion**

The survey of paediatric renal biopsies in the UK confirmed the large variation in the biopsy procedure probably reflecting the lack of an evidence base. Some of the variability may be dictated by local constraints such as physical space and the availability of supporting staff, including radiologists and anaesthetists.

Providing information to children and families in preparation for potentially invasive procedures is an accepted practice in paediatrics [5–7]. However, only half of the centres stated that they provide information beforehand and very few use play preparation prior to the procedure. This study confirms that performing biopsies as a day-case procedure as opposed to inpatient admission is not associated with an increased complication rate. Others have previously emphasized that undertaking biopsies on a day-case basis has great savings for family time and considerable cost savings for the hospital [1,8].

One-third of the centres use a hydration regime and yet the majority of sedated patients are awake and drinking shortly after the procedure. The majority of centres perform the biopsy under GA, which raises logistical issues. In the past, concerns about the use of sedation in treatment rooms on the ward may have arisen. However, with the majority of junior doctors now trained in paediatric life-support skills, many feel that sedation is feasible and the biopsy easier to organize. This may be important in clinically urgent cases. Some centres now offer entonox for cooperative older patients [9]. Some patients had no sedation and the biopsy is performed with ‘verbal sedation’ from a play therapist and local anaesthetic injection using warm lignocaine.

The question of who performs the renal biopsy is very relevant to the training of paediatric nephrologists. A renal biopsy is regarded as one of the essential skills to be acquired by paediatric nephrology trainees. Those who move from a large tertiary centre to a smaller unit for consultant posts may find no interventional radiologists available and difficulties may then arise. There were no differences in complication rates between radiologists and nephrologists. However, it is interesting to note that the unit that was substantially below the standard for achieving adequate biopsy material in native kidneys on three or less needle passes was the unit where the majority of biopsies were performed by a paediatric radiologist. This unit has subsequently changed its practice with fewer cores being taken at each biopsy.

The standard for transplant renal biopsies of ≤2 passes in 80% of cases is a standard that should be revised in view of the Banff 97 criteria [10]. This states that a minimum sample should consist of a cortex with at least 7 glomeruli and one artery, optimally 10 glomeruli and two arteries, in either two separate cores or two separate areas of the cortex from the same core. Benfield et al. demonstrated that when more than one core was obtained and the core length was ≥20 mm, this led to increased specimen adequacy and an increased rate of rejection being diagnosed. Adequacy of the specimen did not vary with other factors [11]. One unit (4) contributed considerably to the number of transplant biopsies and regularly obtained two cores of tissue for transplant kidneys because of the above-mentioned requirement. This led to the standard for transplant kidneys not being achieved in this unit, but there was no increase in complication rates.

The most common indication for the native kidney biopsy in this current large series was proteinuria independent of nephrotic syndrome. Comparisons with other registry data is difficult because many combine adult and paediatric data [12–16]. Proteinuria was the most common indication in this series (36%), comparable to that reported from a large Italian series [17]. Most of the UK units stated a level of sustained proteinuria >40 mg/mmol of creatinine on early morning urine samples as being an indication, with orthostatic proteinuria being excluded. No centres tested specifically for tubular proteinuria. In our series, isolated haematuria was the indication in 9.8% of patients compared to 19.3% quoted in the Italian series [17]. The audit did precipitate discussion about indications for a biopsy in patients with isolated haematuria, and there was much less consensus. Those performing biopsies stated that the isolated haematuria had to be persistent for 1–2 years and the renal lesion not characterized in other family members.

The number of complications reported in children following renal biopsy varied between 0 and 30% for major complications [4,18,19]. This variation may be explained by differences in reporting and definition of complications. Some units in our study also reported small numbers of biopsies and this could have introduced further reporting bias. However, severe complications (death, kidney operation, blood transfusion and severe hypoxia) were very low (1.5%) and the percent of major complications, as defined in this audit, was 6.7 in the four centres in which over 50 biopsies were performed per year. We did not record the timing of complications in this audit. Whittier et al. documented that 42% of complications occur in ≤4 h, 69% in 8 h, 85% in 12 h and 89% in ≤24 h [20]. They suggested that if patients were discharged within 8 h, 32% of complications would be missed. However, in this audit only nine patients (1.7%) were readmitted suggesting once again that day-case procedures are not associated with increased readmission rates.

It is noticeable that although the native kidney biopsies were considered adequate by the histopathologist on light microscopy in 97% of cases, immunofluorescence was only adequate in 80.5% and electron microscopy in 68.9%. Ideally, for consistency all the biopsies should have been reviewed by one histopathologist applying the same criteria although practically this was not feasible.

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Conclusions

Comparisons between units in this audit of a large number of biopsies provide some evidence for units to consider changes in practice that could be instituted without compromising patient safety or biopsy adequacy. Specific areas include preparation of children and day-case procedures with sedation or local anaesthetic.

The application of standards has allowed each unit to monitor their own performance in comparison with other centres and will also allow individuals to assess their own competencies with regard to biopsies. This may be important for revalidation in the future. It is intended to re-evaluate some of the aspects of this process at a future date to see if publication of this audit and standards has influenced practice.

Conflict of interest statement. None declared.

Appendix

Catherine O’Brien—Birmingham Children’s Hospital
Ezzat Afifi—Bristol Royal Hospital for Children
Judith Van Der Voort—Children’s Kidney Centre, University Hospital of Wales, Cardiff
Stephen Marks—Great Ormond Street Hospital, London
Heather Maxwell—Royal Hospital for Sick Children, Glasgow
Chris Reid—Evelina Children’s Hospital, London
Eric Finlay—St James’s University Hospital, Leeds
Caroline Jones—Royal Liverpool Children’s Hospital, Liverpool
Nick Webb—Royal Manchester Children’s Hospital
Milos Ognjanovic—The Royal Victoria Infirmary, Newcastle
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References


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