Intrarenal Reflux: A Retrospective and Comparative Study

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Background/Purpose: Intrarenal reflux (IRR) has been considered a classic indication for surgical intervention in cases with vesicoureteric reflux (VUR). During 1990s, the natural history of VUR and its spontaneous disappearance especially during the first years of life became clearer, leading to the concept of conservative treatment even for the moderate and high grades. This retrospective study aimed at finding if there is an increased incidence of pyelonephritis in spite of proper antibiotic prophylactic treatment of IRR and whether the presence of IRR carries a higher risk in patients with VUR, which dictates earlier surgical intervention.

Materials and Methods: One hundred and eighty five patients less than 5 years old with VUR were operated upon between 1989 and 2000 at the Children's Hospital of Trousseau in Paris. Thirteen (7%) patients (9 females and 4 males) with IRR were diagnosed (Group A). These children were compared with 13 other children with the same age, sex, and grade of reflux but without IRR (control group B) to find out the impact of IRR on the pattern of presentation and prognosis.

Results: The indication of surgical intervention was pyelonephritis under medical treatment (1: 3 episodes) in all patients in Group A except 4 (70%); while for Group B patients, this indication of surgical intervention was present in 6 infants (1: 2 episodes) (46%). The frequency of pre-operative renal scarring (1-3 scars) was higher in group A than in group B (4 cases, 31%, versus 3 cases, 23%).

Conclusion: The results were in favour of higher incidence of pyelonephritis at presentation and in patients under medical treatment. Renal scarring in the pre-operative period was more frequent in patients with IRR. A prospective multicentric study with greater number of patients suffering of IRR is needed, and prolonged surveillance with systematic radio99mTc-DMSA renoscintigraphy scan is highly recommended.

Index Word: Intrarenal reflux, vesicoureteric reflux, renal scarring, pyelonephritis

INTRODUCTION

Radiologically, IRR is the visualization of the contrast material within the renal tubules. It occurs in 5 to 15% all of cases of VUR. Kohler 1 defined 4 types; the most important of them is the pyelotubular type as it can occur without elevation of pressure in pathologic kidneys.

Nowadays, retrograde cystography is not considered as a reliable examination for the detection of IRR (33% sensitivity). The isotopic cystography is...
more reliable because it detects symptomatic intermittent reflux not diagnosed by ordinary cystography. It has the advantage of lower irradiation received than that of classic cystography with better sensitivity in the diagnosis and follow-up.2,3

In Europe, IRR was considered a clear indication for surgical treatment from the start. Nowadays, due to the available detailed studies of the natural history of reflux and the proven incidence of spontaneous disappearance of reflux even that of high grade (40% of cases with prenatal diagnosis in the series of Young2); the tendency is growing towards the conservative management.

PATIENTS AND METHODS

During the period of 1989-2000, 185 patients with ages <5 years presenting with primary VUR were reviewed at the Children Hospital in Trousseau, Paris. An IRR was found in 13 children (9 females and 4 males) with an incidence of 7%.

Our study included 26 children with primary VUR of age and sex matched. The children were classified into 2 groups: Group A (n=13) had IRR (unilateral or bilateral) and Group B (n=13) had the same grade of VUR but without IRR (control group).

Criteria of Inclusion:

All children were younger than 5 years of age with primary VUR (grades III, IV, and V) with or without antenatal diagnosis.

Pre-operative Investigations:

All patients were subjected to urine analysis, culture and sensitivity, serum urea and creatinine assessment. Imaging studies included voiding cystography (VCUG), renal ultrasound, intra-venous urography (IVU). The 99mTc-DMSA renoscintigraphy scan was done sporadically and not systematic.

Treatment:

Conservative medical treatment was tried in all patients. Suppressive doses of cephalosporin, amoxacillin clavulunate (age <3m), and setprin nitrofurantoin (age >3m). Two children in Group A (13%) were operated upon from the start due to severe pyelonephritis. Bilateral uretro-neocystostomy without tailoring using Cohen's technique was used for correction of the VUR.

Follow-up:

Group A patients were followed up for a median of 12 months (range: 3 months-3 years), and Group B patients for a median of 3 years (range: 3 months - 10 years). Urine analysis, culture and sensitivity, serum urea and creatinine assessment were done for all patients. Radiological investigations in the form of renal ultrasound were done every 3 months for 1 year, then every 6 months for another year, then once yearly thereafter. VCUG was done once at 3 months while IVU ± 99mTc-DMSA renoscintigraphy were done once at 6 months post-operatively.

Table 1. Characteristics of IRR

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of refluxing units</td>
<td>20</td>
<td>24</td>
</tr>
<tr>
<td>Side</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Unilateral</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>• Bilateral</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Grade of reflux</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>III</td>
<td>9*</td>
<td>9</td>
</tr>
<tr>
<td>IV</td>
<td>8**</td>
<td>5</td>
</tr>
<tr>
<td>V</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

*7 had RIR  **6 had RIR

RESULTS

The median age at presentation was 6.6 (2 - 20) months for Group A, and 10 (1-24) months for Group B. With a mean follow up period of 8.2 months for Group A (2-20 months), and 9.3 months for Group B (3-30 months). Eleven cases in Group A (85%) and 7 cases in Group B (54%) had acute pyelonephritis in spite of prophylactic medical treatment.

Table 2. Patients’ data

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative scarring.</td>
<td>4 (31%)</td>
<td>3 (23%)</td>
</tr>
<tr>
<td>Pyelonephritis under</td>
<td></td>
<td></td>
</tr>
<tr>
<td>medical treatment.</td>
<td>11(85%)</td>
<td>7 (54%)</td>
</tr>
<tr>
<td>Pyelonephritis as an</td>
<td></td>
<td></td>
</tr>
<tr>
<td>operative indication.</td>
<td>9 (70%)</td>
<td>6 (46%)</td>
</tr>
</tbody>
</table>
The indication of surgical intervention was pyelonephritis under medical treatment (1: 3 episodes) in all patients in Group A except 4 (70%), 2 of them (15%) operated upon for persistence of VUR with IRR at 1 year of age and the other 2 (15%) had severe pyelonephritis on presentation so they were operated upon from the start. The indications for surgical intervention in Group B were pyelonephritis in spite of medical treatment (1: 2 episodes) in 6 infants (46%), persistence of VUR after the age of 2 years in 5 (38%) patients, and the presence of high grade or bilateral VUR after the age of 2 years in the remaining 2 (15%) cases. The median age of surgical intervention was 15 (5 – 30) months in Group A, and 16 (6-32) months in Group B.

None of our patients had impairment of renal function (estimated by serum creatinine before or after the intervention).

IVU was used to detect pre-operative renal scarring in all patients. However 99mTc-DMSA renoscintigraphy scanning of the kidneys was done only in 11 cases (not systematic). In Group A, 4 cases (31%) had pre-operative renal scarring (1-3 scars), and the scars were corresponding to IRR, while in Group B, 3 cases (23%) had pre-operative renal scarring (1-3 scars) and the scars were unilateral on the left side.

IVU was used to detect post-operative renal scarring also in all patients, while 99mTc-DMSA renoscintigraphy scanning of the kidneys was done in 5 infants only in Group A, and in 6 infants in Group B. Deterioration (increase in number of scars) was found in 2 cases (15%) in Group A and in 3 cases (23%) in Group B. After surgical intervention, acute pyelonephritis occurred in 2 cases (15%) in Group A (1 episode in one case and 2 episodes in the other case), while in Group B, only 1 case (7.6%) had 1 episode of acute pyelonephritis.

**DISCUSSION**

In the sixties, Hodson and Edwards discussed the "Dark Age of VUR" and now we can ask ourselves if it is real that we are out of this "Dark Age"?

During the eighties, the presence of IRR was considered as a strong indication for surgical treatment from the start especially in Europe. Actually by the nineties, the natural history of VUR and its spontaneous disappearance became clearer especially during the first years of life and this led to adoption of the concept of conservative treatment even for the moderate and high grades of reflux.

Up till now, the controversy continues regarding the importance of IRR and the proper management for this condition, besides, the studies in the literature concerning this subject are very poor. No study in the literature defines the incidence of renal scarring in case of the presence of IRR and whether the medical or the surgical treatment has an impact on its occurrence. In fact the subject of IRR is poorly studied in the literature and needs more attention and more studies to delineate its natural history.

This retrospective study aimed at clarifying the importance of IRR as a pathology that may be associated with VUR and tried to answer the following question: Is the presence of IRR considered as an indication for early surgical intervention for VUR?

Concerning the incidence of renal scarring in the presence of IRR, our study showed that it was more frequent and correlated to the site of IRR. But the results is not that definite as the 99mTc-DMSA renoscintigraphy scanning of the kidneys was not done systematically in all patients pre-operatively, and due to the small number of patients which makes the statistical significance study invaluable.

In the study by Gorrotxategi and his colleagues in 1993 on 59 cases with IRR the incidence of renal scarring was more frequent and correlated to the site of IRR. But again, 99mTc-DMSA renoscintigraphy scanning of the kidneys was not done systematically in all patients pre-operatively (also it was a retrospective study).

In another retrospective study by Gotoh and his colleagues in 1991, they reviewed 7 cases of IRR, in which VUR was primary in one child and secondary in 6 (anterior urethral ring 2, posterior urethral valve 2, neurogenic bladder 2). They assessed renal scarring by IVP and/or 99mTc-DMSA renoscintigraphy and found that IRR was localized to the upper area in 3, to the lower area in 2, and to the whole kidney in 3. Sixty percent of those with IRR in the polar areas were associated with moderate VUR, whereas all of those...
in the whole kidney were with massive VUR. In our study, 4 cases of Group A (31%) had pre-operative renal scarring (1-3 scars) that were corresponding to IRR, while 3 cases (23%) of Group B had pre-operative renal scarring (1-3 scars) and the scars were unilateral and on the left side. Gotoh and his colleagues, noted that IRR did not necessarily accompany renal scars of the corresponding areas and IRR to the whole kidney did not always lead to multiple scars in the whole kidney.

In the study done by Hannerz and his colleagues in 1987 on 37 children with one or more scars in one or both kidneys, they studied the distribution of renal scars in children with VUR and the past history of urinary tract. They found that scarring was significantly more frequent in the polar areas than in the lateral area. In 7 children with IRR, the distribution of IRR was almost identical with that of renal scarring. When children with marked VUR (grade IV-V) were analyzed separately, a uniform distribution of scars was found. They concluded that fused papillae, which normally are most frequent in the polar area, are a prerequisite for the development of IRR/renal scars.

Regarding the risk of the occurrence of acute pyelonephritis in spite of a correct prophylactic medical treatment and follow up, our study showed that it was higher in the group of patients with IRR. Pyelonephritis was more frequent also in this group as the main presentation and the main indication for surgical intervention.

Arant in 1991 stated that renal injury associated with IRR of urine that is either infected, under high pressure, or both, is a major cause of severe hypertension during childhood and adolescence and of chronic renal insufficiency in patients less than 30 years of age, however, our study can not prove/disprove this role due to the limited number of patients and short follow up period.

CONCLUSION
Up till now, the controversy continues about the importance of IRR and the proper management for this condition. No study in the literature defines the incidence of renal scarring in the presence of IRR and whether the medical or the surgical treatment has an impact on its occurrence.

Our results revealed higher incidence of pyelonephritis as a presentation of surgical in cases of VUR associated by IRR. Renal scarring pre-operatively was more frequent in the presence of IRR.

However, due to the limited number of cases and the short follow-up period and the retrospective nature of the study, prospective multicentric study with larger number of patients, systematic evaluation with 99mTc-DMSA renoscintigraphy scan, and prolonged surveillance of cases of IRR is highly recommended.

REFERENCES