Preliminary data on endoscopic treatment of vesicoureteric reflux with polyacrylate polyalcohol copolymer (Vantris®): Surgical outcome following single injection

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Abstract Purpose: The aim of this study was to evaluate the efficacy of single injection of a new non-biodegradable agent (Vantris®) Manufactured by Promedon, Cordoba, Argentina for treatment of vesicoureteric reflux (VUR).

Patients and methods: 38 children (11 males and 27 females) with a mean age of 5.3 ± 3.8 years underwent endoscopic treatment of VUR using Vantris. VUR was unilateral in 17 and bilateral in 21 patients, comprising 59 renal refluxing units (RRU). The VUR was primary in 42 RRU and 17 comprised complex cases: 3 duplex systems, 1 with prune belly syndrome, and 13 after failed previous endoscopic correction with Deflux®. VUR was Grade I in 5, II in 11, III in 23, IV in 15 and V in 5 RRU.

Results: All patients completed 3 months of follow up. The reflux was corrected in 56 (94.9%) of the 59 RRU (35/38 patients) after a single injection. Of the 38 patients, 21 completed 1 year of follow up, at which time ultrasound demonstrated no change compared with 1 month after injection. Eight of these 21 children underwent 1 year radionuclide cystography, and no reflux recurrence was shown.

Conclusions: Our short-term data show that Vantris injection provides a high level of reflux resolution. Long-term follow up with this tissue-augmenting substance is required.

Introduction

Since the introduction of STING two decades ago, and over the last 9 years since the approval by the FDA of dextranomer/hyaluronic acid (Dx/HA) copolymer (Deflux®, Q-Med Scandinavia, Uppsala, Sweden) for the treatment of VUR,
the endoscopic management of VUR has emerged as a first-line treatment for all grades of reflux in some centers. The overall success rate reported by different groups of authors ranges between 68% and 92%, depending mainly on the VUR grade [1–3]. Complications following this procedure are infrequent and related mainly to obstruction of the vesicoureteric junction and development of a new contralateral VUR following treatment of unilateral VUR [4]. The concept of the endoscopic correction of VUR offers a minimally invasive treatment for the management of UTI or renal parenchymal damage associated with reflux [5–8]. Since endoscopic treatment of UTI has enjoyed a high rate of success in short-term follow-up, it is extremely important to address the issue of the long-term efficacy of the tissue-augmenting substance used. Recently, intriguing data regarding the very high incidence of VUR recurrence following successful Dx/HA treatment was presented [9,10]. These results, which show an overall recurrence rate of up to 21%, are extremely sobering, and lead us to believe that another tissue-augmenting substance may be needed to achieve long-term efficacy in the endoscopic treatment of VUR. Some authors have suggested that the biodegradable nature of Dx/HA is responsible for the eventual VUR recurrence [11].

Polyacrylate polyalcohol bulking copolymer (PPC, Vantris®; Promedon, Cordoba, Argentina) is a new non-biodegradable tissue-augmenting substance. We have conducted a prospective study aiming to evaluate the efficacy of Vantris in children with VUR in the short and long term. Herein, we present our preliminary results with a single Vantris injection.

Patients and methods

Thirty-eight children (11 males and 27 females) with a mean age of 5.3 ± 3.8 years (mean ± SD) underwent endoscopic treatment of VUR utilizing Vantris. Reflux was diagnosed as a result of UTI in 31 (81.6%) of the patients, in 5 (13.2%) following evaluation of antenatal hydronephrosis, and in the remaining 2 (5.3%) due to unrelated causes. We have previously published our standard protocol for evaluation and endoscopic correction of reflux [8]. The reflux grade was based on the VCUG before and after surgery or during conservative treatment, according to the International Classification System (International Reflux Study Committee). DMSA renal scan was used to assess renal scarring. The scan was performed at least 6 months after the last febrile UTI. Kidney uptake of 45%–55% of total renal activity was considered normal. The indication for endoscopic correction in the majority of cases was persistent high-grade VUR or breakthrough infections while on antibiotic prophylaxis. However, in some patients, reflux correction was performed according to guardian request. Of the studied patients, 24 (63.4%) had normal renal function, 12 (31.6%) had moderate renal function, and the remaining 2 (5%) had poor renal function.

Children who had symptoms of dysfunctional voiding or constipation were allocated to conservative treatment prior to endoscopic correction until full resolution of the voiding symptoms was achieved and preoperative reassessment including repeat VCUG was performed. Since 2000, we have utilized a dysfunctional voiding symptoms survey for the evaluation of dysfunctional voiding [8]. None of the children in this series had voiding dysfunction at the time of injection. All patients received antibiotic prophylaxis until VCUG showed spontaneous resolution or definitive cure of the VUR. The technique of endoscopic correction used was similar to that described in the literature [5,6]. In patients with grade I–III VUR, we utilized the usual technique of STING, with the needle introduced submucosally under the ureteral orifice at the 6 o’clock position. In patients with grade IV and V VUR or in those with a widely open orifice, the injection was performed inside the orifice as published previously [6]. Grade I VUR was treated only in children with contralateral high-grade VUR. Recurrent febrile UTI served as the only indication for surgery in 30 (78.9%) patients, Grade 5 VUR in 5 (13.2%), and in 3 (7.9%) reflux correction was performed on parental request.

All injections were performed by a single surgeon (BC) as part of the study protocol. All families gave fully written informed consent regarding the procedure and tissue-augmenting substance used for reflux correction as part of our routine protocol. According to our standard practice, ultrasound scan was performed 1 month after injection in order to identify hydronephrosis, obligatory VCUG was performed 3 months after endoscopic correction, and antibiotic prophylaxis was stopped if VCUG showed no reflux. Reflux was considered cured if VCUG did not demonstrate VUR of any grade. In these patients, ultrasound scan and repeat radionuclide cystography were planned for 1 and 3 years after the first successful injection as part of the routine protocol in order to assess the long-term efficacy of Vantris.

Results

The demographic data and indications for surgery are presented in Table 1. In brief, VUR was unilateral in 17 and bilateral in 21 patients comprising 59 refluxing units (RRU). Of these, primary VUR was present in 42 RRU and 17 were complex cases: 3 duplex systems, 1 with prune belly syndrome, and 13 after failed previous endoscopic correction with Deflux. VUR was Grade I in 5, Grade II in 11, Grade III in 23, Grade IV in 15 and Grade V in 5 RRU.

Reflex correction outcomes are presented in Table 2. The reflux was corrected in 56 (94.9%) of the 59 RRU following the single injection, and this equates to VUR correction in 35 (92.1%) of the 38 patients.

Of those three patients who showed residual VUR, one with Grade V VUR reflux had downgraded to Grade I, was free of UTI and required no further therapy. In another patient with bilateral Grade 4 VUR, reflux was corrected on one side but was persistent on the other; he underwent additional injection and is awaiting the VCUG scheduled for 3 months after injection. As to the third patient, Grade 5 VUR downgraded to Grade 3 and he is awaiting another injection.

The prune belly syndrome patient suffered febrile UTI following successful endoscopic correction. He is on self intermittent catheterization due to incomplete emptying of the urinary bladder, and his repeat VCUG showed no reflux. One patient complained of one episode of a febrile UTI. Two patients demonstrated hydronephrosis on the 1-month
postoperative scan, and one adolescent complained of lumbar pain 2 days following surgery. Her ultrasound scan was completely normal. The mean volume of Vantris used for VUR correction was 0.78 cc (range 0.2–1.0 cc).

Twenty-one (55.3%) of the 38 patients completed the 1-year follow up. Their ultrasound scans demonstrated no change compared with imaging 1 month after injection. Eight (38.1%) had agreed to undergo radionuclide cystography as part of the protocol for this group of patients; in none of these was reflux recurrence shown. The rest of the group refused to undergo the suggested 1-year cystography due to their normal ultrasound examination and the complete absence of urinary symptoms.

Discussion

Recently, we and others have demonstrated that the successful resolution of VUR following endoscopic correction may be as effective as the results of open surgery in the prevention of recurrent UTI and kidney damage [8,12–15]. It follows, therefore, that reflux recurrence following a previous successful endoscopic injection may increase the incidence of febrile UTI and lead to an increased incidence of renal damage.

Since FDA approval of Dx/HA copolymer as a tissue-augmenting substance for endoscopic correction of VUR, Deflux has become the implant of choice in the vast majority of centers around the globe. Recently, Kirsh et al. demonstrated that, utilizing their hydrodistention implantation technique (HIT), the short-term results of endoscopic correction may be close to those of open surgery, and in the case of low-degree reflux even similar to those following open reimplantation [1]. Only the question of Deflux long-term durability remains as a subject of interest and parental concern; however, long-term follow-up data are lacking, as well as strict criteria for what is considered a ‘success’. Since endoscopic treatment of UTI has enjoyed a high rate of success in short-term follow up, it is extremely important to address the issue of long-term efficacy. In recent publications, some authors have raised concern regarding a high incidence of VUR recurrence following short-term success. Lee et al. retrospectively studied VUR recurrence verified by VCUG, which was performed 1 year after successful Deflux injection [9]. The initial experience with Dx/HA was similar to the existing studies, with a postoperative VCUG success rate of 73%, but at 1 year there was a recurrence rate of 26%. These findings lead the authors to believe that other studies, if re-evaluated beyond the initial VCUG, would yield similar findings. Recently, the working group on pediatric urology of the German Association of Pediatric Surgeons published the results of a multicenter prospective trial, which aimed to evaluate the long-term efficacy of endoscopic treatment of VUR utilizing Dx/HA. A total of 284 patients (424 RRU) were treated endoscopically with Deflux injection [10]: reflux was corrected in 68% of the RRU; 46% of the patients completed 3 years of follow up; in 21% of RRU a recurrence of VUR was diagnosed between 6 months and 3 years. Based on this data, the authors strongly recommend continuing to follow patients after a successful injection beyond the first 3 years after surgery.

As we have already mentioned, the biodegradable nature of Deflux may be to blame for VUR recurrence [11]. PPC is a new non-biodegradable substance of synthetic origin belonging to the acryl family. The particles of PPC have an average diameter of 300 μm, thereby reducing the risk of local and distant migration [16]. Once injected, the implant is also stable through time. Our preliminary results from this study on the efficacy of PPC (Vantris) in children with VUR are promising and similar to the previously published series on the endoscopic treatment of VUR. Reflux was cured with a single injection in 92.1% of all patients. It is of note that the failures occurred in patients from the group of complex cases.

Our results are similar to those from the first reported experience with Vantris. A group from South America recently published their experience with 83 patients with all grades of VUR using Vantris as a tissue-augmenting substance [17]. The maximum follow up was 24 months. Overall success rate in this series was 83%. One patient developed ureteric obstruction and required ureteric reimplantation. Some reviewers have raised the issue of increased risk of ureteric obstruction following PPC injection citing the 6% incidence of lumbar pain in the South-American series on the endoscopic treatment of VUR. Reflux was resolved in 100% of patients, and postoperative VCUG was successful in 73% of patients. The maximum follow up was 3 years.

Table 1

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
</tr>
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<tbody>
<tr>
<td>VUR cases (RRU)</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>42</td>
<td>(71.2%)</td>
</tr>
<tr>
<td>Complex</td>
<td>17</td>
<td>(28.8%)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>5.3</td>
<td>(range 1.3–14)</td>
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<table>
<thead>
<tr>
<th>Laterality</th>
<th>Unilateral</th>
<th>Bilateral</th>
</tr>
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<tbody>
<tr>
<td>Grade (RRU)</td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td></td>
<td>5 (8.5%)</td>
<td>11 (18.6%)</td>
</tr>
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</table>

<table>
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<tr>
<th>Indications for surgery</th>
<th>Breakthrough UTI</th>
<th>High-grade VUR</th>
<th>Parental request</th>
<th>Mean injected volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 (78.9%)</td>
<td>5 (13.2%)</td>
<td>3 (7.9%)</td>
<td>0.78 (range 0.2–1.0)</td>
</tr>
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Table 2

<table>
<thead>
<tr>
<th>VUR</th>
<th>RRU</th>
<th>Resolved VUR</th>
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</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>5</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Grade II</td>
<td>11</td>
<td>11 (100%)</td>
</tr>
<tr>
<td>Grade III</td>
<td>26</td>
<td>26 (100%)</td>
</tr>
<tr>
<td>Grade IV</td>
<td>15</td>
<td>14 (93.3%)</td>
</tr>
<tr>
<td>Grade V</td>
<td>5</td>
<td>3 (60%)</td>
</tr>
</tbody>
</table>
American series [17]. In our series one patient suffered lumbar pain, which spontaneously resolved. The ultrasound examination of this patient showed no evidence of hydronephrosis. The routine scan performed 1 month following injection demonstrated hydronephrosis in two patients; they were free of any symptoms, and follow-up ultrasound showed spontaneous resolution of the hydronephrosis. It is speculated that the clinical symptoms in these patients were due to swelling of the ureteric orifice following injection. If further evidence is found for this occurrence in additional studies, consideration should be given to postponing the routine scan in order to spare patients unnecessary anxiety and avoid additional examination.

This study is not without limitations. We present only technical data regarding the short-term efficacy of PPC as a tissue-augmenting substance, and we have demonstrated outcome regarding VUR resolution after 3 months in a relatively small group of patients. We so far have data on long-term efficacy based on the 1-year cystography in only a small group of patients. We do not have data on the characteristic appearance of Vantris on CT; however, we do know that the Vantris implant can barely be demonstrated on ultrasound examination. Finally, we do not know if it will be difficult to perform a ureteric reimplantation in patients following failure of VUR correction with Vantris. These questions are to be addressed in future studies.

In conclusion, our short-term data show that Vantris injection provides a high level of reflux resolution. Long-term follow up with this tissue-augmenting substance is required.

Funding

None.

Conflict of interest

None.

References