Comparison of results of endoscopic correction of vesicoureteral reflux in children using two bulking substances: dextranomer/hyaluronic acid copolymer (Deflux) versus polyacrylate-polyalcohol copolymer (Vantris)

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Comparison of results of endoscopic correction of vesicoureteral reflux in children using two bulking substances: dextranomer/hyaluronic acid copolymer (Deflux) versus polyacrylate-polyalcohol copolymer (Vantris)

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Summary Background: Endoscopic correction of vesicoureteral reflux (VUR) in children offers minimally invasive management and is widely used as a first-line procedure for all grades of reflux. However, there is debate about which tissue-augmenting substance is the best to use. The aim of this study was to evaluate the efficacy of two bulking substances, Deflux (Dx/HA) and Vantris (PPC), for endoscopic treatment of VUR in children.

Methods: From 2009 to 2012, 65 children (50 girls and 15 boys) aged 1.45–9.9 years (mean 4.85 ± 2.52) underwent endoscopic correction of VUR using Deflux. VUR was unilateral in 31 patients and bilateral in 34 patients, comprising 108 renal refluxing units (RRUs) grades: II in 52, III in 47, IV in 7, and V in 2. From 2012, 68 children (43 girls and 25 boys) aged 0.6–17.9 years (mean 4.89 ± 3.46) were treated with Vantris. VUR was unilateral in 33 and bilateral in 35 patients, comprising 109 RRUs grades: II in 48, III in 29, IV in 13, and V in 19. Voiding cystourethrogram was done 3 months after procedure.

Results: All patients completed follow-up (summary Table).
<table>
<thead>
<tr>
<th></th>
<th>RRU (no.)</th>
<th>after first injection no. of RRU (%)</th>
<th>after second injection no. of RRU (%)</th>
<th>after third injection no. of RRU (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deflux</td>
<td>108</td>
<td>68 (63)</td>
<td>30 (27.8)</td>
<td>10 (9.2)</td>
</tr>
<tr>
<td>Vantris</td>
<td>109</td>
<td>101 (92.7)</td>
<td>8 (7.3)</td>
<td></td>
</tr>
</tbody>
</table>

With Deflux, reflux resolved in almost 93% of RRUs after two procedures (in 63% after first injection), with Vantris, VUR was corrected in the same percentage after one procedure.

**Discussion:** The success rate with Deflux ranges between 68% and 92% (only 50-70% after single injection). The reported possibility of reflux recurrence after successful Deflux treatment, and the need for repeated injection led to introduction of the new substance Vantris. The results of a multi-centre survey published in 2014 showed that reflux is corrected in more than 90% of cases after single PPC injection. Our results with PPC confirm a high level of reflux resolution.

**Conclusions:** Our data show that Vantris injection is a safe and effective procedure for treating all grades of VUR with good clinical outcome, and provides a higher and almost complete level of reflux resolution after first injection compared with Deflux.

**KEYWORDS**
Vesicoureteral reflux;
Endoscopic correction of VUR;
Deflux;
Vantris

**Introduction**
Since the introduction of subureteric injection of bulking agents more than three decades ago, endoscopic management of vesicoureteral reflux (VUR) has emerged as a first-line procedure for interventional treatment of reflux in children. Many implant substances have been used in the past, but their safety and efficacy remain major concerns [1-5].
Dextranomer/hyaluronic acid copolymer (Dx/HA, Deflux Q-Med Scandinavia, Uppsala, Sweden), which is a biodegradable material, has been in common use since 2000 [2, 6-8]. In 2010, polyacrylate–polyalcohol copolymer (PPC, Vantris, Promedon, Cordoba, Argentina), a new, synthetic, non-absorbable tissue-augmenting substance, was introduced into clinical practice and is currently used in some centres around the world [9-14].

The aim of the present study was to evaluate the efficacy of the two bulking substances, Deflux and Vantris, in children with VUR. The results of the endoscopic treatment were compared in terms of number of required injections to achieve resolution of reflux.

**Patients and methods**

From 2009 to 2012, 65 children (50 girls and 15 boys) aged 1.45–9.9 years (mean 4.85 ±2.52) underwent endoscopic correction of persisting VUR using Deflux (Dx/HA). Reflux was unilateral in 31 patients and bilateral in 34 patients, comprising 108 renal refluxing units (RRUs) grades: II in 52, III in 47, IV in 7, and V in 2. Primary VUR was noted in 89 (82.4%) RRUs, while 19 (17.6%) RRUs presented complex cases, that is reflux in duplex/bifidus system.

From 2012 to 2015, 68 children (43 girls and 25 boys) aged 0.6–17.9 years (mean 4.89 ±3.46) were treated with a new substance, Vantris (PPC). VUR was unilateral in 33 patients and bilateral in 35 patients, comprising 109 RRUs grades: II in 48, III in 29, IV in 13, and V in 19. In 74 (67.9%) RRUs primary VUR was present, and the remaining 35 (32.1%) RRUs were complex cases (reflux in boys with PUV, in duplex/bifidus system, persistent VUR after Deflux injection).

In the majority of children in both groups, reflux was diagnosed as a result of urinary tract infection.

Indications for endoscopic treatment included persistent VUR grade II-V in patients with a history of previous medical treatment for at least 12 months, with the presence of renal scarring (renal scintigraphy) and with no bladder dysfunction (urodynamic study) at the time of injection.

All procedures were done during cystoscopy under general anaesthesia using a paediatric operating cystoscope (Storz 9.5 FR or Wolf 8/9.8 FR). One millilitre of bulking agent was injected under the ureteral orifice using the STING technique.
A standard injection needle (injection hole at the end of the needle) was used for Deflux injection (Figure 1). For the Vantris injection, two types of needles were used: RIN type (“concave side opening”) with laterally located injection hole to treat high grade primary VUR (IV-V) and complex cases (excluding reflux in bifid/duplex system) (Figure 2), and RINS type (“bevel tip”) with injection hole at the end of the needle for the remaining cases (Figure 1).

Perioperative antibiotic prophylaxis was administered and the child was discharged home the next day after cystoscopy. Each patient underwent ultrasound scan (US) 2 weeks after injection and voiding cystourethrogram (VCUG) 3 months after injection. In the case of immediate post-injection flank/abdominal pain, US was performed to evaluate the degree of possible obstruction of the upper urinary tract.

**Results**

All patients completed follow-up. In the majority of children, after Vantris injection (>90%) US showed an injected substance deposit within the bladder wall visible as apparent bulk compared with Deflux (<50%).

Reflux resolved in 68 RRUs (63%) after the first Deflux injection, in 30 (27.8%) after the second injection, and in 10 (9.2%) after the third injection.

Reflux was corrected in 101 RRUs (92.7%) after the first Vantris injection, and in 8 (7.3%) after the second injection.

Tables 1 and 2 present VUR resolution rate after Deflux and Vantris injections regarding reflux grade.

**Discussion**

Currently, Deflux is the most commonly used tissue augmenting substance applied for endoscopic treatment of VUR using various injection techniques [5-8]. The results of a systematic review published in 2010 showed an overall per-ureter success rate of 77% with Dx/HA after 3 months, although success rates varied widely among reports [6].

The overall success rate reported in the literature after endoscopic treatment of VUR in children with Deflux ranges between 68% and 92%, depending mainly on the reflux grade; however, with only 50–70% success rate after a single injection [1,2,5-7,11]. In our experience with Deflux, the success rate is similar to that published: 63% after the first injection and 90.7% after the second.
The reported possibility of recurrence of VUR after successful Deflux treatment, failures of endoscopic correction with Dx/HA caused by migration mound on re-operation, and the need for repeated injection, resulted in introduction of the new synthetic, non-biodegradable tissue-augmenting substance Vantris, a polyacrylate-polyalcohol copolymer. The biodegradable nature of the dextranomer/hyaluronic acid copolymer is suggested as a factor responsible for the eventual reflux recurrence [7,9-11,13-15].

A high level of reflux resolution is noted using Vantris. The results of a multicentre survey published in 2014 showed that reflux is corrected in more than 90% of cases after single PPC injection [13]. Vantris has been used successfully to treat primary reflux and also for complex cases [12-14,16]. The use of PPC to correct grades IV and V is also very efficient with an overall success rate achieved of over 80% [13,17,18]. All papers estimating the results with Vantris state that PPC can be used to treat VUR with high level of reflux resolution, no recurrence during prospective follow-up, and a low rate of complications. Patients who undergo endoscopic treatment of VUR using Vantris need long-term follow-up because of the possibility of early and delayed ureteral obstruction after PPC injection, which is the main complication encountered [11-14,17].

Our results with Vantris confirm that this new augmenting substance is very effective for treating all grades of primary and also complex VUR in children. Reflux is resolved in almost 93% of all treated RRU after the first procedure, and in 100% after the second procedure. For high grade VUR, that is IV and V, success was achieved in almost 90% after the first injection and 100% after the second injection.

Various injection methods including subureteral transurethral injection (STING), hydrodistention implantation technique (HIT), and double HIT are used for endoscopic treatment of VUR [3,7,8,18]. Recently Kirsch and co-workers reported that the double HIT method for Deflux implantation is the most commonly performed technique by paediatric urologists in the United States [8]. A standard needle with the injection hole located at the end of the needle is used with a single puncture for STING or HIT procedure or two punctures for double HIT. For Vantris, two types of needles are available: a standard needle as described above (RINS type) and RIN type with laterally located injection hole. In our experience, this new type of needle can be used to achieve
the same effect as that observed with double HIT, but using only one puncture. We use the RIN type needle to treat high grade primary VUR (IV-V) and for complex cases (excluding reflux in bifid/duplex system), allowing for achievement of a very high resolution rate using only one puncture.

In conclusion, our experience with the use of Vantris has been favourable. Our data showed that PPC injection is a safe and effective procedure for treating all grades of VUR with good clinical outcome, and provides higher and almost complete level of reflux resolution after first injection compared with Dx/HA. However, extended follow-up after endoscopic correction of VUR with this new tissue-bulking agent is required.

Conflict of interest
None.

Funding

References


### Table 1. Reflux resolution after Deflux injection

<table>
<thead>
<tr>
<th>VUR Grade</th>
<th>RRUs</th>
<th>After first injection % (n)</th>
<th>After second injection % (n)</th>
<th>After third injection % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>52</td>
<td>73.1 (38)</td>
<td>98.1 (51)</td>
<td>100 (52)</td>
</tr>
<tr>
<td>III</td>
<td>47</td>
<td>55.3 (26)</td>
<td>89.3 (42)</td>
<td>100 (47)</td>
</tr>
<tr>
<td>IV</td>
<td>7</td>
<td>43 (3)</td>
<td>43 (3)</td>
<td>100 (7)</td>
</tr>
<tr>
<td>V</td>
<td>2</td>
<td>50 (1)</td>
<td>100 (2)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>108</td>
<td>63 (68)</td>
<td>90.7 (98)</td>
<td>100 (108)</td>
</tr>
</tbody>
</table>

### Table 2. Reflux resolution after Vantris injection

<table>
<thead>
<tr>
<th>VUR Grade</th>
<th>RRUs</th>
<th>After first injection % (n)</th>
<th>After second injection % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>48</td>
<td>97.9 (47)</td>
<td>100 (48)</td>
</tr>
<tr>
<td>III</td>
<td>29</td>
<td>89.7 (26)</td>
<td>100 (29)</td>
</tr>
<tr>
<td>IV</td>
<td>13</td>
<td>84.6 (11)</td>
<td>100 (13)</td>
</tr>
<tr>
<td>V</td>
<td>19</td>
<td>89.5 (17)</td>
<td>100 (19)</td>
</tr>
<tr>
<td>Total</td>
<td>109</td>
<td>92.7 (101)</td>
<td>100 (109)</td>
</tr>
</tbody>
</table>

**Figure 1.** Standard injection needle with the injection hole located at the end of the needle: RINS type (“bevel tip”).

**Figure 2.** Injection needle with laterally located injection hole: RIN type (“concave side opening”).
igła typu RINS „bevel tip”
igła typu RIN „concave side opening”