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Dextranomer/Hyalouronic Acid Copolymer Injection for Treatment of Children with Primary Vesicoureteral Reflux: Long-term Follow-up

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Abstract

Purpose: We aim to present our 5 years results with Dextranomer/Hyalouronic Acid (Dx/HA) sub-ureteral injection for the treatment of children with primary vesico ureteric reflux (VUR).

Patients and methods: The retrospective cohort study, which was performed at tertiary referral center in Cairo.

Children underwent Dx/HA injection for the treatment of the primary VUR were reviewed.

Only those he had full medical record dating 5 years or earlier included into the study.

Results: Sixty patients, 25 boys and 35 girls in total 82 ureters had refluxed underwent DX/HA injections. The patients' average age was 5.70 years. Eight (9.7%) of the 82 ureters that were treated failed all three injections, leaving 74 (90.3%) of them completely cured.

Conclusion: This acceptable improvement sustainability of the DX/HA suburetral injection in children with 1ry VUR highlights the benefits of this procedures. The minimally invasive nature, the short hospital stay are definite advantages.

Keywords: Dextranomer/hyalouronic acid, Endoscopic, Long-term, Vesicoureteral reflux

1. Introduction

One in three children with an active urinary tract infection (UTI) and between one and three percent of pediatric patients have primary VUR.^{1,2}

About 80% of low-grade (I and II) reflux will improved spontaneously, compared to roughly 50% of grade III reflux and 20% of high-degree (IV and V) reflux.³ Preventing recurrent febrile UTI, preventing kidney scarring, and lowering treatment morbidity are the top targets for VUR care.⁴

Active monitoring and continuous antibiotic prophylaxis (CAP) are the first-line treatments for VUR, especially in children with mild reflux.⁵

Ureteral reimplantation (either open or laparoscopic) and endoscopic injection of bulking agent are two pathways that can successfully correct VUR and protect upper tracts.^{6,7}

While the former entails surgical intervention, the later carries the benefits of it's minimal invasiveness.⁸

In the early days bulking agent injection has been reserved for mild and moderate cases with excellent results.⁸

Since the endoscopic injection of Dx/HA was first described by Matouscheck in 1981 and the first clinical cases were documented by O'Donnell in 1984, it has shown to be a successful treatment for VUR.^{1,7,9}

More ever several authors reported acceptable result in severe VUR.^{8,10,11} However the long-term efficacy of these technique have been rarely addressed.

2. Patients and methods

The retrospective cohort study was performed at Al-Azhar University hospitals including children

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with primary VUR who underwent DX/HA injection during the years 2016–2017.

Among seventy child who was treated during this period, sixty child had complete medical records through the past 5 years and were included into the study, we excluded cases with insufficient follow-up data.

The demographic and preoperative data of the cohort study are summarized in [Tables 1 and 2](#).

Indication of injection of DX/HA in low-grade reflux: no spontaneous resolution or improvement after treatment with prophylactic antibiotics.

The early postoperative handling of the children included urine culture & renal ultrasonography (U/S).

Re-injections were performed in children who suffering from recurrent UTI, persistent reflux and increasing kidney scarring.

All children completed 5-years follow-up and including medical history, clinical examination, laboratory data: serum creatinine (S.Cr), complete blood count (CBC), urine culture & imaging study: U/S, voiding cysto-urethrograme (VCUG) and renal isotope scan (DMSA scan) at least twice during the follow-up period.

The success was defined as the resolution of reflux on VCUG. Clinical success means the absence of febrile urinary tract infection, improvement mean the downgrading of reflux (high grade to low grade) while failure is no improvement clinically or radiological.

The statistical program for social sciences, version 20.0, was used to evaluate the recorded data (SPSS Inc., Chicago, Illinois, USA). The mean and standard deviation were used to express quantitative data (SD). Frequency and percentage were used to express qualitative data. When comparing related samples, the paired sample *t*-test was employed. The proportions between qualitative measures were compared using the Chi-square (χ^2) test of significance. The allowable margin of error was set at 5%, while the confidence interval was set at 95%.

Table 1. Demographic data distribution among all studied group ($n = 60$).

Demographic data	Number (%)
Sex	
Female	35 (58.3%)
Male	25 (41.7%)
Age (years)	
Range	2–10 years
Mean \pm SD	5.70 \pm 1.72
Laterality	
Unilateral	38 (63.3%)
Bilateral	22 (36.7%)

Table 2. Preoperative data distribution among all studied group ($n = 60$) child, (82) units & number of injections.

Preoperative data	Number (%)
Febrile UTI	
Absent	50 (83.8%)
Present	10 (14.2%)
S.Cr	
>1 mg/dl	55 (91.6%)
<1 mg/dl	5 (7.4%)
TLC	
>11 g/dl	50 (83.8%)
<11 g/dl	10 (14.2%)
U/S finding ($n = 82$)	
Normal	35 (42.8%)
Mild HUN	23 (28%)
Moderate HUN	10 (12.2%)
Marked HUN	14 (17%)
VCUG	
Grades	
G2	26 (31.7%)
G3	25 (30.5%)
G4	19 (23.2%)
G5	12 (14.6%)
DMSA	
Scaring	
Absent	74 (90.2%)
Present	8 (9.8%)
GFR(n82)	
range	20–80
Mean \pm SD	53.19 \pm 16.31
Number of injections	
2 sessions	52 (63.4%)
3 sessions	30 (36.9%)

Therefore, in terms of probability (*P* value), a *P* value of 0.05 or below was regarded as significant, a *P* value of 0.001 or higher as extremely significant, and a *P* value of >0.05 as inconsequential.

3. Results

The main clinical presentation is recurrent UTI, ante natal hydronephrosis. Indication for intervention were standard and included the following: breakthrough UTI, progressive renal scarring, persistent reflux.

The follow-up data of our cohort study was retrieved medical records showed sixty child and eighty tow renal units, seventy-four (90.3%) units is cured, and eight (9.7%) units is failed after three sessions of injections.

The cure rates as classified according to the pre-operative and operative data are summarized in [Table 3](#).

The success rate after one and three years follow up shown in [Table 4](#).

None of children in our study developed progression in Hydroureteronephrosis (HUN), or obstructed ureter after injection.

Table 3. Shown results in relation to age, sex and grades.

	Success	Failed	χ^2	P value
Age (years)				
>2 (20)	17 cases	3 cases	0.018	0.893
<2 (40)	35 cases	5 cases		
Sex				
Male (23)	21 cases	2 cases	0.196	0.658
Female (37)	31 cases	6 cases		
Laterality				
Unilateral (38)	34 cases	4 cases	0.072	0.789
Bilateral (22)	20 cases	2 cases		
Febrile UTI				
Absent (55)	55 cases	0 case	47.623	<0.001**
Present (5)	0 case	5 cases		
Grades				
G2 (26)	25 unit	1 unit	2.555	0.465
G3 (25)	23 unit	2 unit		
G4 (19)	16 unit	3 unit		
G5 (12)	10 unit	2 unit		
Scarring				
Absent (78)	78 unit	0 case	61.865	<0.001**
present (4)	0 case	4 unit		

Table 4. Shown the success rate at one, three years follow up.

Grade	G2	G3	G4	G5	Total
1st year					
Success	25	25	16	10	76
Failed	1	2	3	2	8
Success %	96.2%	93.0%	84.2%	83.3%	90.5%
3rd year					
Success	26	25	16	11	78
Failed	1	2	2	2	7
Success %	96.3%	92.6%	88.9%	84.6%	91.8%

4. Discussion

Over the past ten years, there has been a considerable global decline in the incidence of ureteral reimplantation. This could be explained by fewer VCUGs being performed and more endoscopic intervention being used to treat primary VUR.¹²

In our study, there were 60 cases, and 82 units underwent DX/HA injections in children with 1ry VUR. The grades of reflux II (26 units), III (25 units), IV (19 units), and V (12 units), respectively. Twenty-five (96.1%) units were cured in grade II, twenty-three (92%) were cured in grade III, sixteen units (84.2%) were cured in grade IV and ten units (83.3%) were cured in grade V reflux, in total 74 units (90.3%) while eight units (9.7%) were failed in different grades.

Regarding the degree of reflux and success rate in our investigation, both clinical and radiographic success evaluations were done. The focus of the clinical assessment was the presence of UTI and accompanying clinical manifestations.

The results reported in our study show no significant differences in curability after one, three and five years follow-up.

Our long-term success rates support earlier reports by MihovilBiočić et al.¹³ Who had a long-term follow-up study, the cure rate is 94%. While better results were conducted by IyimserÜre et al.,¹⁴ Sahned Jaafar et al.,¹⁵ the success rate of the treated patients was 97% and 93.3% respectively. While our results are better than studies conducted by Suleyman et al.,¹⁶ Ling Leung Ivy Hau et al.,¹⁷ The overall resolution rates based on the number of renal refluxing units studied was 70.3%, 65%, respectively.

In comparison with ureterovesical implantation (UVI) the success rate is higher in open UVI over endoscopic injection of DX/HA in the management of high-grade reflux, (IV, V), while endoscopic injection is superior to open surgeries in low-grade reflux. None of the children show progression in HUN or obstruction in the ureter after injection.

4.1. Conclusion

This acceptable improvement sustainability of the DX/HA suburetral injection in children with 1ry VUR highlights the benefits of this procedures. The minimally invasive nature, the short hospital stay are definite advantages encourage further prospective randomized controlled studies between the 2 procedure whatever the grade of reflux.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

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Conflicts of interest

There are no conflicts of interest.

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