



Efficacy of dextranomer/ hyaluronic acid copolymer (DX/HA) injection in management of vesicoureteral reflux in children- A paradigm shift in the management

Mansoor Ejaz, Sharjeel Saulat, Jahanzeb Sheikh, Syed Saeed Uddin Qadri, Awais Ayub, Nauman Sadiq Kiani, Hamza Ashraf

¹Department of Urology, Tabba Kidney Institute, Karachi, Pakistan

*Correspondence: mansurejaz@hotmail.com Received 01-07-2022, Revised: 30-007-2022, Accepted: 31-07-2022 e-Published: 12-08-2022

VUR is one of the most common congenital urological diseases causing Hydronephrosis in children, resulting in significant morbidity ranging from recurrent UTIs to Renal scarring. In this study we will evaluate the efficacy of Deflux Injection in treating various grades of VUR, its cost effectiveness and its different techniques.

This is a prospective, cross-sectional study. Patient with Primary VUR, Grade I, Grade II, Grade III VUR, and patient with American Society of Anesthesiologists (ASA) i, ii were included in the study. Statistical package of social sciences (SPSS) version 23 was used to enter, sort, and analyze the data. Descriptive characteristics included age, gender, weight, and height were analyzed in mean \pm standard deviation. Independent variables were analyzed with frequency. Post-operative complication, success rates were analyzed as end point of study. The gender distribution of participants was 5 (23.8%) males and 16 (76.1%) females with mean weight measuring as 17.5 ± 8.3 Kgs. Post-operative ultrasonography results indicated 100% resolution in Grade I and II VUR, while 75% resolution in Grade III VUR, 50% resolution in Grade IV VUR, whereas 25% resolution in Grade V VUR. Our study shows that endoscopic injection of Dextranomer/Hyaluronic acid copolymer in treating VUR has overall good and comparable success rates in grade I to grade iv VUR with open surgery. For grade V VURs, patients and parents can be counseled that this procedure has a 60% success rate and due to its minimal invasiveness can be undertaken with no extra added risks if further laparoscopic or open surgery is required later on.

Keywords: Vesicoureteral reflux, hydronephrosis, Dextranomer/Hyaluronic acid copolymer

INTRODUCTION

VUR is one of the most common congenital urological diseases causing Hydronephrosis in children (Yeung CK, 1997), resulting in significant morbidity ranging from recurrent UTIs to Renal scarring. It results from developmental defect of superficial trigone which causes decreased intravesical intramural part of distal ureter which leads to incompetent Ureteral orifice trigone complex (Yeung CK, 1997). Due to this incompetent system when bladder contracts there is reflux of urine back to the ureter and can go up to renal pelvicalyceal system. Due to recirculation of urine from lower urinary tract to upper urinary tract, microorganisms easily contaminate the urine and are carried to the pelvicalyceal system causing recurrent urinary tract infection and may lead to renal scarring depending on the grade of VUR (Bomalaski MD, 1997). Untreated VUR can cause significant renal damage ranging from Reflux nephropathy to CKD and may progress to end stage renal disease which may require extensive morbid surgery like

Nephroureterectomy or Renal Replacement therapy i.e., lifelong dialysis or Renal Transplant.

In the past VUR was treated with extensive surgical intervention like Ureteric reimplantation. With passing time, role of prophylactic antibiotics was established but the known risk of antibiotic resistance, compliance, and cost of continuous antibiotic prophylaxis leads to the invention of new treatment modalities. One of the new modalities in treating VUR is the endoscopic treatment of VUR with Dextranomer/Hyaluronic Acid Copolymer (Deflux) Injection (Chertin B, 2013 – Puri P, 2003 – Kirsch AJ, 2003 – Moliterno JA, 2008) after which there is no need for prolonged antibiotics. Multiple trials have been done for the evaluation of efficacy of different modalities in reducing recurrent UTIs, new renal scars and resolution of VUR.

One of the most known trials for the treatment of VUR is Swedish Reflux trial in which they evaluated and compared prophylactic antibiotics, endoscopic treatment in treating VUR vs surveillance and evaluated the

outcome by episodes of UTIs, Renal scarring after treatment, downgrading and resolution of VUR in children with age ranging from 1 to 2 year with dilating VUR. The results were in favor of continuous antibiotics prophylaxis (CAP) and endoscopic treatment with Dextranomer/Hyaluronic acid copolymer vs surveillance with no significant difference in continuous antibiotics prophylaxis (CAP) and endoscopic treatment with Dextranomer/Hyaluronic acid injection. However, there was increased antibiotic resistance in continuous antibiotics prophylaxis (CAP) group.

Our aim was to assess the outcome of endoscopic treatment at our center in children of any age presented to us with dilating and non-dilating VUR in treating recurrent UTIs, prevention of new renal scars and downgrading or resolution of VUR and need of 2nd injection and associated complications. Dextranomer/Hyaluronic acid is one of the safest techniques and the complication rate is very low. However, the complications which can occur includes Ureteral obstruction (0.7%), Urinary Tract infection (4% to 20%) and need for reinjection (8% to 29%). Furthermore, there can be complication of endoscopic instrument which includes urethral trauma, bladder neck trauma and general anesthesia (Lackgren G, 2001 – Vandersteen DR< 2006 – Mazzone L, 2012 – Dwyer ME, 2013- Kim H, 2015).

If VUR don't resolve after 3rd injection it will be labeled as failure of treatment and he will require surgical intervention for the correction of VUR which includes open or laparoscopic ureteric re-implantation.

In this study we will evaluate the efficacy of Deflux Injection in treating various grades of VUR, its cost effectiveness and its different techniques.

MATERIALS AND METHODS

This is a prospective, cross-sectional study. The data was collected at Tabba Kidney Institute from October 2020 till February 2021, after approval of ethical review committee at TKI. Patient with Primary VUR, Grade I, Grade II, Grade III VUR, and patient with American Society of Anesthesiologists (ASA) i, ii were included in the study. Patient with secondary VUR, previous urogenital surgeries, severe hepatic, and renal insufficiency GFR <70 ml / 1.73 m², split function less than 15%, psychiatric illness and patient with Grade IV and Grade V VUR were excluded. A validated questionnaire was filled by urology department residents in the supervision of urology consultant to minimize the chances of error. Statistical package of social sciences (SPSS) version 23 was used to enter, sort, and analyze the data. Descriptive characteristics included age, gender, weight, and height were analyzed in mean \pm standard deviation. Independent variables were analyzed with frequency. Pre-operative laboratory details, co-morbidities, medical history, and imaging reports were included to compare the results of procedure. Post-operative complication, success rates were analyzed as end point of study.

Procedure

After Aseptic measures and draping, patient is placed in lithotomy position. Instruments used are Paediatric nephroscope of 8fr in children and flexible plastic endoscopic needle of 20 gauge with length of 35 cm. Careful evaluation of meatus, anterior and posterior urethra, bladder neck, bladder wall mucosa, ureteric orifices were done to rule out any secondary cause of VUR like meatal stenosis, PUV or cobbs' collar. We usually use 3 techniques for Dextranomer/Hyaluronic Acid Copolymer (Deflux) Injection called STING (subureteric Teflon injection), HIT (hydrodistention-implantation technique) and double HIT technique. In STING technique, we inject Dextranomer/Hyaluronic Acid Copolymer in submucosal subureteric region which results in a slit like orifice and in HIT technique we inject Dextranomer/Hyaluronic Acid Copolymer submucosally in intraureteric region. The technique and amount of injection needed depends on the evaluation of ureteric orifice. After procedure, Foley's catheter is placed which is removed on the 1st post-operative day.

RESULTS

This study includes 21 patients with a mean age of 4.9 \pm 3.4 years (1 month to 10.9 years), who presented with vesico ureteric reflux at the urology department of Tabba Kidney Institute. The gender distribution of participants was 5 (23.8%) males and 16 (76.1%) females with mean weight measuring as 17.5 \pm 8.3Kgs.

Table 1: Demographic details of participants

Demographics (n=34)		
Variables	Mean \pm St. deviation (Range)	
Age (years)	4.9 \pm 3.4 (10.9)	
Weight (Kgs)	17.5 \pm 8.3 (26.9)	
Gender	Male	5 (23.8%)
	Female	16 (76.1%)
Laterality	Unilateral	8 (38.1%)
	Bilateral	13 (61.9%)
Antenatal HDN	Yes	2 (9.5%)
	No	19 (90.4%)
HB	11.1 \pm 1.6 (5.9)	
Hematocrit	32.4 \pm 3.6 (12)	
TLC	10.4 \pm 5.4	
PLT	344 \pm 107.1	
Urea	21.1 \pm 8.0	
Creatinine	0.4 \pm 0.1 (0.6)	

The sample size was calculated with the help of a previously published study from Bahrain* total sample size for 5 years was 30 patients and 50 renal units, upon

adding 50 renal units as population size, we got the minimum sample size of 30 RUs. After obtaining approval from the institutional ethical committee, patients were enrolled based on initial diagnosis. Informed consent was signed by parents and/or guardians of patients with a complete consulting from the primary investigator. Although the study period was decided as 6 months but the mark of 30 renal units was not achieved in the mentioned time; the study, however, was completed over a span of 1 year. Upon categorization of laterality of VUR, 8 (38.1%) had unilateral VUR and 13 (61.9%) had reported bilateral VUR, making it 34 renal units (RU). Patients had 15 (44.1%) right and 18 (52.9%) left refluxing RUs, distributing patients within Grades of VUR results indicated 3 (8.8%) RUs for Grade 1 VUR, 9 (26.4%) RUs for Grade II, 13 (38.2%) for Grade III, 5 (14.7%) RUs for Grade IV, and 3 (8.8%) RUs for Grade V. After an initial assessment, laboratory investigations were performed, results were represented in mean values of hemoglobin,

hematocrit, total leucocyte count, platelets, serum urea, and creatinine level preoperatively as 11.1 ± 1.6 , 32.4 ± 3.6 , 10.4 ± 5.4 , 344 ± 107.1 , 21.1 ± 8.0 and 0.4 ± 0.1 respectively. Range of hemoglobin was measured as 7.6-13.5 and the range of serum creatinine was measure as 0.25 - 0.82. Patients were assessed pre-operatively and post-operatively for Urinary tract infections, Hydronephrosis, and symptoms such as fever, dysuria, and frequency associated with grades of VUR. Upon analysing urinary tract infection, pre-operative results indicated positive urine culture in all patients with a maximum number of E.coli as infecting organism followed by Klebsiella, acinetobacteria, and pseudomonas. After procedure only VUR Grade IV and V VUR patients indicated positive urine culture on the first urine CS reporting 90% resolution; however, all patients of Grades I, II, III and IV had 100% resolution from UTI after the procedure, whereas Grade V VUR patients indicated 70% resolution (Table 02).

Table 2: Pre and post procedure Ultrasonography findings and resolution rate

Pre and post procedure Ultrasonography findings and resolution rate (n=34)							
Variables	MCUG Grading	Pre-OP US HDN		Post-OP US HDN		Resolution	
VUR grading (n=34)	G I (n=3)	No HDN (n=3)	No HDU (n=3)	No HDN (n=3)	No HDU (n=3)	100%	
	G II (n=9)	No HDN (n=4)	No HDU (n=1)	No HDN (n=3)	No HDU (n=3)	100%	
			HDU (n=1)				
		Fullness of PCS (n=4)	No HDU (n=1)				
	G III (n=14)	No HDN (n=2)	No HDU (n=1)	No HDN (n=5)	Fullness of PCS (n=1)	No HDU (n=7)	100%
		Mild HDN (n=3)	HDU (n=6)				
		Mod HDN (n=1)					
		Fullness of PCS (n=1)					
	G IV (n=5)	Mild HDN (n=4)		HDU (n=5)	Mild (n=2)	HDU (n=1)	50%
		Mod HDN (n=1)	No HDN (n=3)		No HDU (n=4)	100%	
G V (n=3)	Mod HDN (n=1)	HDU (n=1)	Fullness of PCS (n=1)	No HDU (n=1)	50%		

The second assessment point was ultrasonography findings as hydronephrosis and hydroureter pre-operatively and post-operatively, results indicated no HDN in Grade I & II, while for Grade III patients only one

indicated fullness in PCS. However, in grade IV, 2 out of 5 RUs indicated mild HDN, but both were symptoms and UTI free on the follow up of three months and further resolution of HDN and HDU on second follow up ultrasound. In Grade V category, 1 out of 3 RUs showed resolution to fullness of PCS on ultrasound while one patient showed treatment failure and was proceeded for laparoscopic ureteric re-implant. 1 patient with moderate HDN of Grade V VUR needed second injection to resolve the HDN. Post-operative ultrasonography results indicated 100% resolution in Grade I and II VUR, while 75% resolution in Grade III VUR, 50% resolution in Grade IV VUR, whereas 25% resolution in Grade V VUR (Table 03).

Symptoms evaluated are represented in Table 04 along with complete or partial resolution post-operatively,

results showed a gradual decline of resolution with increasing grading of VUR, Grade I and II indicated 100% resolution of symptoms, while Grade III showed 90% resolution, Grade IV had 80% resolution and Grade V had only 33% resolution with 2/3 results.

Overall results regarding UTIs, HDN, and symptoms are elaborated in Table 05 and indicated that Grades I and II had 100% resolution in both groups. Grade III had 95% resolution, while Grade IV and V showed 93% resolution and 66.6% resolution respectively.

Overall results regarding UTIs, HDN, and symptoms are elaborated in Table 05 and indicated that Grades I and II had 100% resolution in both groups. Grade III had 95% resolution, while Grade IV and V showed 93% resolution and 66.6% resolution respectively.

Table 3: Pre and post procedure Urine culture

Pre and post procedure Urine culture (n=34)							
Variables	MCUG Grading	Pre-OP Urine CS			Post-OP Urine CS		
		First Urine CS	Second Urine CS	Third Urine CS	First Urine CS	Second Urine CS	Resolution
VUR grading (n=34)	G I (n=3)	E.Coli (n=3)	E.Coli (n=3)		No Growth (n=3)	No Growth (n=3)	100%
	G II (n=9)	E.Coli (n=7)	E.Coli (n=7)	E.Coli (n=1)	No Growth (n=9)	No Growth (n=9)	100%
		Klebsiella (n=1)	Pseudomonas (n=1)				
		Actinobacteria (n=1)	Klebsiella (n=1)				
	G III (n=14)	Klebsiella (n=2)	E.Coli (n=13)		No Growth (n=14)	No Growth (n=14)	100%
		E.Coli (n=11)					
		Actinobacteria (n=1)					
	G IV (n=5)	E.Coli (n=5)	E.Coli (n=5)		E.Coli (n=1) No Growth (n=4)	No Growth (n=5)	100%
	G V (n=3)	E.Coli (n=3)	E.Coli (n=3)	Pseudomonas (n=2)	Pseudomonas (n=1)	No Growth (n=2)	67%

Table 4: Pre and post procedure symptoms and resolution rate

Pre and post procedure symptoms and resolution rate (n=34)					
Variables	MCUG Grading	Pre-OP Symptoms	Post-Op Symptoms	Resolution	
VUR Grading (n=34)	G I (n=3)	Present (n=3)	Resolved (n=3)	100%	
	G II (n=9)	Present (n=9)	Resolved (n=9)	100%	
	G III (n=14)	Present (n=14)		Resolved (n=13)	90%
				No resolved (n=1)	
	G IV (n=5)	Present (n=5)		Resolved (n=4)	80%
				No resolved (n=1)	
G V (n=3)	Present (n=3)		Resolved (n=1)	33%	
			No resolved (n=2)		

Table 5. Overall success rates combining all outcome variables

Overall success rates combining all outcome variables						
Variables	MCUG Grading	Resolution of Symptoms	Resolution of UTI	Resolution of HDN	Success rate	Resolution
VUR Grading (n=34)	G I (n=3)	100%	100%	100%	100%	100%
	G II (n=9)	100%	100%	100%	100%	100%
	G III (n=14)	95%	100%	95%	100%	95%
	G IV (n=5)	100%	90%	90%	90%	93%
	G V (n=3)	67%	67%	67%	67%	67%

DISCUSSION

The treatment of VUR was revolutionized after the introduction of endoscopic subureteral injection of Teflon in 1984 (O'Donnell B, 1984). Dextranomer/Hyaluronic acid was first used by Stenberg & Lackgren in 1995 (Stenberg A, 1995), and is now the most widely used agent for VUR treatment. Multiple studies have been done on the safety and efficacy of DX/HA which shows success of 68% to 92% depending on grades of VUR and it is the only bulking agent approved by FDA in treatment of VUR in paediatric population in 2001.

The Dx/HA is a non-immunogenic inert agent made up of dextranomer microspheres and sodium hyaluronate. Dx/HA injection creates a mechanical barrier and increases the intramural length of distal ureter which helps in VUR resolution. A reviewed study conducted by Mattoo and Greenfield in 2015 stated that, "Subureteric transurethral injection (STING procedure) comprises of injecting dextranomer/hyaluronic acid (Dx/HA), beneath the mucosa of the ureterovesical junction with the help of a cystoscope. This injection changes the angle and perhaps fixation of the intravesical ureter, thereby correcting reflux. The success rate with STING technique is 75% to over 90%. The success rate of a second STING procedure after an initial failed injection is high, ranging from 70% to 90%. We can also use STING technique in patients who had a failed previous open surgical reimplantation." (Aetna, 2021). Although reinjection may be needed after 5-7 years in patients with early success due to migration, biodegradation and absorption of bulking agent.

In a RCT published in World Journal of Urology, (Garcia-Aparicio L, 2018) compared the radiological and clinical success rate of polyacrylate polyalcohol copolymer (PPC) and Dx/HA. He took the results of 44 patients with 73 refluxing renal units (RRUs) and had success rate of 82% with Dx/HA and PPC after 1st injection with no statistical difference in terms of clinical and radiological success rate with mean follow up of 27.6 months. He further observed that ureteric reimplantation in patients previously treated with PPC was difficult as compared to the patients who were treated with Dx/HA due to periureteric fibrosis.

In our study, we achieved total success rate of 91.4%

with endoscopic injection of Dx/HA in terms of clinical and radiological outcomes. Patients with grade I to grade III VUR had 100% success rate in terms of resolution of symptoms, UTIs and radiological findings. In Grade IV VUR patients also had 90% success rate with complete resolution of symptoms and UTIS; however, 1 patient had residual pelvicalyceal system dilatation but his symptoms and UTIs were resolved. We had poor results in patients with grade V VUR. Only 1 patient showed complete success and resolution after 1st injection and 2 patients had positive Urine c/s and hydronephrosis with HDU. 1 patient required 2nd endoscopic injection and his UTI and symptoms resolved and hydronephrosis settled. However, 1 patient underwent ureteric reimplant and we had no difficulty in it.

In 2019, Bele & Bratus also did a retrospective study (Bele U. 2019) in which they compared the efficacy of endoscopic injection of Dx/HA with PPC in 125 patients treated with endoscopic injection of bulking agent and follow up of 12 months with VCUG at 3 and 12 months and found the success rate of 94% with PPC and 88% with Dx/HA with no statistical difference.

In 2016, Pogoreli et al. compared deflux with Vurdex (also a bulking agent) for treatment of VUR in which deflux achieved 93.3% while Vurdex achieved 94.8% success rate. We also achieved success rate of 67% – 100% with DX/HA in our patients depending on the grade of VUR. Patient with Grade I, II and III showed 100% success rate, whereas Grade IV and V showed 90% and 67% success rate respectively (Pogorelic Z, 2016).

A study conducted by Kirsch & Arlen in 2014 (Kirsch AJ, 2014) reported that HIT method (hydrodistention implantation technique) has comparable results to sting technique used for bulking agent and again in 2014, he reported that double HIT method is the most widely used technique for treating high grades VUR by paediatric urologists in United States. We also use all the techniques depending on the ureteric orifice shape, dilation, and grade of VUR. In our study, four patients (2 from Grade IV and 2 from Grade V) were treated by HIT and Double HIT technique.)

In 2018, Friedmacher et al. took the data of 851 patients of grade IV and V VUR patients treated with Dx/HA endoscopic injection and reported in 2018 that Dx/HA is an efficient and safe treatment for Grade IV and

Grade V VUR with success rate of 70% and 61% after 1st injection of Dx/HA, 20.1% after 2nd injection and 10 percent after 3rd (Friedmacher F, 2018) However, in our study

We have achieved success rate of 93% in patients with grade IV VUR and 50% in patients with grade V VUR after 1st injection and 17% after 2nd injection. The reason maybe that we use HIT and double HIT techniques on regular basis depending on the grade of VUR.

In 2019, Lightfoot and her fellow colleagues assessed long term outcomes of endoscopic injection of Dx/HA in 575 patients (Lightfoot M, 209). They contacted and interviewed patients and their parents who were treated with endoscopic injection of Dx/HA and found success rate of 89% with Dx/HA treatment and 94% of parents were highly satisfied with this treatment modality. She also observed that 2 patients underwent ureteric reimplantation; 1 due to failed endoscopic injection and 1 who developed ureteral obstruction after 2.8 years after injection with Dx/HA. We had overall success rate of 91.4% and in our experience patient and parents were also highly satisfied with this treatment modality. Likewise, only one patient having failure of injection in Grade V underwent ureteric reimplantation (Stredle RJ, 2013)

Ureteral obstruction was not observed in any patient. Only Clavien-Dindo 1 complications like catheter irritation and mild hematuria were observed which were self-limiting and resolved spontaneously on 1st pod day. Patient recovery was uneventful.

Patients are still on follow-up up to date. In this study and in our routine practice, VCUG is not routinely performed after endoscopic injection of Dx/HA as it is an invasive and painful investigation and to reduce urethral manipulations on our patients. We believe that VCUG should only be performed in cases of recurrent UTIs post-injection or recurrent and persistent symptoms.

This study, however, has possibility of some limitations as the time period and small no of patients weakens the study which may lead to some biasness. Moreover, long term follow up is not available to assess long term outcomes of Dx/HA in treating VUR.

CONCLUSION

Our study shows that endoscopic injection of Dextranomer/Hyaluronic acid copolymer in treating VUR has overall good and comparable success rates in grade I to grade iv VUR with open surgery. It has lowest complication rate and avoids potential morbidity with open surgery. Patient and parents are mostly satisfied with endoscopic surgery. For grade V VURs, patients and parents can be counselled that this procedure has a 60% success rate and due to its minimal invasiveness can be undertaken with no extra added risks if further laparoscopic or open surgery is required later on.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

ACKNOWLEDGEMENT

I would like to acknowledge the urology department of TKI.

AUTHOR CONTRIBUTIONS

ME: Objective, manuscript writing

SS: Final approval of manuscript, procedure supervision

JH: Procedure assistance, data analysis

SSQ: data collection, ERC

AA: Data collection, surgery assistance

NSK: Data collection, surgery assistance

HA: Data collection, surgery assistance

Copyrights: © 2022@ author (s).

This is an open access article distributed under the terms of the [Creative Commons Attribution License \(CC BY 4.0\)](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author(s) and source are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

REFERENCES

- Abdelwahab HA, Ghoniem GM. Obstructive suburethral mass after transurethral injection of dextranomer/hyaluronic acid copolymer. *International urogynecology journal*. 2007 Nov;18(11):1379-80.
- Bele U, Bratus D. Dextranomer-Hyaluronic Acid and Polyacrylate-Polyalcohol Copolymer are Equally Efficient for Endoscopic Treatment of Vesicoureteral Reflux in Children. *Urology Journal*. 2019 Aug 18;16(4):361-5.
- Bomalaski MD, Hirschl RB, Bloom DA. Vesicoureteral reflux and ureteropelvic junction obstruction: association, treatment options and outcome. *The Journal of urology*. 1997 Mar 1;157(3):969-74.
- Chertin B, Arafeh WA, Zeldin A, Ostrovsky IA, Kocherov S. Endoscopic correction of VUR using vantris as a new non-biodegradable tissue augmenting substance: three years of prospective follow-up. *Urology*. 2013 Jul 1;82(1):201-4.
- Dwyer ME, Husmann DA, Rathbun SR, Weight CJ, Kramer SA. Febrile urinary tract infections after ureteroneocystostomy and subureteral injection of dextranomer/hyaluronic acid for vesicoureteral reflux—do choice of procedure and success matter?. *The Journal of urology*. 2013 Jan;189(1):275-82.
- Lightfoot M, Bilgutay AN, Tollin N, Eisenberg S, Weiser J, Bryan L, Smith E, Elmore J, Scherz H, Kirsch AJ. Long-term clinical outcomes and parental satisfaction after dextranomer/hyaluronic acid (Dx/HA) injection for primary vesicoureteral reflux. *Frontiers in pediatrics*. 2019 Sep 27;7:392.
- Friedmacher F, Colhoun E, Puri P. Endoscopic injection of dextranomer/hyaluronic acid as first line treatment in 851 consecutive children with high grade vesicoureteral reflux:

Ejaz et al. Endoscopic management of VUR

- efficacy and long-term results. *The Journal of Urology*. 2018 Sep 1;200(3):650-5.
- García-Aparicio L, Blázquez-Gómez E, Martín O, Perez-Bertolez S, Arboleda J, Soria A, Tarrado X. Randomized clinical trial between polyacrylate-polyalcohol copolymer (PPC) and dextranomer-hyaluronic acid copolymer (Dx/HA) as bulking agents for endoscopic treatment of primary vesicoureteral reflux (VUR). *World Journal of Urology*. 2018 Oct;36(10):1651-6.
- Kirsch AJ, Perez-Brayfield MR, Scherz HC. Minimally invasive treatment of vesicoureteral reflux with endoscopic injection of dextranomer/hyaluronic acid copolymer: the Children's Hospitals of Atlanta experience. *The Journal of urology*. 2003 Jul;170(1):211-5.
- Kim H, Kim BS, Cheong HI, Cho BS, Kim KM, Kim H, Kim BS, Cheong HI, Cho BS, Kim KM. Long-term results of endoscopic deflux® injection for vesicoureteral reflux in children. *Childhood Kidney Diseases*. 2015 Apr 30;19(1):31-8.
- Kirsch AJ, Arlen AM. Evaluation of new Deflux administration techniques: intraureteric HIT and Double HIT for the endoscopic correction of vesicoureteral reflux. *Expert Review of Medical Devices*. 2014 Sep 1;11(5):439-46.
- LÄCKGREN G, WÅHLIN N, SKÖLDENBERG E, STENBERG A. Long-term followup of children treated with dextranomer/hyaluronic acid copolymer for vesicoureteral reflux. *The Journal of urology*. 2001 Nov;166(5):1887-92..
- Lightfoot M, Bilgutay AN, Tollin N, Eisenberg S, Weiser J, Bryan L, Smith E, Elmore J, Scherz H, Kirsch AJ. Long-term clinical outcomes and parental satisfaction after dextranomer/hyaluronic acid (Dx/HA) injection for primary vesicoureteral reflux. *Frontiers in pediatrics*. 2019 Sep 27;7:392.
- Molitierno JA, Scherz HC, Kirsch AJ. Endoscopic treatment of vesicoureteral reflux using dextranomer hyaluronic acid copolymer. *Journal of pediatric urology*. 2008 Jun 1;4(3):221-8.
- Mazzone L, Gobet R, González R, Zweifel N, Weber DM. Ureteral obstruction following injection of dextranomer/hyaluronic acid copolymer: an infrequent but relevant complication. *Journal of Pediatric Urology*. 2012 Oct 1;8(5):514-9.
- Stredele RJ, Dietz HG, Stehr M. Long-term results of endoscopic treatment of vesicoureteral reflux in children: comparison of different bulking agents. *Journal of pediatric urology*. 2013 Feb 1;9(1):71-6.
- O'Donnell BA, Puri P. Treatment of vesicoureteric reflux by endoscopic injection of Teflon. *Br Med J (Clin Res Ed)*. 1984 Jul 7;289(6436):7-9.
- Puri P, Chertin B, Velayudham M, Dass L, Colhoun E. Treatment of vesicoureteral reflux by endoscopic injection of dextranomer/hyaluronic acid copolymer: preliminary results. *The Journal of urology*. 2003 Oct;170(4 Part 2):1541-4.
- Pogorelič Z, Gudelj K, Budimir D, Todorčić J, Jukić M, Furlan D, Košuljandić Đ, Saraga M. Comparison of dextranomer/hyaluronic acid based bulking agents in the treatment of vesicoureteral reflux in children: Deflux versus Vurdex. *Can J Urol*. 2016 Jun 1;23(3):8312-7.
- Stenberg A, Lackgren G. A new bioimplant for the endoscopic treatment of vesicoureteral reflux: experimental and short-term clinical results. *The Journal of urology*. 1995 Aug;154(2):800-3.
- Vandersteen DR, Routh JC, Kirsch AJ, Scherz HC, Ritchey ML, Shapiro E, Wolpert JJ, Pfefferle H, Reinberg Y. Postoperative ureteral obstruction after subureteral injection of dextranomer/hyaluronic acid copolymer. *The Journal of Urology*. 2006 Oct;176(4):1593-5.
- Yeung CK, Godley ML, Dhillon HK, Gordon I, Duffy PG, Ransley PG. The characteristics of primary vesico-ureteric reflux in male and female infants with pre-natal hydronephrosis. *British journal of urology*. 1997 Aug;80(2):319-27.