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MAY DMSA FINDINGS BE PREDICTIVE OF STING PROCEDURE FAILURE IN CHILDREN WITH PRIMARY VESICOURETERAL REFLUX? (AN EVALUATION OF 132 CASES)

DMSA BULGULARI PRİMER VEZİKOÜRETERAL REFLÜLÜ ÇOCUKLARDA STING PROSEDÜRÜNÜN BAŞARISIZLIĞINI ÖNCEDEN BELİRLEYEN BİR FAKTÖR MÜDÜR? (132 OLGUNUN DEĞERLENDİRİLMESİ)

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ABSTRACT

Purpose: Endoscopic treatment seems to be the first choice of therapy in most of the patients with vesicoureteral reflux (VUR) since it is easily applicable and repeatable without complication. Existence of relation between the DMSA results and recurrence of urinary tract infection in cases with VUR has been demonstrated in previous studies. We aimed to search a relation between the renal functions set by DMSA and the success of STING procedure in patients with primary VUR.

Material And Method: 132 patients on whom STING procedure has been applied for primary VUR at our clinic between the years 2002 to 2009 were evaluated retrospectively in this study. Initial findings of DMSA scintigraphy of the patients in relation to scarring degree at the hospital admission and their improvement after STING procedure were evaluated.

Findings: 132 cases were included in our study consisting of 36 (27%) males and 96 females (73%) in between the ages of 5 months to 16 years (mean 6,59±3,23). 113 cases (86%) referred for the complaints of recurrent urinary tract infection, 14 cases (10%) had enuresis and 5 cases (4%) diagnosed as prenatal hydronephrosis. VUR was detected in 194 ureters of the 132 patients. VUR was bilateral in 62 (47%) patients, on the right side in 29 (22%) patients and on the left side in 41 (31%) patients. Initially, grade II VUR in 10 (5, 1%) cases, grade III VUR in 79 (40,8%), grade IV VUR in 63 (32,4%) cases and grade V VUR in 42 (21,7%) cases were confirmed. Recovery was determined in 105 (54,68%) ureters after the first injection. Second injection was applied to 82 ureters resulting with recovery in 22 ureters. Additional recovery was achieved in 11 ureters after the application of third injection to 50 patients. Thus the initial success rate of 54,68% reached to a success rate of 71,13% with repeated injections. Open surgery was applied to 32 ureters of 24 patients in whom no positive response was noted after STING procedure. DMSA findings were normal in 19 (14%) patients and abnormal in 113 (86%) patients at the initial hospital admission. A significant negative correlation was detected between the grade of VUR and the recovery after STING procedure ($p>0,001$). DMSA findings were not predictive in the success of STING procedure in children with primary VUR on the same degree category ($p>0,05$).

Conclusion: Follow-up results are evaluated on an average of 42 month period in our study. VUR was treated in 54% of the ureters following the first injection and the recovery rate reached to 71% after the third injection. The results of this study revealed that the single meaningful parameter in estimating the recovery by STING application is the degree of VUR. There was no correlation between the initial DMSA findings and the success of STING procedure.

Key Words: Vesicoureteral reflux, DMSA

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ÖZET:

Amaç: Vezikoüreteral reflülü (VUR) olgularda endoskopik tedavi komplikasyonsuz, kolay uygulanabilir ve tekrarlanabilir olması nedeni ile pek çok hastada ilk tedavi seçeneği olarak görülmektedir. VUR'lu olgularda DMSA sintigrafi sonuçları ile idrar yolu enfeksiyonunun tekrarlaması arasında ilişki olduğu yapılan çalışmalarda gösterilmiştir. Çalışmamızda primer VUR'lu olgularda DMSA ile belirlenen renal fonksiyonlar ile STING uygulamasının başarısı arasında ilişki olup olmadığının araştırılması amaçlandı.

Materyal ve Metod: Kliniğimizde 2002 ile 2009 yılları arasında primer VUR nedeni ile STING uygulaması yapılan 132 olgu hastane kayıtlarından geriye dönük olarak değerlendirmeye alındı. Bu araştırmada olguların yaşı, cinsiyeti, reflünün tek ya da çift taraflı olması, reflünün derecesi, başvuru anındaki bulguları ve ilk DMSA sintigrafi bulgusundaki hasarlanma derecesi ile STING uygulaması ile VUR iyileşmesi arasındaki ilişki araştırıldı.

Bulgular: Çalışmamıza yaşları 5 ay ile 16 yaş (ortalama 6.59+3.23) arasında değişen 36 erkek (%27), 96 kız (%73) toplam 132 olgu alındı. 113 olgumuz (%86) tekrarlayan idrar yolu enfeksiyonu yakınması ile başvururken, 14 (%10) olgu enürezis nedeni ile yapılan araştırma sırasında, 5 olgu (%4) prenatal saptanan hidronefroz bulgusunun araştırılması sırasında tanı aldı. Reflü 62 (%47) olguda bilateral, 29 olguda (%22) sağ, 41 olguda (%31) sol tarafta belirlendi. 132 olguda toplam 194 üreterde reflü saptandı. Başlangıçta 10 olguda grade 2 VUR (%5.1), 79 olguda grade 3 VUR (%40.8), 63 olguda grade 4 VUR (%32.4), 42 olguda grade 5 (%21.7) VUR saptandı. İlk enjeksiyon sonrası 105 üreterde iyileşme saptandı (%54.68). İkinci enjeksiyon 82 üretere uygulandı. İkinci enjeksiyon sonrası 22 üreterde iyileşme saptandı. 50 olguya yapılan üçüncü enjeksiyon sonrası 11 üreterde daha iyileşme izlendi. Başlangıçta %54.68 olan başarı oranı, tekrarlanan enjeksiyonlar ile % 71.13'e kadar ulaştı. 24 olgumuzdaki 32 üretere STING uygulamasına yanıt alınamadığı için açık cerrahi girişim uygulandı. 19 olguda (%14) DMSA sintigrafisi normal iken, 113 olguda (%86) anormal olarak bulundu. STING ile iyileşen ya da açık cerrahi uygulamasına alınan olgularımız yaş, cinsiyet, VUR'un tek yada bilateral olması, başlangıç bulguları ve başlangıç DMSA bulguları açısından karşılaştırıldığında anlamlı herhangi bir fark bulunmadı. Reflü derecesi ile STING sonrası iyileşme arasında ise negatif corelasyon mevcuttu ($p<0.001$). Aynı grade'deki olgularda DMSA bulguları arasındaki farkın STING uygulamasına yanıtı etkilemediği görüldü ($p>0.05$).

Sonuç: Ortalama 42 aylık izlem sonuçlarının irdelendiği serimizde endoskopik ilk enjeksiyon sonrası üreterlerin % 54'ünde reflünün iyileştiği saptanırken, üçüncü enjeksiyon sonrası bu oranın % 71'e yükseldiği görüldü. Bu çalışmanın sonuçlarına göre STING uygulaması ile reflünün düzelmesinde anlamlı olan tek parametre reflünün derecesi olduğu ve başlangıç DMSA incelemesinde saptanan fonksiyon bozukluğu ile STING uygulaması başarısı arasında herhangi bir ilişki olmadığı saptandı.

Anahtar Sözcükler: Vezikoüreteral reflü, DMSA

INTRODUCTION

Vesicoureteral reflux (VUR) is defined as the backflow of urine from bladder to ureter and kidney and is the most frequent urinary system anomaly leading to recurrent urinary tract infection in childhood. 30 to 60% of the children with VUR have renal scars at the time of diagnosis (1,2). Reflux nephropathy resulting from renal scarring causes hypertension in 20% of the cases and leads to the end stage renal disease in 10% of the cases (3,4). The aim of VUR treatment is to protect the patient from renal function loss by preventing urinary tract infection (5,6).

Long term antibiotic prophylaxis, open surgery and endoscopic approaches are the main options of the treatment of VUR. Especially endoscopic subureteric injection practice has gained importance for the last 20 years and is substituting open surgical approaches and long term antibiotic prophylaxis (7,8). Endoscopic treatment seems to be the first choice in many of the patients since it is easy to apply without complication and repeatable when required (9, 10,11). Although success rates of endoscopic applications are noted between 64% to 100%, there are publications reporting the recovery rates dropping to 45% on follow-up exceeding 1 year (12,15,16). It has been demonstrated that recurrence of urinary tract infection is more frequent in patients with VUR who have renal function disorders in scintigraphy (17,18). Recurrent urinary tract infections leads to a vicious cycle by increasing reflux (19,20). Unpreventable urinary tract infection and occurrence of renal scarring on follow-up are the main indications for surgical treatment options (21).

CASES AND METHODOLOGY

132 cases on which STING procedure was applied for primary VUR during 2002 to 2009 in our clinic were evaluated retrospectively on hospital records. The diagnosis and degree of VUR was set by Voiding Cystouretrography (VCUG) on the basis of international reflux classification between I to V in all of the cases (22). Cases with neurogenic bladder, posterior urethral valve, ectopic ureter, extrophy and epispadias complex and the cases with ureterocele were not included in the study. DMSA surveys were made at least 3 months after the cease of urinary tract infection in all of the cases to exclude the temporary focal ischemic image due to acute pyelonephritis. Urodynamic studies were also ruled on our patients suspected of dysfunctional urination.

Subureteral injection was applied to patients over 1 year age with grade II and III reflux who had recurrent urinary tract infection despite the antibiotic prophylaxis and to cases with grade IV and V VUR. STING procedure was also applied to children under 1 year age with high degree (Grade IV-V) VUR. Injection procedure was carried out by using at the amounts of 0.5 cc to 3 cc injection material to provide a bump at the ureteral orifice. Injection by double hit technique was not applied to any of our cases included in the study.

According to DMSA functions, the cases were evaluated as mild disturbance with 40% to 45%, moderate disturbance with 20% to 40% and as severe with findings below 20% (23). The initial DMSA findings were evaluated in terms of effecting the success of STING application; besides this, effects of sex, age, complaints at admission, degree of reflux and the side of the reflux on the response to injection were also evaluated. Results were analyzed on SPSS program with t-test and Logistic regression; $p<0,05$ was accepted as meaningful.

FINDINGS

36 (27%) males and 96 (73%) females between the ages of 5 months to 16 years (mean 6.59±3.23 years) were included in our study. Average follow-up time was 42.5 ±8.3 months. 113 (86%) of the cases referred with the complaints of recurrent urinary infection. 14 (10%) of the cases were diagnosed during the investigation of enuresis and 5 (4%) cases were diagnosed while searching prenatally diagnosed hydronephrosis. Reflux was bilateral in 62 (47%) of the cases, on the right side in 29 (22%) and on the left side in 41 (31%) of the cases. Reflux was demonstrated in totally 194 ureters of the 132 cases. Initially there was grade II VUR in 10 (5.1%) ureters, grade III VUR in 79 (40.7%) ureters grade IV VUR in 63 (32.4%) ureters and grade V VUR in 42 (21.7%) ureters.

Following the first injection recovery was noted in 105 (54.68%) ureters. Second injection was applied to 82 ureters. Recovery was noted 22 more ureters after the second injection. Following the application of third injection to 50 cases, healing was assessed in 11 more ureters. Initial success rate of 54.68% reached to 71.13% with repeated injections (Table 1). Median age of the healing patients (6.43 years) was higher in respect to non-recovering patients (4.49 years). It was estimated that STING application was successful in a total of 149 (76.8%) ureters when taking into consideration the cases whose reflux dropped to grade II. Our cases whose reflux has decreased are on the follow-up and they are free of recurrent urinary tract infection. There is no knowledge about 13 ureters since they failed follow-up.

19 (14.49%) of the cases had normal DMSA results. 54 (40.9%) of the cases had mild degree functional depression. Functional loss was moderate in 24 (18.2%) cases and severe in 35 (26.5%) (Table 2). 18.5% of the cases recovering after STING application were from the cases with normal DMSA findings, 37% from the group with mild function loss, 18.5% from the group with moderate function and 25.9% from the group with severe function loss group respectively.

No positive response was deducted in 32 ureters of our 24 cases so open surgery was applied to them. Grade of the reflux has an important effect on the recovery ($p=0,001$). According to regression analysis sex ($p=0,460$) and age ($p=0,052$) of the patients, side of the reflux ($p=0,839$) and DMSA findings ($p=0,068$) are not

Table 1. The results of STING application

The number of ureter that applied STING	Healing ureter		Number of ureter which went to open surgery
	Number	%	
First injection (n= 194)	105	54.68	2
Second injection (n= 82)	22	26.82	7
Third injection (n= 5 0)	11	22	23
Total	138	71.13	32

Table 2. The distribution of renal scars

The degree of feflux	No scar	Mild Scar	Modarate Scar	Serious Scar	Total
2	9	1	-	-	10
3	13	39	9	18	79
4	4	26	14	19	63
5	2	13	12	15	42
Total	28	79	35	52	194

influencing the recovery (p>0,05). Grade I to III reflux on the contralateral side was determined in 10 of the cases undergoing STING procedure. In 11 cases, the degree of the reflux reduced and no recurrent urinary tract infection was encountered therefore additional therapeutic measures were not required. Recurrent urinary tract infection was noted in 6 of our cases during follow-up. In one of our cases, hematuria lasting for two days was noted with no additional complication.

DISCUSSION

Relation between urinary tract infection and VUR with renal parenchymal injury has been outlined with all details (24). Renal scarring may occur related to the interstitial inflammation caused by infective urine or to mechanical or immunological processes caused by sterile urine. It can also be due to renal dysplasia occurring in relation to abnormal embryological development (25). Cases with reflux nephropathy compose 3% to 25% of the end stage renal insufficiency patients in the pediatric age group (26). In many of the cases, VUR recovers spontaneously however it has been reported that renal scarring occurs at the rates of 4.7% to 23% during the waiting time (27).

There is no consensus on when to prefer surgery or when to prefer medical treatment in the cases of VUR (8.28%). In the preference of the surgical attempt not only the degree of the reflux but function of the contralateral kidney, bladder capacity and function, presence of additional urinary system anomaly is important. Age of the patient and harmony to taking medicine and preference of the family must be taken into consideration. Surgical interventions has high complication rates especially in high degree reflux with dilated ureters and in infants. It is expressed that reflux persists at a rate of 19.3% following open surgical procedures in cases with high degree reflux. Obstruction requiring reoperation is also encountered at the rates of 0.3% to 9.1% after the operation in cases with high degree reflux (8). Tending to subureteric injection is increasing in relation to surgical reimplantation procedures being apt to complications. It is reported in a study that the parents have preferred endoscopic treatment practice at a rate of 80% among the three treatment choices being explained to them in details (29).

Endoscopic treatment of VUR is widespread administered with success in children since 1984 as an alternative to open surgical approaches or medical treatment (13, 15, 30). In series in which endoscopic treatment and antibiotic prophylaxis has been practiced randomly STING has been successful at a rate of 69% where a success rate of 38% has been provided in the medical treated group (14). Subureteric injection procedures are getting widespread in relation to the safety and ease in application of the injection material. The preferred material must be easily injected, must not migrate, must not have systemic side effects and must have permanent efficiency. The injection material we used in our series is a copolymer of hyaluronic acid and we did not encounter any complication or allegic reaction. In the rates of 100% success with repeated injections has been reported and successful outcomes are published after application in complicated cases of VUR following open surgery which has increased the popularity of the procedure (13, 14).

The success of STING procedure is reported as 78.5% in grade I and II reflux, 72% in grade III, 63% in grade IV and 51% in grade V reflux at the meta analysis evaluation (32). VCUG results 3-4 months after the procedure are taking place in most of the evaluations but long term follow-up results are not explained (16).

Results in an average of 42 month follow-up are explicated in our series. Reflux was treated after the first injection at a rate of 54% and increased to 71% after the third endoscopic injection. Recovery was provided in all of the cases with grade II VUR. Success was obtained in 96% of the ureters with grade III, 55% of the ureters with grade IV and 40% in grade V respectively (Table 3).

It is observed both from our results and the literature that the most significant factor designating the success of STING procedure is the degree of the reflux. Cases at the low age group are not responsive to STING application. The regression analysis showed that age was not effective on recovery as an independent variable (p=0,052). A relation between the gravity of VUR and abnormal DMSA results is stated in a lot of studies (33,35). No meaningful difference was noted in comparison of the cases in the series of VUR according to their response to STING application in relation to DMSA findings (p=0,068).

As for a result, it is deducted that endoscopic VUR treatment is the first choice of treatment modality to be applied because of its high success rate in cases with low grade VUR and low complication rate. Grade of the VUR is the most important factor to affect the success of STING application. Initial DMSA findings are not important in predicting the success of STING application.

Table 3. The distribution of resolution after STING according to the degree of VUR

The degree of reflux	1st injection		2nd injection		3rd injection		Total	
	Number	%	Number	%	Number	%	Number	%
II	10	100	-	-	-	-	10	100
III	58	73.4	11	13.9	7	8.8	76	96.2
IV	26	41.2	7	11.1	2	3.1	35	55.5
V	11	26.1	4	9.5	2	4.7	17	40.4
Total	105		22		11		138	71.1

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