

## Current Perspectives in Management of Vesicoureteral Reflux

SHANDIP KUMAR SINHA<sup>1</sup> AND AMIT AGARWAL<sup>2</sup>

*From the Departments of <sup>1</sup>Pediatric Surgery and Pediatric Urology, and <sup>2</sup>Pediatric Nephrology;*

*Madhukar Rainbow Children Hospital, Delhi, India*

*<sup>1</sup>shandips@gmail.com*

Vesicoureteral reflux (VUR) is a major contributor to renal morbidity in children and its management is controversial. The two major goals of management of VUR have been prevention of urinary tract infection (UTI) and renal damage. The treatment options for VUR include watchful waiting, continuous antibiotic prophylaxis (CAP), and endoscopic (injection of tissue bulking substances) and surgical (open, laparoscopic, robotic) strategies. Each of these has certain advantage and disadvantages. Continuous antibiotic prophylaxis (CAP) has been efficacious in reducing the risk of UTI in children with VUR and evidence for the same is based on sufficiently powered studies [1]. However, CAP may be hampered by poor compliance; the Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) trial showed that one-third of the participating children needed to be withdrawn from the study because of non-compliance [1]. Whether CAP can reduce the risk of renal damage is another area of concern, as in a recent meta-analysis, it was not associated with decrease in new renal scarring [2]. In this context, the endoscopic management of VUR seems to be an attractive option, more so in our set-up, where compliance and long-term follow up can be problematic.

It is with great interest that we read the article by Rao, *et al.* [3] published in the current issue of *Indian Pediatrics*, on the long-term outcomes of more than 500 children and 767 renal units, in which endoscopic management of VUR has been done. As was evident from this study, endoscopic management offers a one-time solution for majority of children with VUR, with a resolution rate of 90% of children. However, we need to remember that resolution of VUR is never the end-point in its management, as the primary aim of treatment remains prevention of UTI and renal damage.

The incidence of febrile UTI after endoscopic treatment had been reported to be in 0.75% of children in a meta-analysis [4]. Rao, *et al.* [3] have shown 96% success in symptomatic relief (preventing UTI),

establishing endoscopic therapy as a reliable treatment option for preventing UTI.

The other major treatment goal, *i.e.*, ability of endoscopic therapy to protect against renal damage is still unclear with only few studies evaluating this outcome. In the present study by Rao, *et al.* [3], a fresh scar was seen in 1% of cases at mean follow-up of 27 months after endoscopic treatment; although, approximately 50% of cases had scars before injection. Similar results in terms of development of new scars have been documented earlier by Chertin, *et al.* [5]. However, they raised concern regarding renal function deterioration on follow-up. Rao, *et al.* [3] have not commented on the deterioration in renal functions; albeit, they have reported that there was no improvement in renal units who had poor function before endoscopic treatment and few of them had to undergo nephrectomy. It will be interesting to know what happens to those renal units on long-term follow-up, in which VUR had been corrected and no fresh scars are formed.

The open surgical treatment of VUR has had a long history, but now with increased knowledge about natural history of VUR, it is now being used more selectively. In a meta-analysis, Wheeler, *et al.* [6] analyzed that surgery has only a minimal benefit over antibiotics alone. Although compliance can be an issue with CAP, open surgery is associated with abdominal incision, hospital stay, temporary urinary catheter, possible damage to trigone, and possibility of bladder dysfunction. In an interesting article published recently, it was seen that after careful explanation, although CAP was parental preference of all children with VUR, approximately 30% of parents also considered open surgery as a mode of treatment [7].

Since the approval of endoscopic treatment of VUR by dextranomer/hyaluronic acid co-polymer in 2001 by FDA, concerns regarding its long-term success rates and long term complications like delayed ureteral obstructions have emerged [8-10]. Swedish reflux trial reported a recurrence rates of 20% after two years of

endoscopic treatment [8]. Lee, *et al.* [9] reported overall recurrence of 46%. Rao, *et al.* [3], in this study, reported only six late recurrences after many years. This suggests that regular follow-up is required to evaluate the long-term durability of endoscopic treatment, even though postoperative VCUG had shown success of procedure.

It is interesting to note that the popularity of endoscopic injection has decreased in last few years, although the number of open surgical interventions have remained same [11]. The decrease in the popularity of endoscopic treatment can be attributed to evolving concept of benign nature of lower grade reflux, which neither require too much investigations or treatment. For higher grade reflux, open surgical interventions have been used, based on a belief that endoscopic treatment is not dependable for higher grade reflux. In this context, the current study is relevant as it suggests that even for higher grades of reflux, endoscopic treatment by an experienced person can provide good results. The other reasons for decreasing popularity of endoscopic treatment, as suggested by Rao, *et al.* [3], are cost and availability of tissue bulking substance – dextranomer/hyaluronic acid co-polymer.

To conclude, although many guidelines are available for management of VUR, it is still a clinical art in which the clinician has to incorporate many variables like age, grade of reflux, history of previous febrile UTI, existing renal scarring, other urogenital malformations, compliance to treatment, patient's preferences, availability of resources, and available scientific evidence for each mode of treatment, in order to decide the appropriate management strategy with ultimate aim of prevention of recurrent UTI and renal damage.

*Funding:* None; *Competing interests:* None stated.

## REFERENCES

1. RIVUR Trial Investigators, Hoberman A, Greenfield SP, Mattoo TK, Keren R, Mathews R, *et al.* Antimicrobial prophylaxis for children with vesicoureteral reflux. *N Engl J Med.* 2014;370:2367-76.
2. Wang HH, Gbadegesin RA, Foreman JW, Nagaraj SK, Wigfall DR, Wiener JS, *et al.* Efficacy of antibiotic prophylaxis in children with vesicoureteral reflux: systematic review and metaanalysis. *J Urol.* 2015;193:963-9.
3. Rao KLN, Menon P, Samujh R, Mahajan JK, Bawa M, Malik MA, *et al.* Endoscopic management of vesicoureteral reflux and long-term follow-up. *Indian Pediatr.* 2018;55:1046-9.
4. Elder JS, Diaz M, Caldamone AA, Cendron M, Greenfield S, Hurwitz R, *et al.* Endoscopic therapy for vesicoureteral reflux: a meta-analysis. I. Reflux resolution and urinary tract infection. *J Urol.* 2006;175:716-22
5. Chertin B, Natsheh A, Fridmans A, Shenfeld OZ, Farkas A. Renal scarring and urinary tract infection after successful endoscopic correction of vesicoureteral reflux. *J Urol* 2009;182(4Suppl): 1703-6.
6. Wheeler D, Vimalachandra D, Hodson EM, Roy LP, Smith G, Craig JC. Antibiotics and surgery for vesicoureteric reflux: a meta-analysis of randomised controlled trials. *Arch Dis Child.* 2003;88:688-94.
7. Tran GN, Bodapati AV, Routh JC, Saigal CS, Copp HL. Parental Preference Assessment for Vesicoureteral Reflux Management in Children. *J Urol.* 2017;197:957-62.
8. Holmdahl G, Brandstrom P, Lackgren G, Sillen U, Stokland E, Jodal U, *et al.* The Swedish reflux trial in children: II. Vesicoureteral reflux outcome. *J Urol.* 2010;184:280-5.
9. Lee EK, Gatti JM, Demarco RT, Murphy JP. Long-term followup of dextranomer/hyaluronic acid injection for vesicoureteral reflux: late failure warrants continued followup. *J Urol.* 2009;181:1869-74.
10. Okawada M, Murakami H, Tanaka N, Ogasawara Y, Lane GJ, Okazaki T, *et al.* Incidence of ureterovesical obstruction and Cohen antireflux surgery after Deflux® treatment for vesicoureteric reflux. *J Pediatr Surg.* 2018;53:310-2.
11. Herbst KW, Corbett ST, Lendvay TS, Caldamone AA. Recent trends in the surgical management of primary vesicoureteral reflux in the era of dextranomer/hyaluronic acid. *J Urol.* 2014;191 (5 Suppl):1628-33.