Does the ureteric jet Doppler waveform have a role in detecting vesicoureteric reflux?

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Abstract Data reported in this issue of *Pediatric Nephrology* suggest that the ureteric jet Doppler waveform can predict the occurrence of vesicoureteric reflux (VUR). Many different methods are currently used to detect VUR, including traditional X-ray micturating cystourethrogram, indirect and direct nuclear imaging and contrast enhanced ultrasonography. These methods are invasive, do have some radiation burden and are also quite uncomfortable to paediatric patients. This relatively new non-invasive method is therefore of interest, but its efficacy needs to be confirmed in further studies and, in particular, in babies and infants before it can possibly be considered as a good method to provide clinical information on VUR. Once such studies have been performed, this method may also prove to be a useful approach to obtain modern knowledge on the occurrence of VUR in healthy children.

Keywords Vesicoureteric reflux · VUR · MCUG · Prophylactic antibiotics · Kidney scarring · Ultrasonography · Ureteric jet Doppler waveform

Introduction

The clinical importance of vesicoureteric reflux (VUR) has, during the last decade, become a highly debated issue. Most older guidelines recommend a micturition cystography (MCUG) for children who have had a urinary tract infection (UTI). More recent guidelines, written by the National Institute of Health and Clinical Excellence (NICE) in the UK and the American Academy of Pediatrics, recommend a

more selective and much more restrictive approach on when to do an MCUG [1, 2].

Reasons for changes

This change in recommended practices has several underlying reasons. Questions have been raised on the actual benefit in terms of clinical management of knowing about VUR in a child who has experienced a single uncomplicated episode of acute pyelonephritis [3]. The efficacy of anti-reflux surgery has been compared to that of prophylactic antibiotics in several well-performed studies [4–7]. In these studies, surgery could not be shown to reduce the number of children who developed new renal scars; this was true also for children with quite marked reflux, namely, Grade III or IV.

The efficacy of prophylactic antibiotics in preventing UTIs and further renal scarring has been tested in a number of recent studies [8–12] which were summarised in a meta-analysis in American guidelines [1]. This meta-analysis could not show any benefit from antibiotic prophylaxis over placebo treatment—irrespective of grade of VUR.

Another important reason to radically reduce the use of MCUG is that most children find the procedure quite challenging and painful. The procedure is also associated with a small radiation burden and the risk of introducing an infection.

Natural prevalence of VUR

The prevalence of VUR in healthy children is not fully known. It has, based on results from early studies, been assumed to be very low (only a few percent). In contrast, one early study did show that 30 % of 102 healthy children between the age of 2 days and 5 years had VUR [13] and

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that as many as 64.7 % of infants showed reflux. The reflux seemed to disappear with age, and none of the older children who were studied at the age 5 years showed VUR. This study has, however, been criticised for using a too high filling pressure of the bladder during the MCUG and thus of “creating” VUR.

A recent retrospective Finnish study re-evaluated the diagnosis of UTI in 406 children aged less than 5 years who had had an MCUG [14]. The children were categorised into three groups on the basis of their initial urine findings [14]: those having had a certain ($n=276$), possible ($n=46$) or improbable ($n=25$) UTI. The occurrence of VUR was very similar in the three groups, namely, 36, 28 and 36 %, respectively.

In another study conducted by the same group, the UTI diagnosis in 2,036 children who had had an MCUG was reclassified. The children were grouped into five groups according to their initial urine data: proven, likely, unlikely or false UTI and no microbial data. The occurrence of VUR was 37.4 % in those with proven UTI and 34.8 % in those with a false diagnosis [15]. These data bring the previously found strong relationship between VUR and febrile UTI into question.

Interestingly, similar occurrences of VUR have been found when siblings were screened for VUR due to one sibling previously being diagnosed with reflux. A meta-analysis showed a prevalence of 27.4 (2.9–51.9)/100 screened siblings [16].

Gender difference

Modern guidelines and most clinicians still acknowledge that there are clinical circumstances where knowledge of the reflux status of a certain child is clinically important and will influence further management. The meta-analysis in the American guidelines did not separately analyse boys and girls [1]. The largest study on prophylactic antibiotics in children with high-grade reflux, the Swedish reflux study, did however find a significant gender difference [1, 8]. Treatment with prophylactic antibiotics in girls, but not in boys, reduced both the number of infections and the number of new renal scars [17]. The lack of benefit in the boys was due to the low number of recurrent infections that occurred in those boys who were not treated with antibiotics. The use of antibiotics in boys thus had very small chance to improve the outcome.

Other imaging modalities

Several other imaging modalities have been developed to investigate the occurrence of VUR, such as direct and

indirect nuclear studies and ultrasound imaging with ultrasound contrast medium injected into the bladder [18]. Both direct nuclear imaging and ultrasound with contrast medium involves catheterisation of the bladder. Indirect nuclear imaging can only be performed in potty trained children and is thus not possible in the most important group, namely, infants and toddlers. All of these methods also show a lower sensitivity than a regular MCUG [19].

It is therefore of great interest to develop accurate non-invasive methods to detect VUR. Consequently, the study by D’Souza et al. on the ureteric jet Doppler wave form as a marker for VUR in this issue of *Pediatric Nephrology* is an interesting step forward [20].

Researchers from Hong Kong have previously analysed the ureteric Doppler wave form in 1,010 subjects of all ages [21]. They found six different patterns, one of which was monophasic and seemed to represent an immature form. In a later study, the same group investigated 241 healthy and 98 other children who had a UTI [22]. The monophasic pattern was found in 29 % of the healthy children and varied greatly with age; in comparison, it was present in most infants before the age of 6 month and in 90.5 % of the children with proven VUR.

A research group in Slovenia has also investigated whether wave form analysis is a reliable predictor of VUR. In one study [23], they compared the waveform method with echo-enhanced voiding ultrasonography in 75 children between the age of 3 and 12 years. They found that the Doppler method had 88.5 % sensitivity and 82.3 % specificity compared to the voiding ultrasonography. In another study, the same group showed a good correlation between voiding ultrasonography and conventional X-ray MCUG [24].

In the study reported in the present issue of *Pediatric Nephrology* researchers from Bangalore in India take these findings further and compare analyses of the wave form pattern with the present gold standard, MCUG [20]. They unfortunately excluded the most interesting group of children, those younger than 2 years of age. These authors found the sensitivity for the wave form analyses to be 80.3 % and specificity 87.9 % in children aged 2–18 years.

In summary, analysis of the ureteric Doppler wave form may provide a future tool to investigate children for VUR. However, further studies are needed that compare this method with the present gold standard, X-ray MCUG. Such studies must also be performed in children in the youngest age group. A high proportion of infants show an immature Doppler pattern, and for this reason they were excluded from the recent study of D’Souza et al. [20]. An alternative interpretation of the findings could be that a large group of young children actually have VUR. This possibility is supported by the studies described above from the Finnish group.

If the wave form analysis approach is properly evaluated it might provide a tool that could provide a great deal of

information on the physiology and pathology of VUR. This method may also provide the possibility to learn more about the natural occurrence of VUR.

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