INTRODUCTION

Vesicoureteric reflux (VUR) is the most common urinary tract abnormality in children. In recent years, its exact role in chronic kidney disease development has become controversial (1, 2). While the exact clinical role of VUR cannot be uniformly determined and the correlation between VUR, urinary tract infection, and chronic kidney disease development is very hard to predict, we believe that in some groups of children, the awareness of VUR’s existence or nonexistence is still a very important issue.

Three types of voiding cystography are currently used to identify VUR, namely, X-ray voiding cystourethrography (VCUG), radionuclide voiding cystography (RNVC), and echo-enhanced voiding urosonography (VUS). The voiding cystographies differentiate according to the type of contrast agent installed in the bladder and the equipment required for depicting the contrast agent (Table 1). All of these techniques require catheterization of the urinary bladder. In addition, VCUG and RNVC involve exposure to ionizing radiation.

Since 1997, the American Urology Association has stated the necessity to find "less traumatic methods of determining whether reflux is present as well as techniques of voiding cystourethrography that results in less radiation exposure" (3). O’Hara described what characteristics should the perfect screening cystographic examination have: no radiation, no bladder catheterization, no sedation, low cost, high sensitivity and excellent anatomic details (4). All these factors considered, echo-enhanced VUS with a second-generation ultrasound contrast agent (USCA) is fairly close to the mark.

First reports on the first-generation USCA Levovist-enhanced VUS were published in 1998 (5, 6). University Medical Centre, Children’s hospital in Ljubljana was also among the first who performed echo-enhanced VUS and published the results (7). The manufacturer Bayer-Schering Pharma had already stopped marketing first-generation USCA Levovist (99.9% microcrystalline galactose microparticles and 0.1% palmitinic acid). Therefore, there is a need to switch to using second-generation USCA like SonoVue (phospholipid-stabilized micro bubbles of sulphur-hexafluoride; Bracco, Milan, Italy). SonoVue has been proved to have a potentially higher safety profile since so far no adverse effects have been reported during intravesical administration. Also, USCA has become relatively cheaper, particularly when performing the examination by using small doses (1 ml per bladder filling). It means that with one vial of SonoVue, one can examine 4 children.

In the last decade, the sensitivity of echo-enhanced VUS has been greatly improved, also due to improvements in...
contrast-specific US techniques, such as contrast harmonic imaging. Contrast-specific US techniques produce artifact-free images with high contrast resolution and not only increase the conspicuity of micro bubbles contained in the USCA, but also the sensitivity of the procedure. It is important to set a mechanical index (MI) below 0.10 in order not to break the micro bubbles of the second-generation USCA, since with an increase of MI the rate of micro bubbles destruction increases.

PROCEDURAL DETAILS

The basic procedural steps of echo-enhanced VUS encompass:

- US of the kidneys and bladder;
- the bladder catheterization and intra-vesical administration of normal saline and USCA;
- repeated scan of the bladder and kidneys during bladder filling and voiding.

Echo-enhanced VUS is performed on a US machine using a 2-5 MHz convex probe, in accordance with the widely accepted recommendations (8). Contrast-specific software dedicated to the second-generation USCA should be used during the procedure. The MI is set in the low specific mode (below 0.10). The second-generation USCA SonoVue is used in small doses.

At the beginning of the procedure, a 6 or 8-Fr urinary catheter is inserted into the urinary bladder under aseptic conditions, and the urine is allowed to drain. With a child in the supine position, the bladder is then slowly filled with saline solution kept at body temperature and under hydrostatic pressure (40-70 cm H2O). It is important that the normal saline instilled into the bladder is not from a container sealed under vacuum (9). When the predicted half of volume (bladder capacity in children younger than one (in milliliters) ~ 10 ml/kg body weight and bladder capacity in children older than one (in milliliters) ~ age (years) + 2×30) is reached, the USCA is administered intravesically through the catheter in order to evaluate the bladder and the distal parts of both ureters. While SonoVue accumulates on the roof of the bladder at the beginning of its injection, we continue with normal saline infusion immediately after the contrast agent in order to ensure the homogenous distribution of micro bubbles. The kidneys are thereafter scanned alternately while a child is turned in the supine and prone positions. The procedure is continued until the child bladder is empty, and the presence or absence of VUR is assessed. The length of the procedure therefore depends on the time taken from the application of the USCA into the bladder until the child has stopped voiding, but on average it takes 15-20 minutes.

THE GRADING OF VESICOURETERIC REFUX

Commonly, the diagnosis of VUR is based on a real-time examination decision at the time of the study. Reflux is diagnosed when echogenic micro bubbles are detected in the ureter or pelvicalyceal system (Figure 1). Two classifications of VUR grading exist: five or three grade classification (Figure 2). Generally, the severity of reflux is graded in a similar manner to the international reflux grading system for VCUG, and like the VCUG grading, this sonographic grading also has five categories based on the extent of reflux and the hydrodynamic behavior of reflux.

Table 1. The difference between various types of voiding cystoscopy

<table>
<thead>
<tr>
<th>contrast agent/ kontrastno sredstvo</th>
<th>equipment/uređaj</th>
<th>sensitivity/posebnosti</th>
<th>anatomical details/ anatomski detali</th>
<th>radiation/izravenje</th>
</tr>
</thead>
<tbody>
<tr>
<td>VCUG iodine/jod</td>
<td>roentgen machine</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>RNVRC radionucleide</td>
<td>gama camera</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>VUS ultrasound</td>
<td>ultrasound machine</td>
<td>++++</td>
<td>++++</td>
<td>0</td>
</tr>
</tbody>
</table>

Legend VCUG - voiding cystourethrography, RNVRC - radionucleide voiding cystography, VUS - voiding urosonography; + - anatomical details are close to those seen on VCUG, depending on the capacity of US machine/Legenda: VCUG - mikcijska cistouretrografija, RNVRC - direktna radionuklidna cystografia, VUS - ultrazvучна микцијска цистографија; + - анатомски детаљи су слични онома које се виде на VCUG, овом о машиналима уltrazvучног aparата

where many medical centers and include not only follow-up examinations, first examinations in girls and screening high-risk patients, but also children younger than one, including boys without voiding problems. VCUG should be limited only to the following cases:

- where the urethral imaging is of importance (patients referred specifically for a diagnosis of urethral anomaly);
- where potential voiding problems are suspected (evaluation of bladder morphology and function are of primary importance);
- where VUS was non-diagnostic due to poor patient cooperation, or in cases where bladder or one of the kidneys cannot be visualized on US due to malposition in severe scoliosis;
- before surgical intervention after consultation with the urologist;
- where complex malformations exist.

There are recently more reports of imaging urethra by VUS, which showed that imaging of the urethra is no longer a minor importance.

CONCLUSION

Echo-enhanced VUS is now incorporated into international guidelines for VUR detection. It is starting to be used as the primary imaging modality for all cases of VUR detection, regardless of age, and is changing the conventional diagnostic and management algorithms of VUR. It has proved to be a safe, highly...

Figure 1
ECHO-ENHANCED VOIDING UROSONOGRAPHY

Echo-enhanced VUS is now described in standard pediatric radiology and urology textbooks and incorporated into guidelines (12, 13). The diagnostic accuracy of VUS in terms of reflux detection and grading has been evaluated in a number of comparative studies with VCUG and RNVRC. All these studies were collected and analyzed in two extensive reviews, which have shown that more VUR were detected by echo-enhanced VUS compared to VCUG. In addition, the refluxes missed by VCUG were of higher grades compared to those missed by VUS, what might be important in the management of children (14, 15). These results suggested echo-enhanced VUS as a method of choice when looking for VUR. It was shown to be a safe, highly sensitive, and radiation-free alternative for the detection and grading of VUR in children. In addition, the visualization of intrarenal reflux is easier with echo-enhanced VUS (16). Therefore, VCUS and RNVRC are increasingly being replaced by VUS. The election criteria for VUS is becoming wider in...
sensitive, and radiation-free alternative for the detection and grading of VUR in children. VCUG should be mostly limited to cases where the bladder and/or urethra pathology are in question.

LITERATURE


Sažetak

ULTRAZVUČNA MIKCIJSKA CISTOGRAFIJA U DJECE: NOVE SPOZNAJE

D. Ključevšek


Deskriptori: VEZIKOURETERALNI REFLUKS, ULTRAZVUČNA MIKCIJSKA CISTOGRAFIJA, DRUGA GENERACIJA ULTRAZVUČNOG KONTRASTNOG SREDSTVA

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