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IS EARLY PROPHYLACTIC INTERVENTION BENEFICIAL FOR THE MANAGEMENT OF THE LOWER URINARY TRACT DYSFUNCTION IN CHILDREN WITH SPINA BIFIDA?

Hypothesis / aims of study

Spina bifida is often associated with lower urinary tract dysfunction (LUTD), leading to renal dysfunction. Optimal treatments are often needed to prevent the renal dysfunction. However, it is still controversial whether routine serial urodynamic evaluation initially starting at the infantile term and early prophylactic intervention with clean intermittent catheterization (CIC) and anticholinergic medication based on detection of urodynamic risk factors are needed or not [1, 2]. To determine whether early prophylactic intervention has advantage for the management of LUTD, we retrospectively reviewed and compared clinical records of the spina bifida children with LUTD managed with early or delayed intervention.

Study design, materials and methods

We retrospectively reviewed the medical records of children with spina bifida who underwent video-urodynamic study (V-UDS) at least once at their ages of 5 to 10 years old. Children who had undergone the initial V-UDS at their ages under 3 years old and underwent V-UDS periodically and had been managed with early prophylactic intervention based on detection of urodynamic risk factors were defined as the early intervention group (group E). Others were defined as the delayed intervention group (group D). Children who had normal lower urinary tract function were excluded. Urodynamic parameters obtained when those children were between 5 and 10 years of age were compared. In children who underwent V-UDSs more than two times during a period of age 5 to10 years, the last V-UDS was evaluated. In those who underwent bladder augmentation at age under 10 years, the results of the last V-UDS before bladder augmentation was used for evaluation. Children younger than 5 years old who showed the urodynamic risk factors (low compliance bladder, high detrusor leak point pressure (>40 cmH_2O), existence of detrusor sphincter dyssynergia or large amount of residual urine) were diagnosed as the high-risk group and the others classified as the low-risk group. In all children classified as the high-risk group CIC was introduced immediately and the low-risk group of children were just followed by watchful waiting until school age. In children elder than 5 years of age, CIC was introduced to improve continence. But children in whom CIC did not effective because of severe incompetent urethral closure mechanism were just followed by watchful waiting. Both groups of children were periodically checked up with history taking, urinary analysis and ultrasound of the kidneys and urinary tract. When urodynamic results indicated a low compliant bladder or DO, anticholinergic agents were administered unless severe incompetent urethral closure mechanism was not concomitantly detected. The V-UDS was carried out without any anaesthesia or sedatives. Bladder capacity was defined as the volume when detrusor pressure reached 40cmH_2O, continuous leakage occurred or the child felt the strong desire to void. Expected bladder capacity(EBC) was calculated using the formula; age(years)×30+30(ml) [3].Unpaired t-test, 2x2 Chi square test and Fisher's test were applied for the comparisons of urodynamic parameters between the groups, and $p<0.05$ is taken as statistically significant.

Table 1

	Early intervention (group E)	**Delayed intervention (group D)**
number of patients	24 (MMC 18, lipoma 6)	18 (MMC 15, lipoma 3)
age at the first intervention introduced(years)	1.3±1.9(0-7)	6.6±2.5(3-9) ***
age at the first V-UDS (months)	5.8±7.8 (0-32)	70.0±25.8(27-129) ***
managed with CIC	21 (88%)	12 (67%)
anticholinergic medication	21 (88%)	5 (28%)***
indwelling catheter	0	1 (6%)
age at V-UDS evaluated (years)	6.7±2.3	8.3±1.9
compliance (ml/cmH2O)	20.1±14.9(1.9-65.0)	8.6±7.1 (0.6-25)**
low compliance (<10 ml/cmH2O)	6 (25%)	14 (78%)**
% bladder capacity / EBC x 100(%)	96.5±41.4	65.6±34.1*
DO (>15cmH2O)	7 (29%)	1 (6%)
ALPP (<60cmH2O)	11 (46%)	10 (56%)
VUR	7 (29%)11uu	7 (39%) 8uu
augmentation at 5-10 years	1 (4%)	6 (33%) *

*; $p<0.05$, **; $p<0.01$, ***; $p<0.001$ significantly different from the value in the group E

Results

There were 54 children with spina bifida (36 myelomeningocele (MMC) and18 spinal lipoma). Seven children underwent surgery for a tethered cord or spinal lipoma during follow-up because of progression of LUTD, and LUTD improved in 3 out of these children after the surgery. Twelve children including these 3 were excluded because they had normal lower urinary tract function. There were 24 children aged 9.1±2.9 (5-14) years in the group E and 18 children aged 18.9±3.6 (13-29) years in the group D.

In the group E, at the first V-UDS, 11 children were classified as the high-risk group and the remaining 13 as the low-risk group. CIC was introduced immediately after the first V-UDS in the high-risk group of children. VUR was detected in 64% (7/11 children) of the high-risk group at the first V-UDS, but during follow-up, VUR was disappeared in 4 children and newly appeared in one ureteral unit. Among the 13 children classified as the low-risk group at the first V-UDS, 10 children shifted to the high-risk group during follow-up [0-7(mean 2.8) years later] and CIC with anticholinergic medication was applied to these children. None of the 13 children

initially classified as the low-risk group had VUR at the first V-UDS, but VUR was detected in 7 of the 10 children who shifted to the high-risk group when they shifted. VUR disappeared in 5 children after treatment.

In the group D, before the first V-UDS, CIC was introduced in 2 children and 1 was managed with an indwelling catheter because of repeated urinary tract infection. At the first V-UDS mean bladder compliance of the group D was 10.6±10.2ml/cmH_2O, and VUR was detected in 9 children (50%; 10 ureteral units). After the first V-UDS, CIC was introduced in 6 of them at the age of 6.1(5-10) years and 2 children with severely low compliant bladder underwent bladder augmentation and then managed with CIC. All the remaining 10 children had incompetent urethral closure mechanism, and thus they were just followed. During follow-up, VUR disappeared in 3 and newly appeared in 1 child.

Table 1 shows comparative data between the two groups on the background of patient-management at the V-UDS evaluation performed at the age of 5 to 10 years old and its findings. Compliance and the percentage of bladder capacity for EBC were significantly higher in the group E. The proportion of low compliant bladder (<10ml/cmH_2O) and the percentage of children who underwent bladder augmentation were significantly higher in the group D. Finally bladder augmentation was performed in 1 (at 8 years) of the group E and in 10 children [at 5-14 (mean 10) years] of the group D.

Interpretation of results

The results of the present study suggest that early and prompt intervention with CIC and anticholinergic medication based on periodic video-urodynamic monitoring may be beneficial to keep the bladder compliance and bladder capacity being well, and thus to limit a risk of receiving bladder augmentation and lead to preserving the renal function, although it can not be denied that the lower percentage of anticholonergic medication in the delayed intervention group may influence the urodynamic results. Early detection of LUTD by serial urodynamic monitoring may provide good information for neurosurgeons who need to decide the timing of untethering. However, further studies with longer follow-up until post-puberty are necessary to clarify the advantage of early prophylactic intervention to maintain renal function and establish continence.

Concluding message

The present results support the view that periodic video-urodynamic monitoring starting from the infantile term and early and prompt intervention with CIC and anticholinergic medication can provide better storage bladder function in children with spina bifida. However, prospective randomized trials with a longer follow-up are needed to verify this advantage.

References

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What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**No**
This study did not require eithics committee approval because	**this study is retrospective review of medical records obtained our ordinary outpatient clinic.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**