Urodynamic Evaluation in Primary Enuresis: An Investigative and Treatment Outcome Correlation

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Summary
A prospective study was done in pediatric out-patient department of a tertiary care hospital to evaluate the role of urodynamics in the management of primary enuresis in the 5–14-year-old children and to compare the effectiveness of multidimensional behavioral therapy with pharmacological therapy. Hundred and nineteen children between 5–14 years with primary enuresis were evaluated clinically and investigated. Three patients with obvious organic causes were then excluded. The remaining patients were given either behavioral or pharmacological treatment on the basis of urodynamic assessment. Urodynamic abnormalities were seen in 80/116 (68.9%) patients namely uninhibited bladder contraction 50/116 (43.1%), small bladder capacity 20/116 (17.2%), large bladder capacity 4/116 (3.4%), decreased bladder compliance 3/116 (2.5%) and detrusor sphincter dyssenergia 3/116 (2.5%). Combination of abnormal micturition history stating daytime urgency or frequency or dysfunctional voiding symptoms like squatting and/or abnormal voiding charts could predict abnormal results of urodynamics correctly with sensitivity of 81% and specificity of 86.2%. Ultrasound identified only 38/80 enuretics with urodynamic abnormalities although it was 100% specific. Additionally one patient who was identified as having a small bladder capacity on voiding chart was seen to have mild pelvicalyceal dilatation on ultrasound and subsequently on urodynamic assessment was found to have Detrusor sphincter dyssenergia (DSD). Behavioral therapy as compared to drug therapy produced more complete remission (17/18 vs. 14/18) and lesser relapse rate (2/17 vs. 5/14) in monosymptomatic enuretics with normal urodynamics. In patients with urodynamic abnormality, response rates with behavioral therapy, imipramine, oxybutynin and flavoxate were 73.9% (CI 56–91.8%), 89.4% (CI 75.7–100%), 94.2% (CI 84.7–100%) and 89.4% (CI 75.7–100%), respectively. Specific drug therapy as per the urodynamic abnormality was significantly more effective 49/57 [86% (CI 77–95%)] vs 17/23 [73.9% (CI 56.1–91.9%)] at P < 0.05 than behavioral therapy in patients with underlying abnormal urodynamics. Micturition history and voiding chart can be used as screening tool for enuretics. Behavioral therapy should be the first line treatment for mono symptomatic and drug therapy for polysymptomatic enuretics. Urodynamic testing may be reserved for polysymptomatic enuretics with abnormal ultrasound or those who fail to respond to first line treatment.

Introduction
Enuresis is a common but difficult and controversial problem affecting 10–15% of all children at 5 years of age [1]. The embarrassment and emotional trauma to children with enuresis may be profound. Moreover the associated parental anxiety and frustration adversely affects the entire family unit.

A number of anatomical, psychological and endocrine disorders have been incriminated as underlying factors for enuresis. More recently, lower tract urodynamics, the study of bladder and its outflow mechanism, has been used in the investigation of wetting to elucidate lower urinary tract dysfunction and intrinsic bladder abnormalities. However, these are extremely invasive, expensive and distressing for the child. Whether a thorough clinical assessment of each individual child to delineate the exact causative factor needs to be accompanied by precise but invasive technique like urodynamics is a topic of hot debate. To the best of our knowledge, there is no previous study that has scientifically compared the results of urodynamics with micturition history, voiding chart and ultrasound in investigation of enuretics using urodynamics as the gold standard.
In addition, there is considerable controversy regarding the most appropriate treatment for this common condition. Thus the present study was undertaken to find out if preliminary detailed clinical assessment and non-invasive investigations could suffice in postulating the underlying cause of bed wetting in a given patient, to define the exact role of urodynamics in management and to compare the effectiveness of behavioral therapy with pharmacological therapy in a resource poor nation.

Methods

A total of 119 children in the age group of 5–14 years attending pediatric out-patient department with the complaint of bedwetting were enrolled and evaluated in this study as per the following definitions:

Nocturnal enuresis was defined as two or more wet nights per month after 5 years of age and diurnal enuresis as two or more wetting per month while awake after 3 years of age [2]. Moderate to severe enuresis was defined as ≥3 wettings per week [3].

Primary enuresis was defined as wetting that occurred in the children who never had control on micturition. Secondary enuresis was defined as the situation in which the child had a consistent period of dryness of 6 months preceding the onset of wetting [2].

Exclusion criteria were taken as overt psychiatric disturbance requiring urgent referral to child guidance clinic, moderate to severe mental handicap, secondary enuresis, unconscious patients and underlying organic cause of incontinence. Informed consent was taken from the parents of the participants and approval was taken from institutional ethical committee.

A detailed history and comprehensive physical examination was done. Investigations included urine for albumin, sugar, culture, specific gravity; X-ray lumbosacral spine, blood sugar and ultrasound abdomen to look for bladder wall thickness, dilated ureter or pelvicalyceal dilatation in each child. Three children with organic causes namely epispadias, diabetes insipidus and phimosis were excluded from further study. The remaining 116 children were subjected to urodynamic assessment also.

Voiding chart was maintained for 3 days for frequency and volume of urine voided. The maximum volume of urine voided at any one micturition was assessed as functional bladder capacity.

Expected bladder capacity was calculated by Berger’s formula [4].

bladder capacity = [Age (in years) + 1] × 30ml

A total of 116 children were subjected to lower urinary tract urodynamic assessment by slow fill water cystometry. A transurethral bladder catheter recorded the intravesical pressure (Pves). Intrabdominal pressure (Pabd) was recorded by a rectal catheter. The detrusor pressure (Pdet) was computed as:

\[ P_{\text{det}} = P_{\text{ves}} - P_{\text{abd}} \]

Perineal patch electrodes were used to record the bioelectric activity in sphincter muscle. The parameters that were recorded were functional bladder capacity, bladder compliance, uninhibited bladder contractions and presence of detrusor sphincter dyssnergia. The mode of therapy was either behavioral or pharmacological decided according to the result of urodynamics.

Multidimensional behavioral modification therapy included many components. Firstly, positive reinforcement of the patient with praise/stickers for toddlers and special privileges for the youth for dry days or nights was encouraged. Secondly, scheduled awakening of the child was advised to a simple preset alarm clock. The child’s parents initially had to determine the critical time when the bladder would be full by monitoring the child for 2–3 days to see when bedwetting occurred. The alarm was then set to go off 15 min prior to this enabling the child to wake up and void in the bathroom. The therapy also included mild restriction of fluids after dinner. Another component was retention control and bladder training by lengthening the interval between daytime voidings. Each child also maintained a progress chart (star chart) in a voiding diary with a sequential reward system for longer and longer dry intervals. Family motivation consisted of reassurance of absence of any underlying organic factors in the enuretic child and motivating the family especially the mother to be supportive of the child.

Pharmacological therapy consisted of either of anticholinergic drug like oxybutynin (5 mg BD in 6–9 years and 5 mg TDS in 10–14 years) or musculotrophic relaxant flavoxate (3 mg/kg TDS) or tricyclic antidepressant imipramine (0.9–1.5 mg/kg given 1–2 h before bedtime). Drugs were given for 3 months followed by tapering over 1 month. Desmopression and tolterodine were not used in either group because of resource constraints.

Thirty-six children without cystometric abnormalities were divided into two groups of 18 each and were started on behavioral or drug therapy (oxybutynin, flavoxate or imipramine), respectively. Seventy-six children with cystometric abnormalities other than Large Bladder Capacity (LBC) were divided into four groups of 19 each randomly. They were prescribed behavioral therapy, oxybutynin chloride, flavoxate and imipramine, respectively. Remaining four children with LBC were given behavioral therapy.

Thus 41 children received behavioral therapy and 75 children received drug therapy and were assessed for immediate outcome.

\[ \text{Age} \times (\text{in years}) + 1 \times 30 \text{ml} \]
Evaluation was done fortnightly. Complete remission of wetting was defined as 14 consecutive dry days and nights within 4 months use of a treatment program.

Partial remission was taken as ≥50% reduction in frequency. More than two episodes of wetting by day or night over a 1-month interval was considered as relapse and continued success was if there was no relapse for 6 months after treatment was discontinued [2]. Twenty of hundred and sixteen patients who did not respond to treatment initially and also failed to respond later and those who completed 4-month treatment program but did not enroll for long-term assessment protocol were excluded from the assessment of long-term outcome.

Statistical analysis for univariate variable was done by chi-square test. Significance was taken at $P < 0.05$.

**Results**

The mean age of male enuretics was 8.8 ± 2.3 years and that of females was 9 ± 2.3 years, 80/116 (68.9%) patients had urodynamic abnormalities. The most common abnormality was unstable bladder contractions (43.1%). Other abnormalities are as shown in Table 1.

<table>
<thead>
<tr>
<th>Cystometrogram</th>
<th>Male (n = 64)</th>
<th>Female (n = 52)</th>
<th>Total (n = 116)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>17</td>
<td>19</td>
<td>36</td>
<td>31.03</td>
</tr>
<tr>
<td>Unstable bladder contractions</td>
<td>29</td>
<td>21</td>
<td>50</td>
<td>43.10</td>
</tr>
<tr>
<td>Small bladder capacity</td>
<td>10</td>
<td>10</td>
<td>20</td>
<td>17.2</td>
</tr>
<tr>
<td>Reduced bladder compliance</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Large bladder capacity</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>3.4</td>
</tr>
<tr>
<td>Detrusor sphincter dyssnergia</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>2.5</td>
</tr>
</tbody>
</table>

**Table 1**

*Results of cystometrogram of the study group*

Validity of various modalities for screening of patients with wetting is compared in Table 2. Micturition history stating daytime urgency or frequency or dysfunctional voiding symptoms like squatting could identify 57/80 (71.2%) enuretics with underlying urodynamic abnormality whereas voiding chart and ultrasound alone could pick up 50/80 (62.5%) and 38/80 (47.5%) patients, respectively. Combination of either abnormal micturition history or abnormal voiding chart could predict urodynamic abnormality in 65/80 enuretics with a fairly good sensitivity of 81.2% and a specificity of 86.2%. Thus this could be used as a screening test.

The immediate and late outcome with behavioral therapy and different pharmacological treatments based on urodynamic results are shown in Tables 3–6.

In patient with normal urodynamics, with behavioral therapy complete remission is more common (17/18 vs. 14/18) and with lesser relapse rate (2/17 vs. 5/14) as compared to pharmacological therapy. Although this difference is statistically not significant probably due to small numbers, a trend was noted.

With behavioral therapy, imipramine, oxybutynin and flavoxate response rates were 73.9%, 89.4%, 94.2% and 89.4%, respectively in enuretics with urodynamic abnormality. Thus specific drug therapy is significantly more effective (17/23 vs. 49/57 at $P < 0.05$) in patients with underlying abnormal urodynamics. Oxybutynin had best immediate outcome of all drugs. Oxybutynin was effective in patients with or without urodynamic abnormality. Flavoxate was significantly more effective in patients with small bladder capacity than in population with normal bladder function.

**Discussion**

Bedwetting continues to be a major problem seen globally, is of multifactorial causation and has controversial treatment options. Yet few conditions evoke such anxiety and a symptomatic cure is very gratifying for the child, the family and the physician.

In the present study, irritative symptoms of daytime frequency and urgency and dysfunctional voiding symptoms like squatting were seen in...
57/116 (49.1%) of patients which is comparable to 59% seen by Juneman, et al. [5].

Cutler, et al. [6] believed that daytime wetting is associated with a high incidence of urinary tract abnormalities. However, Burke, et al. [7] opined that most daywetters have urge incontinence secondary to an immature bladder that improves with age. Whether or not such children should be subjected to detailed radiographic examination or urodynamics has been subject of dispute for a long time.

Despite the increasing use of urodynamics in children, these investigations are invasive, upsetting and difficult to interpret. So in the present study, an attempt was made to predict the results of urodynamics studies from the data collected from a detailed micturition history, voiding chart and ultrasonography.

The predictions were compared with the actual urodynamics results and their accuracy was recorded.

In the present study, cystometric abnormalities were seen in 68.4% patients with the most common urodynamic abnormality being unstable bladder contractions (43.1%). Other studies have also reported a high incidence of cystometric abnormalities (80%) with bladder instability as the commonest cause [8]. These included both monosymptomatic (45) and polysymptomatic (130) patients.

Similarly another study from Argentina has reported cystometric abnormality in 49% (17/33) of monosymptomatic and 79% (35/47) of polysymptomatic enuretics. The abnormalities seen in this study were detrusor instability, low compliance bladder and small bladder capacity [9].

Moreover in the present study, both males and females were found to have an equal number of urodynamic abnormalities (Table 1). However in contrast, in a study by Lal et al. [10], three out of four girls who had abnormal cystometry were >8 years of age while males in this group had normal cystometry. So they suggested that older girls with nocturnal enuresis form a group where urodynamic studies may be indicated. However their sample size of 15 patients with 9 boys and 6 girls is too small to reach this conclusion.

In the present study, 71% of the abnormal patients were identified by micturition history of daytime or dysfunctional voiding symptoms. Voiding chart picked up eight additional patients, thus increasing the sensitivity to 81%. No additional patients could be identified by ultrasound. In fact only 38 of 116 patients subjected to ultrasound showed abnormalities in form of bladder wall thickening (>0.3mm) or altered bladder capacity that were subsequently found to have urodynamic abnormality.

However, one patient who was identified as small bladder capacity (SBC) on voiding chart was seen to have mild pelvicalyceal dilatation on ultrasound and subsequently on urodynamic assessment was found to have DSD.

Moreover two more patients labeled erroneously as SBC by voiding chart were seen to have normal bladder capacity on urodynamics. It was presumably because if the voiding of the children at different times are unsupervised or on command by mother, the chart might give on erroneous results which is not representative of the true bladder capacity.

In a study by Yeung, et al. [11], Ultrasound measurement were performed on 514 children 5–18 years old with primary nocturnal enuresis and compared with those of 339 normal age matched controls. A total of 218 children with severe enuretic

<table>
<thead>
<tr>
<th>Immediate outcome</th>
<th>Behavioral therapy (n=18) (%)</th>
<th>Drug therapy (n=18) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete remission</td>
<td>13 (72.2)</td>
<td>10 (55.6)</td>
</tr>
<tr>
<td>Partial remission</td>
<td>4 (22.2)</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>No improvement</td>
<td>1 (5.6)</td>
<td>4 (22.2)</td>
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</table>

<table>
<thead>
<tr>
<th>Long-term outcome</th>
<th>Behavioral therapy (n=17) (%)</th>
<th>Drug therapy (n=14) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continued success</td>
<td>14 (82.3)</td>
<td>7 (50.0)</td>
</tr>
<tr>
<td>Relapse</td>
<td>2 (11.8)</td>
<td>5 (35.7)</td>
</tr>
<tr>
<td>Lost for follow up</td>
<td>1 (5.9)</td>
<td>2 (14.3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immediate outcome</th>
<th>Behavioral therapy (n=23)</th>
<th>Imipramine (n=19)</th>
<th>Oxybutynin (n=19)</th>
<th>Flavoxate (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete remission</td>
<td>13 (68.4)</td>
<td>14 (73.7)</td>
<td>11 (57.9)</td>
<td></td>
</tr>
<tr>
<td>Partial remission</td>
<td>4 (21.1)</td>
<td>4 (21.1)</td>
<td>6 (31.5)</td>
<td></td>
</tr>
<tr>
<td>No improvement</td>
<td>2 (10.5)</td>
<td>1 (5.2)</td>
<td>2 (10.5)</td>
<td></td>
</tr>
</tbody>
</table>
symptoms underwent urodynamic assessment. Bladder Volume Wall Thickness Index (BVWI) calculated by ultrasound studies was compared in normal and enuretic children in correlation with functional bladder capacity. A high predictive value of bladder function and treatment response was found with BVWI. Thus it is a very specific tool but has a low sensitivity.

In patients with normal urodynamics, behavioral therapy had significantly better immediate as well as long-term outcome as compared to drug therapy.

However, with underlying urodynamic abnormality, imipramine and oxybutynin had better treatment benefit that was more frequent in patients with low bladder capacity, low bladder compliance or bladder instability.

Thus it may find its place in patients with daytime symptoms where above-mentioned abnormalities may be suspected.

Also in the present study, there was 89.4% treatment benefit with flavoxate in the group with urodynamic abnormality (17/19) and only 16.6% (1/6) in normal group. So it may have a role in treatment of polysymptomatic primary enuretics who experience side effects with anticholinergics.

Thus monosymptomatic primary enuretics with normal voiding chart may be started on behavioral therapy without subjecting them to urodynamic test. Even in polysymptomatic enuretics, drug therapy may be started empirically. Urodynamic testing may be reserved for polysymptomatic enuretics who show abnormal ultrasound or who fail to respond to first line treatment.

Whether polysymptomatic enuretics need to have a combination of drug therapy with behavioral therapy to improve long-term outcome needs to be established by further studies.

**References**


**Table 6**

Comparison of long-term outcome in patients with abnormal urodynamics

<table>
<thead>
<tr>
<th>Long-term outcome</th>
<th>Behavioral therapy (n = 17)</th>
<th>Imipramine (n = 17)</th>
<th>Oxybutynin (n = 14)</th>
<th>Flavoxate (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continued success</td>
<td>12 (70.6)</td>
<td>7 (41.7)</td>
<td>10 (71.4)</td>
<td>6 (40.0)</td>
</tr>
<tr>
<td>Relapse</td>
<td>3 (17.6)</td>
<td>7 (41.7)</td>
<td>3 (21.4)</td>
<td>7 (46.6)</td>
</tr>
<tr>
<td>Lost for follow up</td>
<td>2 (11.8)</td>
<td>3 (17.6)</td>
<td>1 (7.14)</td>
<td>2 (13.3)</td>
</tr>
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