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ORIGINAL ARTICLE

Urodynamic Findings in Children with Refractory Nocturnal Enuresis

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ABSTRACT

Background: Nocturnal enuresis or bedwetting is the most common type of urinary incontinence in children. It has significant psychological effects on both the child and the family. The Aim of study was to evaluate the role of UDS in management of refractory Nocturnal Enuresis (MNE).

Methods: This Prospective Study was carried out in Urology Department, Zagazig University Hospital that included 24 Patients, 14 boys and 10 girls. The patient ages was ranged from 10–18 years old with mean age (SD) of 11.91 ± 1.95 years. All patients were treated with mono pharmacotherapy (desmopressin). The duration of treatment before UDS at last six months.

Results: bladder sensation was intact in 41.7%, increased in 50.0% and decreased in 8.3% of patients. The value of a single test PVR was ranged from 20-150 ml. 21 of patients were no post voiding volume (87.5%) and 3 cases had post voiding volume (12.5 %). The filling cystometry was normal in 6 patients (25%) and abnormal in 18 patients (75%). Bladder sensation intact in 10 patients (41.7%) and decrease in 2 patients (8.3%) and increase in 12 patients (50%) with p-value (< 0.05).

Conclusions: it is recommended to perform urodynamic studies in the form of uroflowmetry and cystometry for those with refractory nocturnal enuresis who failed ADHC (desmopressin) for at last 6 months as initial monotherapy. Also a combination therapy of anticholinergics with desmopressin could be applied as treatment for those with refractory monosymptomatic nocturnal enuresis

Keywords: Monosymptomatic nocturnal enuresis, urodynamic studies, detrusor overactivity.



INTRODUCTION

The International Children's Continence Society (ICCS) defined nocturnal enuresis as both a symptom and a condition of intermittent incontinence that occurs during periods of sleep. Previously it was wetting in discrete portions while asleep after the age of five [1]. Refractory Nocturnal enuresis is defined as less than 50% improvement in symptoms with an adequate trial of treatment (3 months). Children with refractory enuresis showed abnormal sleep architecture, high incidences of periodic limb movements in sleep, and increased cortical arousability, leading to awakening [2]. Patients with primary enuresis that is refractory to treatment are usually referred for urodynamic assessment. The referring physician is looking for an urodynamic explanation for the failure of treatment, which has usually been given with the aim of improving the storage function of the bladder. How far these patients would benefit

from urodynamic testing as part of their management [3]. The monosymptomatic nocturnal enuresis (MNE) is recommended by the International Children's Continence Society (ICCS) to distinguish MNE from non-monosymptomatic nocturnal enuresis (NMNE), which is accompanied by lower urinary tract symptoms (LUTS) such as daytime urinary frequency, urgency, or urinary incontinence. In general, indications for urodynamic studies (UDS) in children include the following: neurogenic bladder, sphincter dysfunction, anorectal malformations, voiding dysfunction including urge syndrome and underactive bladder, vesicoureteral reflux, urinary incontinence, infravesical obstruction, or obstructive uropathy. [4]. It was thought that patients with a diagnosis of MNE had normal bladder function. Thus, invasive urodynamic studies (UDS) was not generally performed in children in order to manage MNE.

However, several studies have revealed an important role of the reduced functional bladder capacity and bladder dysfunction in the progression of refractory MNE. [5]. The Aim of this study was to evaluate the role of UDS in management of refractory Monosymptomatic Nocturnal Enuresis (MNE).

METHODS

This prospective study was carried out in Urology Department, Zagazig University Hospital from March 2020 to December 2020, Twenty four patients with refractory MNE were enrolled in the study. The included patients with MNE were treated with mono pharmacotherapy (desmopressin) for at least six months without response. Written informed consent was obtained from all children's parents and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board) ZU-IRB .The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. **Inclusion criteria:** Any patient above 10 and less than 18 years who has refractory enuresis according to the ICCS guidelines, meaning failure of medical treatment after at least 6 months of continuous treatment in form desmopressin 0.2mg up to 0.6 mg / day and patients with monosymptomatic enuresis. **Exclusion criteria:** Patients with Neuropathic bladder disorder, Diabetes-mellitus, spinal dysraphism, dysfunctional voiding, or anatomical abnormalities of urinary tract were excluded.

All patients were subjected to: Complete history was taken including sex, age, fluid intake, urological symptoms as frequency, urgency, nocturia, urge incontinence, holding maneuvers (e.g., standing on tiptoes, crossing the legs, pressing the heel or hand into the perineum), number of bed wetting per week. Medical history including types of drugs as desmopressin, , or other drugs and the duration of treatment. Family history to NE. History of constipation. or other medical diseases. History of previous pelvic or urological procedure. All patients undergoing physical examination which include general examination as body build, back to exclude spina bifida, abdominal examination to exclude supra pubic fullness, examination of genitalia and perineum to exclude meatal stenosis or any congenital anomalies. Complete urine analysis, urine culture and sensitivity to exclude active urinary tract infections and hematuria. Random blood sugar, Pelvic abdominal ultrasonography (U/S) and Plain X-ray (KUB) to evaluate the size of the kidney, parenchymal thickness, degree of echogenicity and to exclude renal, ureteric or

bladder stones, spina bifida and other abnormalities.

Methods: All patients were subjected to urodynamic study using Laborie Machine model triton (**Figure 1**), using 6 Fr double lumen urethral catheter to measure intravesical pressure (Pves) and 6 Fr water filled rectal catheter to measure intraabdominal pressure (Pabd). **The Urodynamic tests done in this study:** **Uroflowmetry:** is a measurement of the urine flow rate over time. It is also an assessment of bladder emptying (**Figure 2**). **Post-void residual urine volume:** Post-void residual volume (PVR) is the amount of urine retained in the bladder after a voluntary void and functions as a diagnostic tool. A post-void residual volume helps in the evaluation of many disease processes, including but not limited to neurogenic bladder, cauda equina syndrome, urinary outlet obstruction, mechanical obstruction, medication-induced urinary retention, postoperative urinary retention, and urinary tract infection. **Filling cystometry (CMG):** is the method by which the pressure/volume relationship of the bladder is measured during bladder filling. The filling start by 10 cc/sec and then increase gradually up to 50 cc/sec to avoid overstimulation for dartose muscle, ask patient cough to make sure there isn't blocked to rectal catheter and for exceeded stress incontinence also ask patient about first bladder sensation and strong desire to void. The filling phase starts when filling commences and ends when the patient cannot maintain continence or urinary leakage occurs and urodynamicist given permission to void..start by 10 cc/sec and then increase gradually up to 50 cc/sec to avoid overstimulation for dartose muscle, ask patient cough to make sure there isn't blocked to rectal catheter and for exceeded stress incontinence also ask patient about first bladder sensation and strong desire to void .CMG can be performed by double lumen urethral catheter to measure Pves and rectal catheter to measure Pabd. To calculate Pdet the following equation is used: **$P_{det} = P_{ves} - P_{abd}$** . Measurements obtained during cystometry include bladder sensations, compliance, bladder capacity .

STATISTICAL ANALYSIS

The collected data were analyzed by computer using Statistical Package of Social Services (SPSS) version 25. Data was presented in tables and figures. Quantitative data was presented as mean and standard deviation. Qualitative data was presented as frequencies and proportions. For testing the differences for significance, the variance and association of qualitative variable have been clarified by Chi square test (X^2) while variances between independent quantitative multiple groups

are assessed by (ANOVA) analysis of variances and the presence or absence of detrusor overactivity.

RESULTS

Table (1) showed that the mean age was 11.91±1.95 years; males were majority with 58.3%. Table (2) showed that bladder sensation was intact in 41.7%, increased in 50.0% and decreased in 8.3% of patients. Table (3) showed that detrusor stability had Phasic uninhibited detrusor contractions and 29.2% had No uninhibited detrusor contractions, regard Bladder compliance 70.85 were normal and 29.2% decreased. Table (3) showed that regarding detrusor stability 17 patients had Phasic

uninhibited detrusor contractions and 7 patients had No uninhibited detrusor contractions, while regarding Bladder compliance, 17 patients were normal and 7 patients decreased. Table (4) showed that NIL Post voiding volume was normal in 21 patients and 3 patients cases had Post voiding volume. Table (5) showed that regarding diagnosis, 25% were normal and 66.7% were Idiopathic detrusor over activity and only 2 cases (8.3%) had Hypo contractile bladder and only 2 cases had Low compliance. Table (6) showed that abnormal cases significantly associated with abnormal Bladder sensation and also with Phasic uninhibited detrusor contractions.

Table1: age and sex distribution among studied group (N=24)

		Age/ years	
Median (Range)		11.0 (10-18)	
		N	%
Gender	Female	10	41.7
	Male	14	58.3
	Total	24	100.0

Table2: bladder sensation distribution among studied group (N=24)

		N	%
Bladder sensation	Intact	10	41.7
	Decrease	2	8.3
	Increase	12	50.0
	Total	24	100.0

Table 3: Detrusor stability and Bladder compliance distribution among studied group (N=24)

		N	%
Detrusor stability	No uninhibited detrusor contractions	7	29.2
	Phasic uninhibited detrusor contractions	17	70.8
Bladder compliance	Decrease	7	29.2
	Normal	17	70.8
	Total	24	100.0

Table 4: Post Voiding volume distribution among studied group (N=24)

		N	%
Post voiding volume	NIL	21	87.5
	20	1	4.2
	40	1	4.2
	150	1	4.2
	Total	24	100.0

Table 5: diagnosis distribution among studied group (N=24)

		N	%
Diagnosis	Normal	6	25.0
	Hypo contractile bladder	2	8.3
	Idiopathic detrusor over activity	16	66.7
Low compliance	No	22	91.7
	Yes	2	8.3
	Total	24	100.0



Figure (1): Laborie triton.



Figure (2): Uroflowmetry.

DISCUSSION

Patients with enuresis that is refractory to treatment who are referred for urodynamic study usually have tried several kinds of medical and behavioral therapy without any response. The referring physicians are hoping to find a urodynamic explanation for this treatment failure that will affect management. However, if the result of urodynamic study is in the form of a bladder filling abnormality such as reduced bladder capacity, detrusor overactivity or hypocompliance, this will not be of much help, as these patients have already

received medical treatment for such problems[6].It was thought that patients with a diagnosis of MNE had normal bladder function. Thus, invasive UDS was not generally performed in children in order to manage MNE. However, several studies have revealed an important role of the reduced functional bladder capacity and bladder dysfunction in the progression of refractory MNE [7]. Unlike MNE, it has been suggested that children with NMNE present with symptoms mainly due to underlying lower urinary tract dysfunction [8]. Therefore, this study sought to

determine whether or not a UDS is beneficial for NE management in pediatric patients, especially in cases of pharmacoresistant MNE. The urodynamic test should be indicated in patients with symptoms of overactive bladder refractory to treatment, as well as those patients in whom an organic cause is suspected during the diagnostic investigation. The use of such conduct could result in a decrease in the number of invasive procedures, reducing the discomfort of the patient and family, time until the start of the treatment, and hospital costs [9]. So, this study was aimed to evaluate the role of UDS in the diagnosis of the causes of refractory nocturnal enuresis after 6 months of treatment with mono pharmacotherapy. In this study 24 patients including, 14 boys and 10 girls (male 58.3%-female 41.7%) the patient ages were ranged from 10–18 years old with mean age (SD) of 11.91 ± 1.95 years. No patients were found to have any relevant psychological history, medical diseases or other urological symptoms. All patients were treated with mono pharmacotherapy (desmopressin). The duration of treatment before UDS ranged from six to ten months. **Naseri and Hiradfar [10]** reported that of 60 there were 33 boys and 27 girls with mean age 8.8 ± 2.3 years (range 5-14 yr) met the inclusion criteria. Also, **Conkar and Mir [11]** reported that their study included two hundred and seventy-seven (30.8%) boys and 620 (69.1%) girls with a mean age of $7.52 (\pm 2.6)$ years (range: 5-18) underwent UDS in their study. Bladder sensation intact in 10 patients (41.7%) and decrease in 2 patients (8.3%) and increase sensation in 12 patients (50%). **Saber-Khalaf and Abdallah [10]**, Reported that abnormal cystometric findings was detected in the form of detrusor overactivity in 52.5% and abnormal bladder sensations in 24% of patients. Regarding detrusor stability, there was overactive bladder in 17 patients (70.8%) and normal detrusor function in 7 patients (29.2%). Which in agreement with the study of **Conkar and Mir [11]** who reported that the overactive bladder detected in 630 patients (70.2%) and 29.8% of patients were normal. While in contrast, **Elmissiry et al. [3]** found that detrusor overactivity was reported in 45% of patients and 55% were normal. The value of PVR was ranged from 20-150 ml, 21 of patients were no post voiding volume (87.5%) and 3 cases had post voiding volume (12.5%) 2 case of them hypocontractile bladder. While **Conkar and Mir [11]** reported that the post voiding volume was represented in 450 patient (50.1%). The filling cystometry was normal in 6 patients (25%) and abnormal in 18 patients (75%). 8 patients out of 18 have idiopathic detrusor overactivity (IDO) in patients (66.7%) and hypocontractile bladder in 2 case (8.3%) low

bladder compliance in 7 patients (38.9%). **Naseri and Hiradfar [10]**, reported in his study on 48 patients that The detrusor overactivity (DO) was the most common findings in (56.2%). Also **Elsiad et al, [4]** reported in his study on 30 patients with MNE, normal filling cystometry in (43.3%) and abnormal filling cystometry 17 patients (56.6%) in the form of detrusor overactivity (DO) in 12 patients (40%) and low bladder compliance in 5 patients (16.6%). Higher percentage of abnormal UDS findings were reported by **Ryu et al, [14]** in combined study including 19 patients with MNE and 61 patients with NMNE. In the MNE arm of the study, (36.8%) had normal filling cystometry and (63.2%) had abnormal filling cystometry in the form of (31.6%) Detrusor overactivity (DO), (21.1%) had DO with decreased cystometric bladder capacity, and (10.5%) had DO with detrusor sphincter dyssynergia (DSD). Another study by **Sehgal et al, [14]**, on large No of patients (116) who are not classified. when compared to our study, it reported that the filling cystometry of 116 patients, (68.9%) had abnormal filling cystometry and (31.03%) had normal filling cystometry. The most common abnormality was overactive bladder (OAB) in (43.1%), small bladder capacity in (17.2%), reduced bladder compliance in (2.5%) and detrusor sphincter dyssynergia in (2.5%). **RYU, et al [13]**, reported in this study 80 children (50 boys and 30 girls), 19 of which were diagnosed with MNE and 61 of which were diagnosed with NMNE, were included in the final analysis. Of the 19 MNE children, 12 (63.2%) demonstrated abnormal UDS findings which is comparable to our study (75%). Ten demonstrated detrusor overactivity (DO) with or without decreased cystometric bladder capacity (CBC) We should note the differences between our study and these previous studies. Our study included small number of patients with only MNE, while in the studies by **Sehgal et al, [14]** a large number of patients with unclassified NE were evaluated. **Elmissiry et al, [3]** when compared to our study we included only MNE with no day time symptoms or dysfunctional voiding so, we use only uroflowmetry and cystometry without EMG also According to AUA/SUFU guidelines on urodynamic, EMG of pelvic floor muscles is recommended in patients with relevant neurological disease at risk for neurogenic bladder **Vignoli [15]**.

CONCLUSIONS

Based on the current study, it is recommended to perform urodynamic studies in the form of uroflowmetry and cystometry for those with refractory nocturnal enuresis who failed ADHC (

desmopression) for at last 6 months as initial monotherapy. Also a combination therapy of anticholinergics with desmopressin could be applied as treatment for those with refractory monosymptomatic nocturnal enuresis.

No Conflict of Interest

No financial disclosure

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SUPPLEMENTARY FILES

Table (S1): Comparison between urodynamically abnormal and normal patients.

			Abnormal	Normal	t/ X²	P
Age			12.0±2.08	11.66±1.63	0.355	0.726
Bladder capacity			225.83±82.96	265.0±49.29	1.084	0.290
Pdet Q max			51.27±8.32	57.83±4.02	1.839	0.079
Q max flow			14.94±2.33	15.16±1.16	0.225	0.824
Voiding volume			214.16±61.21	265.0±49.29	1.836	0.080
Gender	Female	N	7	3		
		%	38.9%	50.0%		
	Male	N	11	3	0.229	0.633
		%	61.1%	50.0%		
Bladder sensation	Intact	N	4	6		
		%	22.2%	100.0%		
	Decrease	N	2	0	11.20	0.004*
		%	11.1%	0.0%		
	Increase	N	12	0		
		%	66.7%	0.0%		
Detrusor stability	No uninhibited detrusor contractions	N	1	6		
		%	5.6%	100.0%		
	Phasic uninhibited detrusor contractions	N	17	0	19.42	0.00**
		%	94.4%	0.0%		
Bladder compliance	Decrease	N	7	0		
		%	38.9%	0.0%		
	Normal	N	11	6	3.29	0.07
		%	61.1%	100.0%		
Total		N	18	6		
		%	100.0%	100.0%		