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THE ROLE OF URODYNAMIC STUDY IN EVALUATION OF 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 evaluation of refractory Nocturnal Enuresis in children. **Patients and 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 urodynamic studies (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). **conclusion:** 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

Keywords: 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

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(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).

PATIENTS AND 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 or their relatives and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board IRB#:5949-l-3-2020). 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 then 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 desmopression 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**,** 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**.**

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 infections

Filling cystometrography (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 exceled stress incontinence also ask patient about first

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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 exceled 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: **Pdet = Pves – Pabd**.

Measurements obtained during cystometry include bladder sensations, compliance, bladder capacity and the presence or absence of detrusor overactivity.

RESULTS

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**

Table (1) showed that the mean age was 11.91±1.95 years; males were majority with 58.3

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 (2) showed that bladder sensation was intact in 41.7%, increased in 50.0% and decreased in 8.3% of patients.

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

		N	%
Detruser stability	**No uninhibited detruser contractions**	**7**	**29.2**
	Phasic uninhibited detruser contractions	**17**	**70.8**
Bladder compliance	**Decrease**	**7**	**29.2**
	Normal	**17**	**70.8**
	Total	**24**	**100.0**

Table (3) showed that detruser stability had Phasic uninhibited detruser contractions and 29.2% had No uninhibited detruser contractions, regard Bladder compliance 70.85 were normal and 29.2% decreased. Table (3) showed that regarding detruser stability 17 patients had Phasic uninhibited detruser contractions and 7 patients had No uninhibited detruser contractions, while regarding Bladder compliance, 17 patients were normal and 7 patients decreased.

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 (4) showed that NIL Post voiding volume was normal in 21 patients and 3 patients cases had Post voiding volume.

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

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

Table (5) showed that regarding diagnosis, 25% were normal and 66.7% were Idiopathic detruser over activity and only 2 cases (8.3%) had Hypo contractile bladder and only 2 cases had Low compliance.

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 i Lebl n 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 (±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 Abdellah [10], Reported that abnormal cystometric finings 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.

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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 cystomettric 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 dyssenergia 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 cysyometry without EMG. also **Vignoli [15]** reported that 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 **.**

Conclusion

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.

Recommendations :

We recommended performing 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.

Abbreviations:

SD: mean age; USD : Urodynamic studies; ICCS : International Children's Continence Society; MNE : monosymptomatic nocturnal enuresis; LUTS : lower urinary tract symptoms.

-Authors' contributions

AAA, AMZ, KMT and MMA collected patients' samples and clinical data. MMA prepared sample for laboratory investigations and wrote the paper. Statistical analysis, interpretation of data, and preparation the paper for submitting international was done by AAA. Critical revision of the manuscript was performed by all of the authors. All authors have read and approved the final manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

Presentation at a meeting: no

Conflicting Interest (If present, give more details): No Conflict of Interest

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Declarations

-Ethics approval and consent to participate

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board) lRB#:5949-l-3-2020.

-Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

REFERENCES

1- **Hashim H, Blanker M, Drake M, Djurhuus J, Meijlink J, Morris V et al.** International Continence Society (ICS) report on the terminology for nocturia and nocturnal lower urinary tract function. Neurourol Urodyn 2019; 38(2): 499-508.

2- **El-Mitwalli A, Bediwy AS, Zaher AA, Belal T, Saleh AB.** Sleep apnea in children with refractory monosymptomatic nocturnal enuresis. Nat Sci Sleep. 2014;6:37-42.

3- **Elmissiry M, Abdelkarim A, Badawy H, Elsalmy S, Ali GA.** Refractory enuresis in children and adolescents: how can urodynamics affect management and what is the optimum test? J Pediatr Urol. 2013; 9 (3):348-52.

4- **Elsiad I, Ibrahim H, Aldaqadossi H, Youssof H.** The role of urodynamic study in evaluation of patients with refractory monosymptomatic nocturnal enuresis. FUMJ 2019; 3(1): 12-14.

5- **Yeung CK, Sit FK, To LK, Chiu HN, Sihoe JD, Lee E, Wong C.** Reduction in nocturnal functional bladder capacity is a common factor in the pathogenesis of refractory nocturnal enuresis. BJU Int. 2002; 90(3):302-7.

6- **Ismail MB.** Urodynamic findings in patient above 15 years old with primary refractory nocturnal enuresis. Merit Res. J. Med. Med. Sci. 2016; 4(8): 374-378

7- **Yeung CK, Chiu HN, Sit FK**. Bladder dysfunction in children with refractory monosymptomatic primary nocturnal enuresis. J Urol, 1999 ; 162: 1049–54.

8- **Neveus T, von Gontard A, Hoebeke P, Hjälmås K, Bauer S, Bower, W et al:** The standardization of terminology of lower urinary tract function in children and adolescents: report from the Standardisation Committee of the International Children's Continence Society. J Urol**.** 2006 ; 176:314-324.

9- **Lebl A, Fagundes SN, Koch VH.** Clinical course of a cohort of children with non-neurogenic daytime urinary incontinence symptoms followed at a tertiary center. J Pediatr (Rio J). 2016 Mar-Apr;92(2):129-35..

10- **Naseri M, Hiradfar M.** Abnormal urodynamic findings in children with nocturnal enuresis. Indian Pediatr 2012**;** 49 (5) :401-403.

11 **Conkar S, Mir S.** Are Urodynamic Studies Really Necessary in Voiding Dysfunction in Children?. Haseki Tip Bulteni 2018; 56(3): 192.

12- **Saber-Khalaf, M., & Abdellah, A. (2017).** Abnormal Urodynamic Finding in Monosymptomatic Nocturnal Enuresis. SMJ 2017; 21(3): 329-332.

13- **Ryu D, Lee H, Kwak K, Park K, Baek M.** Role of Urodynamic Study in Nocturnal Enuresis: Urodynamic Findings and Treatment Outcome Correlation in Children with Pharmacotherapy-resistant Monosymptomatic Nocturnal Enuresis or Severe Non-monosymptomatic Nocturnal Enuresis. LUTS 2014; 6(2):88-93.

14- **Sehgal R, Paul P, Mohanty NK.** Urodynamic evaluation in primary enuresis: an investigative and treatment outcome correlation. J Trop Pediatr 2007 ; 53 (4) : 259-63.

15- **Vignoli G.** Electromyography of Pelvic Floor Muscles**.** In: Urodynamics. Springer, Cham, 2017. p. 129-141.