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TREATMENT SYSTEM FOR NOCTURNAL ENURESIS ACCORDING TO A NEW CLASSIFICATION SYSTEM

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Introduction: Failure of conventional medical treatment in nocturnal enuretic children is often frustrating. Classification system based on urodynamic studies is proposed.

Material & Methods: 120 nocturnal enuretic patients were referred for urodynamic studies after poor response to conventional medical treatment. A full questionnaire, frequency volume chart, clinical examination and full urodynamic studies were performed.

Results: 36% of enuretics showed presence of detrusor instability, 64% of them were observed late in cystometric curve, decreased ability to inhibit voiding in 17%, post micturition contraction in 27%, low bladder capacity in 12%. Based on the above findings:

Patients with enuresis were classified into four groups: Group I with no abnormal findings, Group II with increased detrusor activity, Group III with immature bladder capacity and Group IV with nocturnal polyuria. Group I may responded well to any sort of medical treatment including assurance. Group II can carry good response to parasympatholytics and antidepressants. While Group III may respond to bladder retention training or bladder drilling programs. Group IV can respond excellently to vasopressin.

Conclusion: Treatment based on this information can offer good results and prevents years of unnecessary therapy.

Key words: Nocturnal enuresis, Detrusor instability and Classification

INTRODUCTION

Nocturnal enuresis is the involuntary passing of urine during sleep after the age at which bladder control would be normally anticipated. It is common in children with spontaneous cure rate of approximately 15% per year. [1] Originally it was referred to as primary (if the child had never experienced a dry period), or secondary enuresis (if the enuretic child had a dry period at least 6 months).The distinction between primary and secondary enuresis is simplistic. Despite extensive research on nocturnal enuresis, the pathophysiology remains controversial and multiple factors are considered responsible for its etiology.

Several subtypes were classified in the literature for nocturnal enuresis, based on its time of onset, primarily or secondary, [2] symptomatology (monosymptomatic or polysymptomatic nocturnal enuresis), [3, 4] response to vasopressin (responders, non responders), [5] presence of nocturnal polyuria[6] (polyuric, non polyuric), mechanism of bladder function and arousal function, (Type I, IIa, IIb).[7, 8]

Failure of conventional medical treatment is often frustrating. The aim was to propose a classification based on clinical and urodynamic work up in-patients with nocturnal enuresis.

PATIENTS AND METHODS

The study included 12O child with nocturnal enuresis with refractory response to medical treatment after a trial of several months. Urologists and pediatricians referred them for urodynamic work up. Patients were excluded when they were known to have an overt organic urological disease as; obstruction, neuropathy, ectopic ureter, congenital sphincteric impairment, and central diabetes insipidus or urinary tract infection. All patients were evaluated with complete history and full questionnaire including; age, sex, symptoms, accidents during sleep, psychiatric distress (parent view) and constipation. Physical and neurological examination, urine analysis, urine culture and sensitivity. Frequency/volume chart and voiding history was taken including; urgency, largest voided volume, and functional capacity.

Maximal functional capacity was determined in all patients by instructing them to collect and measure the volume of multiple voids when they had a sensation of fullness. The largest voided volume for each patient was considered to be the maximal functional bladder capacity. The maximal functional capacity was compared to the estimated age adjusted bladder capacity based on the formula by Berger et al 1983 [9] and Koff et al. 1983 [10] where, bladder capacity = patient age (years)+2x30.

Complete urodynamic testing was done in each patient including cystometery with concomitant measurements of rectal pressure, urethral pressure profilometery (UPP), and pressure flow study. Urodynamics were done on Urodyn 5500 apparatus (Dantec). Plain KUB to assess spina bifida and skeletal anomalies.

Children were asked to urinate immediately before urodynamic evaluation so that an accurate assessment of residual urine could be made. The results were analyzed using student's "t" test. The definition of detrusor instability, maximum cystometric capacity confirms to those of the International Continence Society.[11]

RESULTS

The mean age of the 120 studied children was 14 years, (range from 7 to 30 years). There were 71 females, (59.2%), and 49 males (40.8 %). Fourteen (12%) were less than 10 years, 83 (69%) were more than 10 years, and 23 (19%) were adults (>18 years). (Table 1). It was observed that the difference in sex was statistically significant in adults only. There was a positive familial history in 33.3%, (40/120). Thirty one percent (37/120) of patients had monosymptomatic nocturnal enuresis (MNE) as the only presenting symptom, 69% (83/120) had polysymptomatic nocturnal enuresis (PNE). These symptoms included; urgency in 72% (86/120), frequency in 72% (86/120), urge incontinence in 44% (53/120), and mixed symptoms in 42% (50/120). It was observed that adult cases (>18 years) had only polysymptomatic nocturnal enuresis (Table 1). In monosymptomatic nocturnal enuresis wet night accidents occurred only once a night in all enuretics in this group, while in polysymptomatic nocturnal enuresis the majority (55%) had more than one accident per night number (Table 2). Day sleep accidents happened in 30.5% of enuretics. It did not occur in monosymptomatic nocturnal enuresis cases, but it was observed in 41% of polysymptomatic nocturnal enuresis cases. Sixty four percent (77) of enuretics were deep sleepers. Parents reported psychological distress and poor self-esteem in 28% of enuretics, mainly in the females (70%).

Urodynamic studies were performed to all cases. A decrease in bladder volume at first sensation was observed in 23%. While a decrease in cystometric capacity was noted in (13.8%). Postmicturition contraction was seen in 27% of enuretics studies. Thirty three percent of postmicturition contractions were detected in monosymptomatic nocturnal enuresis leaving 64% in polysymptomatic nocturnal enuresis. Bladder instability was noted in 36% (43) of all the studied patients. Cases we considered only had detrusor instability of high amplitude. The instability was frequent in 80% of cases, 64 % of instability occurred in late curve, while 38% of detrusor instability occurred at both early and late cystometric curves. Detrusor instability was noted in association with polysymptomatic nocturnal enuresis in 33% (40/120) of all enuretics and in association with monosymptomatic enuresis in 3% (3) of all enuretics. (Table 3). It was observed that in polysymptomatic enuretic group 28% had multiple mixed symptoms despite the absence of detrusor instability in their cystometric studies. The compliance was reduced in l8.9% of all enuretic cases, range from 12.5 to 91 (mean=50), 59% had associated bladder instability and 41% were pure low compliance. Urethral pressure profile studies were not significant.

The maximal functional capacity (the largest voided volume) was 170-470 cc. The functional capacity was reduced in 55 % of cases. The polysymptomatic nocturnal enuretics, with bladder instability showed reduction in bladder capacity in 33% (40/120) of cases, while those with stable bladder showed reduction in bladder capacity in only 12% (14/120) cases. In monosymptomatic nocturnal enuresis, it was observed that only in l %(3) had reduced bladder capacity with stable bladder. The total number of reduction in maximal functional bladder capacity in stable bladder was 12% (14) (Table 3).

Nocturnal polyuria (Group IV) was detected in 28% of case (34/120), [11% (13/120) in monosymptomatic nocturnal enuresis, and 17% (21/120) in polysymptomatic nocturnal enuresis]. (Table 3). It was observed that patients in Group I had normal functional bladder capacity,

dynamically stable bladder, and nocturnal urine out put equivalent to the daily output. This was observed in 24% of the total number of enuretics studied. The majority (16%) of these cases was monosymptomatic nocturnal enuresis.

Table (1): *Age of presentation.*

	< 10 years		*10-18*		*> 18 years*	
MNE 37 (31%)	7	(6%)	30	(25%)	0	(0%)
PNE 83 (69%)	7	(6%)	53	(44%)	23	(19%)
	14	(12%)	83	(69%)	23	(19%)
X^2			5.21			
P			<0.01*			

* Significant difference

Table (2): *Wet night accidents/night.*

	1/night		*> 1/night*	
MNE 37 (31%)	37	(31%)	0	(0%)
PNE 83 (69%)	17	(14%)	66	(55%)
X^2		4.1		
P		<0.01*		

* Significant difference

Table (3): *Application of classification to enuretic patients.*

	No abnormality		*Det. Instability*		*Reduced Bl. Cap*		*Noct. Polyuria*	
	Group I		*Group II*		*Group III*		*Group IV*	
MNE 37 (31%)	20	(16%)	3	(3%)	1	(1%)	13	(11%)
PNE 83 (69%)	10	(8%)	40	(33%)	13	(11%)	20	(17%)
Total 120 (100%)	30	(24%)	43	(36%)	14	(12%)	38	(28%)
X^2				1.32				
P				>0.05 N.S.				

NS = Not significant

Table (4): Classification of nocturnal enuresis.

Group I	No abnormal findings
Group II	Increased detrusor activity
Group III	Immature bladder
Group IV	Nocturnal polyuria

DISCUSSION

The rational for management of nocturnal enuresis revolve around improving and preserving the child's self esteem. [12] The pathogenesis of nocturnal enuresis remains controversial,[13] multiple factors are considered responsible. The presented classification (Table 4) was based on clinical evaluation, frequency/volume chart and simple urodynamic work up, to identify the prominent etiological factor, thus facilitating the choice of a suitable treatment. Various therapeutic modalities are currently available. The treatment option should be tailored to each individual situation. Norgaard et al[1] in accordance with the presented study emphasized the importance of the division of enuretic patients into different subtypes according to the underlying mechanisms to obtain better treatment results. Watanabe et

al,[7] proposed a treatment classification system for monosymptomatic nocturnal enuresis based on simultaneous sleep cystometery and EMG recordings, they subdivided children to; Type Ia, with mild arousal disturbance with stable bladder. Type IIa with sever arousal disturbances, and Type IIb with latent neurogenic bladder and continuous uninhibited bladder contractions during sleep. This classification although theoretically attractive, is not applicable for routine use and need a sophisticated setup including sleep laboratories.

The studied population of enuresis represents a group of cases referred after failure of empirical treatment. We observed 89% were more than 10 years, of these 19% were adults. This older age justifies the need for a thorough evaluation and classification to improve the outcome.

Children with stable bladder, normal bladder capacity, non-polyurics with no abnormal findings, can respond to any sort of medical treatment including assurance, motivational therapy, and conditioned therapy. Family positive reinforcement is essential.

Children observed with detrusor instability and increased detrusor activity may have good response to anticholinergics,[13,14] in accordance with Type IIb in Watanabe classification.[7] Although theoretically anticholinergics could help bed wetters by reducing uninhibited bladder contractions and increasing bladder capacity,[15] its role alone was debatable by some authors.[16,17] The combination (with tricyclic antidepressant (Imipramine)[15] for its alternation in arousal and sleep mechanisms, anticholinergic, antispasmodic effects as well as antidepressant action,[18] may enhance its action. Unstable bladder contractions were reported to be frequent in diurnal[16] and nocturnal enuresis.[18] Almost half of studied patients with polysymptomatic nocturnal enuresis exhibited, detrusor instability. Cystometric studies[19] consistent with our studies showed that the detrusor contractions observed in enuretics occurring in the final phase of cystometery.

Bed-wetting occurs when the functional capacity is reached. Results of our study showed that there was a group of patients with immature reduced bladder capacity with stable bladder. Recent studies[20,21] showed that the response of children with monosymptomatic nocturnal enuresis to desmopressin as a single drug therapy is adversely affected by reducing functional bladder capacity. Normal nocturnal urine output of patients with small functional bladder capacity may exceed bladder capacity when the child fails to wake up, enuresis results. Thus this group of patients may respond to anticholinergic drugs to increase bladder capacity in association with bladder retention training[20] or bladder drilling programs.[22]

Norgraad et al, [23] noted that children with monosymptomatic nocturnal enuresis routinely produce urine volume exceeding their functional capacity some as much as 2-3 folds. We reported 28% of our children have nocturnal polyuria as recorded by frequency volume chart of children. Nocturnal polyuria seen in nocturnal enuresis is caused by relative nocturnal deficiency of antidiuretic hormone .It was reported that the plasma level of ADH did not increase during sleep in enuretic children as it usually does in non-enuretic sleeping children. [23] Recent studies indicate that some enuretic children with nocturnal polyuria show an excellent response to treatment with desmopressin. However there is a small subgroup of enuretics with nocturnal polyuria have a normal circadian rhythm of vasopressin secretion and do not respond to desmopressin. Thus nighttime polyurics respond to vasopressin therapy, [24] and nighttime non-polyurics does not respond to vasopressin. [25] New horizon on nocturnal polyuria is starting to evolve, there is accumulating evidences in the literature that a full bladder may be able to inform the kidneys to reduce urine production. [26] A protein Aquamarine 2 which under the influence of ADH develops water channels through the epithelial cells of the collecting tubules allows water to escape from the urine to the blood stream thus reduces urine production. [27]

The available evidences indicate that nocturnal enuresis has a multifactorial, [1] etiology it may best be regarded as a group of conditions with differing etiologies rather than a single entity. Obviously therapy must be match to etiology. Nocturnal enuresis classification may guide to suitable therapy, it may offer better results and prevent years of unnecessary therapy.

REFERENCES

1. Norgaard JP, Djurhuus JC, Watanabe H, Stenberg A, Lettgens B. Experience and current status of research into the pathophysiology of nocturnal enuresis. Br J Urol 1997;79:825-35.

2. Haligren B. Enuresis, A clinical and genetic study. Acta Psychiatr Neurol Scand 1957; 144 (Suppl): 27-40.

3. Chiozza ML. An update on clinical and therapeutic aspects of nocturnal enuresis. Pediatr Med Chir 1997;19(5): 385-90.

4. Walle JV, Hoebeke P, Raes A. Difference in the profile of nocturnal diuresis. Arch Pediatric 1997; 4 (Suppl 1): 7s-9s.

5. Djurhuus JC, Ritting S. Current trends, diagnosis and treatment of enuresis. Eur Urol 1998; 33 (Suppl 3): 45-8.

6. Hurisballe JM, Hensen TK Ritting S, Norgaard W, Pedersen GB, Djurhuus JS. Polyuric and nonpolyuric bedwetting-pathogenesis differences in nocturnal enuresis. Scand J Urol Nephrol 1995 b; (Suppl 173): 77-9.

7. Watanabe H, Kawauchi A, Kitamori T, Azum Y. Treatment system for nocturnal enuresis according to an original classification system. Eur Urol 1994; 25:43-50.

8. Kawauchi I, Tanaka Y, Yamao Y, Watanabe H, Takeuchi Y. Classification based on overnight simultaneous monitoring by electroencephalography and cystometery. Eur Urol 1998; 33 (Suppl 3): 45-8.

9. Berger RM, Maizales M, Moran GC, Conway J, Firlit CF. Bladder capacity (ounces) equals age plus 2 predict normal bladder capacity and aids in diagnosis of abnormal voiding patterns. J Urol 1983; 21:248-9.

10. Koff SA. Estimating bladder capacity in children. Urology 1983248-9.

11. Abram PH, Blavis JG, Stauton SL, Andersen JT. Standardization of terminology of lower urinary tract function. Neurourol urodyn. 1988; 403-27.

12. Hagglof B, Andren O, Bergetron C, Marklund L. Self esteem before and after treatment in children with nocturnal enuresis and urinary incontinence. Scand J Urol Neph 1997; (Suppl 183): 78-82.

13. Husmann D. Enuresis. Urology 1996:48(2): 184-93.

14. Loverin JV, Tallet SE, Mckendry JB, Oxybutinine efficacy in the treatment of primary enuresis. Pediatrics 1988; 82(1): 104-6.

15. Banerjee S, Srivastav A, Palan BM. Hypnosis and self hypnosis in the management of nocturnal enuresis. A comparative study with Imipramine therapy. American Journal of Clinical Hypnosis 1993; 36(2): 113-19.

16. Rhouston HG. Nocturnal enuresis: Epidemiology, evaluation, and current available treatment options. Journal of Pediatrics 1989; 114 (4pt2): 691-96.

17. Khan A, Staten P, Singh VK, Zaman N. Role of detrusor instability in primary enuresis. Urology 1993; 41(2): 189-91.

18. Medel R, Ruarte AE, Caetera R, Podesta ML. Primary enuresis: a urodynamic evaluation. Br J Urol 1998; 81 (Suppl 3): 50-2.

19. Norgaard JP, Hansen JH, Wilschiodz G, Sorensen S, Rittings, S, Djurhuus JC. Sleep cystometries in children with enuresis. J Urol 1989a; 141: 156-9.

20. Rushton HG, Belmann B, Zaontz MR, Skoog SJ, Sihelnik M. The influence of small functional bladder capacity and other predictors on the response to desmopressin in the management of monosymptomatic nocturnal enuresis. J Urol 1996; 156: 651-55.

21. Eller D, Austin PF, Tanguary S, Homsy YL. Daytime functional bladder capacity as a predictor of response to desmopressin in monosymptomatic nocturnal enuresis. Eur Urol 1998;33(Suppl 3):25-29.

22. Joek XL, Wyndaele J, Vermandel A. The role of bladder biofeedback in the treatment of children with refractory nocturnal enuresis associated with idiopathic detrusor instability and small bladder capacity. J Urol 1998; 160: 858-860.

23. Norgaard JP, Pederssen EB, Djurhuus JC. Diurnal antidiuretic hormone levels in enuretics J Urol 1985; 134: 1029-31.

24. Hjalmas K, Hanson E, Hellstrom AL, Kruse S, Sillen U. Long term treatment with desmopressin in children with primary monosymptomatic nocturnal enuresis: an open multicentric study. Br J Urol 1998; 82: 704-9.

25. Norgaard JP, Jonler M, Rittin S, Djurhuus JC. A pharmacodynamic study of desmopressin in-patients with nocturnal enuresis. J Urol 1995; 153: 1984-6.

26. Hvistendal J, Kopp U, Schmidt F, Pedersen T, Jorgensen JM, Djurhuus JC, Frokiar J. Vesico-renal reflex mechanisms modulate urine output and renal blood flow during elevated bladder pressure in the pig. 8th Annual Meeting of European Society of Pediatric Urology-Rome, 1997.

27. Frokiaer J, Nielsen S. Do aquaporines have a role in nocturnal enuresis? Scand J Urol Nephrol 1997 (Suppl 183): 31-32.