

Single Vs Combined Therapy in the Treatment of Enuretic Children in Kirkuk District

*Dhahir H. Bra**

*Ziad M. Sadiq***

*Lyla H. Mohammed****

**Department of surgery, college of medicine - University of Kirkuk*

***Department of pediatrics, college of medicine - University of Kirkuk*

****Technical Institute _ Kirkuk*

Accepted: 2011/3/8, Received: 2010/4/1

Abstract

This is a prospective study done in urology polyclinic of Azadi teaching hospital in Kirkuk governorate from 1st of April 2009 to 1st December 2009. The study involved 75 patients complaining from enuresis and does not respond to non pharmacological treatment.

The results of the study showed a higher rate of enuresis in males 45 (60%) than females 30(40%), the peak age incidence 11- 13 years (37.3 %).

Regarding treatment the study showed that children received combination treatment (Imipramine and Oxybutenine) has a better response rate (84.8 %) with fewer relapse rate (15.6 %) after discontinuation of treatment than children received Imipramine alone in which the response rate where (73.3%) and relapse rate (26.7%).

The study recommend combination treatment as a safe and effective treatment for children who didn't respond to single drug therapy.

Introduction

Nocturnal enuresis refers to involuntary passage of urine during sleep by a child old enough to have gained urinary control. The American Psychiatry Association has defined bed wetting as children older than age five who are incontinent of urine at night. Mentally disabled children should have reached a mental age of four years before they are considered enuretic. (Allen, 1997).

It is estimated that 15-20% of children have some degree of bedwetting at five years of age, with a spontaneous resolution rate of 15% per year. Bedwetting has been reported to be higher in males – 60% of bedwetters and more than 90% of nightly bedwetters are males. However this finding has been disputed by other reports (Rittig *et al.*, 1989).

The frequent changing and washing of bedding and night-clothes can place an additional workload and financial burden on the family. Parents may become intolerant of the situation, and this may even lead to physical punishment of the child. (Redsell & Collier, 2001).

Nocturnal enuresis is a common problem, affecting an estimated 5 to 7 million children in the United States and occurring three times more often

in boys than in girls. For the diagnosis of nocturnal enuresis to be established, a child five to six years old should have two or more bed-wetting episodes per month, and a child older than six years of age should have one or more wetting episode per month. (Miller, 1993)

A single explanation for nocturnal enuresis has been elusive. The current belief is that the condition is multifactorial. Numerous etiologic factors have been investigated, and various theories have been proposed.

A Family history of nocturnal enuresis is found in most children. If one parent was a bedwetter the probability of having enuresis in the child is 45%; if both parents were bedwetters the probability increases to 77%. On the other hand only 15% will be affected if neither parent had enuresis (Tarun *et al.*, 2001)

It is postulated that functional immaturity of the central nervous system results in decreased sensory perception of bladder filling, inability to inhibit bladder emptying and poor arousal mechanisms. The proponents of this theory cite the spontaneous cure with increasing age as evidence in support of their postulate.

Nocturnal enuresis is also associated with episodes of obstructive sleep apnea in children with upper airway obstruction and surgical correction in such cases (*viz.* tonsillectomy, adenoidectomy etc.) diminishes the episodes of bedwetting (Weider *et al.*, 1991).

Children with primary enuresis have essentially the same behaviour pattern as normal children. If a child develops secondary enuresis after a psychological event it is usually a relapse physiologic enuresis, and is usually also accompanied with daytime symptoms. (Feehan *et al.*, 1990).

Some studies have found functional bladder capacity to be low in patients with nocturnal enuresis. If the bladder is small, the patient would also manifest accompanying symptoms, such as daytime frequency, wetness every night, occasional wetness several times in a night and the problem being primary.(Mayo & Burns, 1990).

Children with nocturnal enuresis have not been found to have an increased incidence of emotional problems. (Wan & Greenfield, 1997).

No correlation has been found between urethral or meatal stenosis and bed-wetting. Furthermore, congenital, structural, or anatomic abnormalities rarely present solely as enuresis. (Yeung *et al.*, 1999).

Treatment of nocturnal enuresis can be divided into two broad categories: non pharmacologic and pharmacologic. Non pharmacologic treatment of enuresis includes motivational therapy, behavior modification (conditioning therapy), bladder-training exercises, psychotherapy, diet therapy and hypnotherapy. Because of increased awareness that primary nocturnal enuresis can be a significant psychosocial stressor, pharmacologic treatment of primary nocturnal enuresis has evolved

significantly over the past 15 years. Combination drug therapy may be tried in older patients with refractory primary nocturnal enuresis when neither the alarm nor pharmacologic therapy has been effective. Drug therapy can be combined with the use of alarms to optimize effectiveness. (Wille, 1989).

Combination drug therapy may be tried in patients with refractory nocturnal enuresis when neither alarm nor single pharmacologic therapy is effective. In such cases combination therapy using 2 or more drugs has been shown to be effective. Several studies with various combination modalities are published. With deferent success rate. (Tarun *et al.*, 2001)

In a study done in United Kingdom involve Twenty-three patients (17 boys and six girls from nine to 16 years of age) in whom prior medical therapy had failed were treated with desmopressin acetate and hyoscyamine. Twelve patients (52 %) were considered dry and off all medications (Wille, 1989).

In another study done by Austen and Paul at 2008 on 41 children who had enuresis refractory to treatment with intranasal desmopressin alone; after 1 month of treatment, there was a significant reduction in the mean number of wet nights in the combination therapy group, compared with the placebo group. With a generalized estimating equation approach, there was a significant (66%) decrease in the risk of a wet episode, compared with the placebo group (Paul *et al.*, 2007).

Patients and method

This is a prospective study for total 75 whom complain from nocturnal enuresis that didn't respond to non pharmacological treatment. The study start from 1st April 2006 to 31 marches 2007, and involve patients who consult the urosurgical polyclinic of Azadi general hospital in Kirkuk governorate.

Data on sex, age, age at presentation, were taken. These patients divided into tow groups according to the drug that they received, first group receive Imipramin (0.5 mg/kg/day) alone, while the second group receive Imipramine together with Oxybutenine (0.2 mg/kg/day).

Statistical analysis was carried out to assess the deference between the results. Chi square was applied, statistically significant value was defined as ($p < 0.05$).

Results

There was a satirically significant difference in the frequency of nocturnal enuresis between males (45 patients) (60%) and females (30 patients) (40%) (Table.1).

Diagnosed patients grouped according to their age; it's found that enuresis is more frequent among age group (11-13) years (28 patient) 37.3%, followed by patient with age group (8-10) years (17 patient) 22.7% and (5-7) years (15 patients), 20% respectively; after 14 years the frequency start to decrease. (Table.2).

Table No. 3 shows that patient who received combined therapy with Imipramin and Oxybutenine had better response (38 patients- 84.4%) and less relapse rate (7 patients- 15.6%) than Imipramin alone whom only (22 patients - 73.3%) shows response to treatment and had relapse rate (8 patients - 26.7%) this deference in both success rate and relapse rate was statistically significant.

Table (1): Distribution of enuretic patients according their sex.

Sex	Nocturnal enuresis	%
Male	45	60%
Female	30	40%
Total	75	100%

p<0.05

Table (2): Distribution of enuretic patients according to their age

Age(year)	F	%
5-7	15	20%
8-10	17	22.7%
11-13	28	37.3%
14-16	12	16%
17-19	3	4%
Total	75	100%

p<0.05

Table (3): Distribution of enuretic patient according to pharmacologic treatment

Drug	No.	%	Response rate		Relapse rate	
			No.	%	No.	%
Imipramin (Tofranil)	30	40.0%	22	73.3%	8	26.7%
Imipramin with Oxybutenine	45	60%	38	84.4%	7	15.6%
Total	75	100%	60	80.5%	15	19.5

p<0.05

Discussion

In this study; enuresis found to be more frequent in males (45 patients- 60%) than female (30 patients- 40%) as shown in table No.1. This result is similar to a study done in Cambridge between March 1997 - April 2002 and there was a gender imbalance in patients presenting for treatment with the sample containing (65.1%) males and (34.9%) females.

However some reports show more prevalence of enuresis between female. (Ritting *et al.*, 1989).

Frequency of enuresis found to be gradually increased up to (11- 13) age group, this result is not in agreement to a similar study done by Kimberly in which the frequency of enuresis gradually decline after 5 years age (Kimberly, 2002). The discrepancy between these tow studies probably due to some social believe in our nation that regard enuresis as normal habit even after fifth years age so they do not bring their children to medical attention even after 5 years age.

The treatment approach for enuresis is controversial due to the lack of consensus as to the exact causes of nocturnal enuresis. Despite various treatment modalities, pharmacotherapy still appears to be the common choice. (Lütfü *et al.*, 2000)

In our study combination of Imipramin and Oxybutenine show better response (38 patients- 84.4%) and less relapse rate (7 patients- 15.6%) from those patient who received Imipramin alone in which only (22 patients - 73.3%) shows response to treatment and had relapse rate (8 patients - 26.7%).

Combination therapy with Imipramine and Oxybutenine appear to be superior to other drug combinations regarding the response rate, this combination is also appears to be safe, and with lesser chance of relapse after discontinuation of the therapy.

References

- Allen, T.D., (1977): The non-neurogenic neurogenic bladder. *J Urol*, vol.117, pp.232-238.
- Feehan, M., McGee, R., Stanton, W., Sil, (1990): A six-year follow-up of childhood enuresis: prevalence in adolescence and consequences for mental health. *J Paediatr Child Health*, vol.26, pp.75-9.
- Kimberly M. Sanborn (2002): Nocturnal Enuresis in Children. American Psychological Association Publication Manual, Fourth Edition 37 p.
- Lütfü Tahmaz, Yusuf Kibar, Ibrahim Yildirim, Süleyman Ceylan, Murat ayanç (2000): Combination Therapy of Imipramine with Oxybutynin in Children with Enuresis Nocturna *Urol Int*, vol.65, pp.135-139
- Mayo, M.E., Burns, M.W., (1990): Urodynamic studies in children who wet. *Br J Urol*, vol.65, pp.641-5.
- Miller, K., (1993): Concomitant non pharmacologic therapy in the treatment of primary nocturnal enuresis. *Clin Pediatr*, pp.32-7.
- Paul F. Austin, Genoa Ferguson, Yan Yan, Mary J. Campigotto, Michele E. Royer, and Douglas E. Coplen. (2008): Combination Therapy with Desmopressin and an Anticholinergic Medication for Non responders to Desmopressin for Monosymptomatic Nocturnal Enuresis: A Randomized, Double-Blind, Placebo-Controlled Trial *pediatrics* Vol. 122, No. 5 November, pp.1027-1032.
- Rittig, S., Knudsen, U.B., Norgaard, J.P., Petersen, E.B., Djurhuus, J.C., (1989): Abnormal diurnal rhythm of plasma vasopressin and urinary output in patients with enuresis. *Am J Physiol*, vol. 256, pp.664-71.
- Redsell, S., Collier, J., (2001): Bedwetting, behaviour and self-esteem: a review of the literature. *Child Care Health Dev*, vol.27, pp.149–62.
- Rushton, H.G., (1989): Nocturnal enuresis: epidemiology, evaluation, and currently available treatment options. *J Pediatr.*, Vol 114, pp.691-6.
- Tarun, Gera, A., Seth, & J. L. Mathew, (2001): Nocturnal Enuresis in Children. *The Internet Journal of Mental Health*. Volume 1 Number 1
- Weider, D.J., Sateia, M.J., West, R.P., (1991): Nocturnal enuresis in children with upper airway obstruction. *Otolaryngol Head Neck Surg* vol.105, pp.427-32.
- Wan, J., Greenfield, S., (1997): Enuresis and common voiding abnormalities. *Pediatr Clin North Am*, vol.44, p.1117-31.

- Wille, S., (1989): Comparison of desmopressin and enuresis alarm for nocturnal enuresis. Sutton Coldfield, England: Horus Medical Publications, pp.209-214.
- Yeung, C.K., Chiu HN, Sit FK. Bladder dysfunction in children with refractory monosymptomatic primary nocturnal enuresis. J Urol 1999: 162(3 pt 2):1049- 54.

مقارنة بين استخدام الدواء المزدوج والدواء المفرد لعلاج الأطفال المصابين بالتبول الليلي اللاإرادي

ظاهر حميد برا* زياد محمد صادق** ليلى حسن محمد***

*فرع الجراحة، كلية الطب_جامعة كركوك
**فرع طب الأطفال، كلية الطب_جامعة كركوك
***معهد التقني – كركوك

تاريخ الاستلام: ٢٠١٠/٤/١، تاريخ القبول: ٢٠١١/٣/٨

الخلاصة

هذه دراسة استباقية أجريت على الأطفال الذين يعانون من التبول الليلي اللاإرادي من الذين لم يظهروا استجابة للعلاجات غير الدوائية . أجريت الدراسة على ٧٥ طفلاً من الأطفال الذين يراجعون عيادة الأمراض البولية في مستشفى أزاوي العام في مركز محافظة كركوك في الفترة بين الأول من آذار ولغاية الأول من كانون أول (٢٠٠٩).

أظهرت نتائج الدراسة أن نسبة الإصابة أكثر بين الذكور ٤٥ (٦٠%) مقارنة بالإناث ٣٠ (٤٠%). وكانت نسبة تقديم المرض أكثر في الفئة العمرية (١١-١٣) سنة. أظهرت نتائج الدراسة أن الأطفال الذين عولجوا باستخدام دوائين (امبرامين مع اوكسيبوتولين) اظهروا معدل استجابة أحسن (٨٤,٤%) مع نسبة انتكاسة اقل (١٥,٦%) بعد قطع الأدوية مقارنة بالأطفال الذين عولجوا باستخدام امبرامين فقط حيث كانت الاستجابة عند هذه المجموعة (٧٣,٣%) مع نسبة انتكاسة وصلت إلى (٢٦,٧%) بعد قطع الأدوية. أوصلت الدراسة باستخدام مجموعة (امبرامين مع اوكسيبوتولين) كعلاج مؤثر و أمين للأطفال الذين لا يستجيبون لعلاج امبرامين فقط.