Original Article

OUTCOME OF COMBINATION THERAPY VERSUS BEHAVIOR THERAPY IN TREATMENT OF NOCTURNAL ENURESIS

Hafiza Nuzhat[*], Imran Qadir[*], Muhammad Tahir Bashir Malik[**], Shazia Nazar[*]
[*]Department of Pediatric Urology, Children Hospital, Faisalabad
[**]Department of Urology, Madinah Teaching Hospital, The University of Faisalabad

ABSTRACT:

Nocturnal Enuresis (NE) is the involuntary urination during sleep after the age at which bladder control usually occurs. It is a socially stigmatizing and stressful condition which affects around 15%-20% of five years old. Various treatment options for PNE include behavioral therapy, alarm therapy, pharmacotherapy and combinations. Current study was aimed to evaluate outcome of behavioral therapy alone and in combination with pharmacological treatment.

OBJECTIVE: To compare the outcome of behavioral therapy alone and in combination with pharmacotherapy in management of NE.

OPERATIONAL DEFINITION: Behavioral therapy was performed with prompted voiding (voiding by clock) at day time & reducing fluid intake at bedtime. Pharmacotherapy was performed with orally administered imipramine at bedtime.

MATERIAL AND METHOD: **STUDY DESIGN:** Comparative study.

SETTING: Urology department, Children Hospital, Faisalabad.

SAMPLING: One hundred & thirty consecutive children in age range of 5-13 years with nocturnal enuresis were enrolled in the study and randomly allocated in two groups. One group was advised behavioral treatment alone and other was advised pharmacotherapy (imipramine) along with behavioral therapy.The children with known urinary tract pathologies/congenital anomalies, active urinary tract infection, acquired urologic disease, neurologic diseases and children with daytime LUTS were excluded from the study.

Results: At first follow up (15-days), in group-A (behavioral therapy alone), 7.7% children reported complete resolution of NE, 23.1% showed improvement (reduction in episodes of NE) and 69.2% showed no improvement.
At first follow up (15-days), in group-B (combination therapy), 15.4% children reported complete resolution of NE, 61.5% showed improvement (reduction in episodes of NE) and 23.1% showed no improvement.
At second follow up (30-days), in group-A (behavioral therapy alone), 38.5% children reported complete resolution of NE, 38.5% showed improvement (reduction in episodes of NE) and 23% showed no improvement.
At second follow up (30-days), in group-B (combination therapy), 38.5% children reported complete resolution of NE, 46.2% showed improvement (reduction in episodes of NE) and 15.4% showed no improvement.

CONCLUSION: Behavioral therapy can be offered as an initial treatment step in management of nocturnal enuresis. However, combination therapy (behavioral +pharmacotherapy) gives an overall better outcome in the treatment of Nocturnal Enuresis as compared to behavioral therapy alone.
KEYWORD: Nocturnal enuresis, Behavioral therapy, Imipramine

INTRODUCTION:

Nocturnal Enuresis (NE) is the involuntary urination during sleep after the age at which bladder control usually occurs. Mono symptomatic enuresis is defined as enuresis in children without any other urinary tract symptoms and without a history of bladder dysfunction[1,2]. Primary mono-symptomatic nocturnal enuresis is the most frequent (85%) type of enuresis in children[3]. It is a socially stigmatizing and stressful condition which affects around 15%-20% of five years old. The incidence falls to 1-2% at the age of 15 years. Despite high rate of spontaneous remission[4,5], this condition leads to social, emotional and psychological issues in the affected children[6]. An association of NE has been found with male gender and obesity[1]. Management of NE should be adapted to the child and his/her family requirements. Prescribing the right medication and ensuring compliance is important[7]. Treatment options depending on the underlying etiology include simple behavioral intervention, conditioning alarm regimen and pharmacotherapy with Impiramine, Desmopressin and anticholinergic drugs[8] . Sometimes psychotherapy is important in enuresis as well because psychological factors do have potential role in the pathogenesis of NE.[9]

It is noted that simple behavioral methods are better than giving no treatment, however, alarm and drug therapy are more effective when compared to using simple behavioral methods only. Behavioral therapies are defined as interventions that require a behavior or action by the child which promotes night dryness and includes strategies which reward that behavior[10]. Pharmacotherapy includes tricyclic antidepressants and Desmopressin[10]. Unfortunately, 20 to 60 % of children with monosymptomatic enuresis are desmopressin-resistant[11]. Behavioral therapies could be tried as first line treatment before considering other therapies[10] . The purpose of this study was to compare the efficacy of two treatment modalities for NE, namely behavioral intervention and combination therapy which includes behavioral interventions and Imipramine, in local population of Faisalabad presenting to Hospital OPD.

Corresponding Author:
Dr. Muhammad Tahir Bashir Malik
Assistant Professor Urology, Madinah Teaching Hospital, The University of Faisalabad
Email: drtahirbasheer@gmail.com

Objective: To compare the outcome of behavioral therapy alone and in combination with pharmacotherapy in management of Nocturnal Enuresis.

Operational Definition: Behavioral therapy was performed with prompted voiding (voiding by clock) at day time & reducing fluid intake at bedtime. Pharmacotherapy was performed with orally administered Imipramine in dose of 25mg at bedtime.

MATERIAL & METHODS:

This comparative study was conducted in the Urology Department of Children Hospital, Faisalabad from April to October, 2016. One hundred & thirty consecutive children of both genders, of age range of 5-13 years with mono-symptomatic Nocturnal Enuresis were enrolled in the study. Sampling was performed with non-probability convenient sampling technique.

The children with known urinary tract pathologies/congenital anomalies, active urinary tract infection, acquired urologic disease, neurologic diseases, children with daytime LUTS were excluded from the study. Detailed history & examination was performed on all children. They were randomly allocated in two groups A & B. Group-A was advised behavior therapy alone while Group-B was given Imipramine along with behavioral therapy.

METHODOLOGY:

Management of NE was done by two methods. The first method was **behavioral therapy** which includes lifestyle modifications by the child in a supportive environment provided by parents/family**.** Patients included in this study were advised to follow some instructions including restricted water intake two hours before bedtime, avoiding tea, coffee, milk, juices and cold drinks after evening and going to washroom right before going to bed. Parents or families were advised to note the usual time of

child wetting the bed after going to sleep, and wake him/her up about fifteen minutes before that time either by themselves or by using alarm (whichever option is more convenient for family and child) and that time should be fixed to wake up the child every night throughout the course of therapy. Special emphasis was put on avoiding any kind of insult, punishment and teasing the child, for wetting bed, both at home by family and at school by friends or peers. Verbal praise/appreciation by parents/family (and if possible some minor reward) after every dry night was encouraged. In the day time, the child was advised bladder re-training i.e. to go to toilet at fixed intervals (prompted voiding) by clock. Parents were motivated to supervise their children for timed voiding. The second method of treatment used was combination therapy that includes drug therapy and behavioral therapy. Drug used for this study was Imipramine which is a tricyclic antidepressant used for management of NE. A dose of 25mg orally was administered at bed time.

Outcome measures: There were three possible outcomes of patients being included in this study. First was *no-response group* when there is no change/improvement in symptoms after a specific period of taking treatment. Second was *improved but not cured group* that includes patients who had only some improvement in symptoms (reduction in number of episodes of NE) after a specific period of taking treatment. Third category is *cured group* including patients with complete remission of the symptoms after taking treatment for specific period.

The children were reviewed after fifteen days and then at one month. Data was recorded on predesigned proforma & statistical analysis was performed via SPSS.

DATA COLLECTION:

After the approval of the research proposal from the "Hospital Ethical Committee", as per inclusion and exclusion criteria, data of patients were collected in the Department of Urology, CHF from the Outpatient Department of the Hospital. Informed consent was taken from parents of all the children for investigations and use of the data for research purpose.

Descriptive statistics: Total number of patients was 130. This included 75 boys (57.7%) and 55 girls (42.3%) with age ranging from 5 to 13 years (mean age: 7.65 & SD: ±2.15). All patients were divided into two groups by computer generated random number table. Group A (n=65, 50%) were advised only behavior therapy for the treatment of Nocturnal Enuresis and group B (n=65, 50%) were given Imipramine plus behavior therapy for the treatment of NE. Total period of treatment was one month and treatment response was assessed in terms of improvement in the NE. The data was recorded twice, first at 15th day follow up and then at 30th day follow up. Depending on response patients were grouped in three categories named, No Response (0), Improved but not cured (1) and completely cured (2). Data was entered on a Performa (attached herewith). Chi-square test was applied

RESULTS:

On first follow up (after 15 days of treatment), there was statistically significant difference in the outcome of both treatment options (behavioral therapy alone verses combination) on depicted by P- value 0.0000. Group-A patients who were treated with only behavioral therapy, 45(69.2%) reported no improvement of symptoms, 15 (23.1%) patients were improved but not cured. The patients who were completely cured were 5 (7.7%). While among group-B patients, who were treated with combination therapy, 15(23%.1) patients had no improvement in symptoms, 40 (61.5%) patients had some improvement in symptoms and 10 (15.4%) were completely cured.

On second follow up (after 30 days of treatment, there was no statistically Significant difference in the outcome of both treatment options (behavioral therapy alone verses combination) on depicted by P- value 0.4832. Group-A patients showed following results. Fifteen (23%) patients reported no improvement of symptoms, 25(38.5%) had some improvement of symptoms and same number i.e. 25 (38.5%) patients were completely cured. From group B patients who had no improvement of their symptoms were

Table 1. 15-days Analysis

Groups	Responses			
	Cured	Improved	Not responded	Total
Group - A	05 7.7% 33.3%	15 23.1% 27.3%	45 69.2% 75%	65 (50%)
Group-B	10 15.4% 6.7%	40 61.5% 72.7%	15 23.1% 25%	65 (50%)
Total	15 11.5%	55 42.3%	60 46.2%	130

X-squared = 28.03 P-value=0.0000

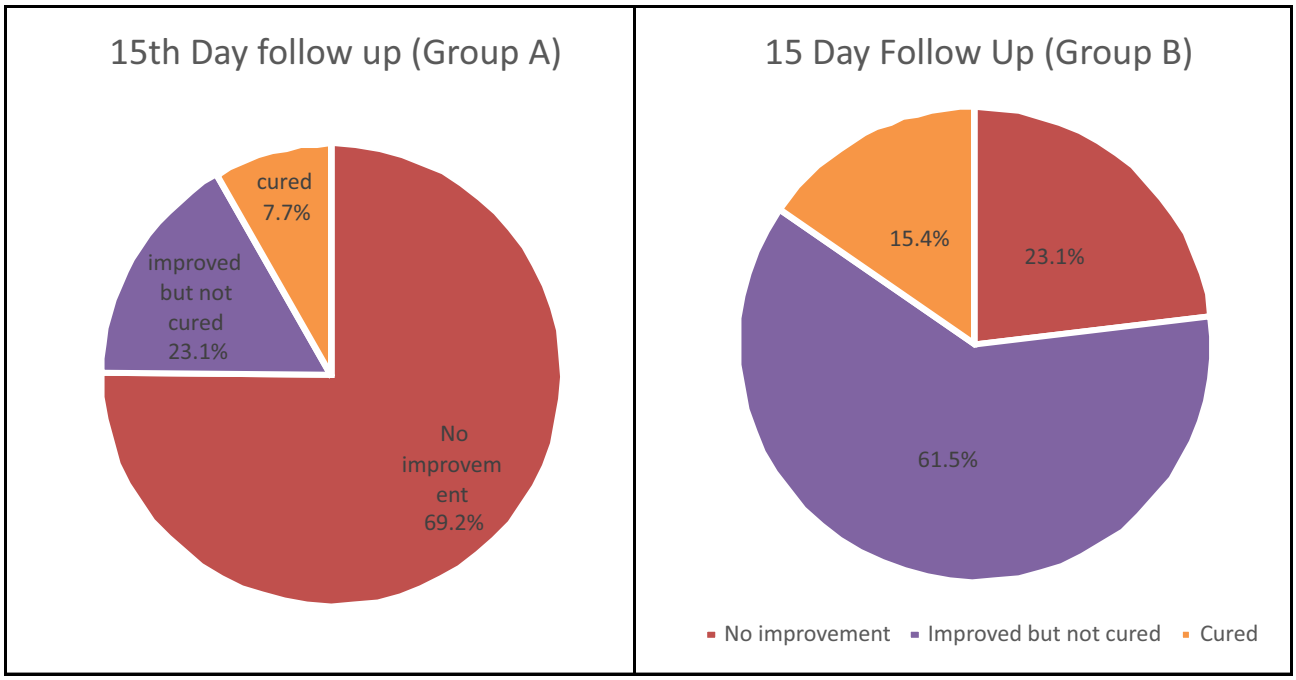

Fig:1 15-days Analysis

Table 2. 30-Days Analysis

Groups	Responses			
	Cured	Improved	Not responded	Total
Group - A	25 38.5% 50.0%	15 38.5% 45.0%	15 23.1% 60.0%	65 (50%)
Group-B	25 38.5% 50%	30 46.2% 45.5%	10 15.4% 40.0%	65 (50%)
Total	50 38.5%	55 42.3%	25 19.2%	130

X-squared+28.03, df=2, P-value=8.19e-07

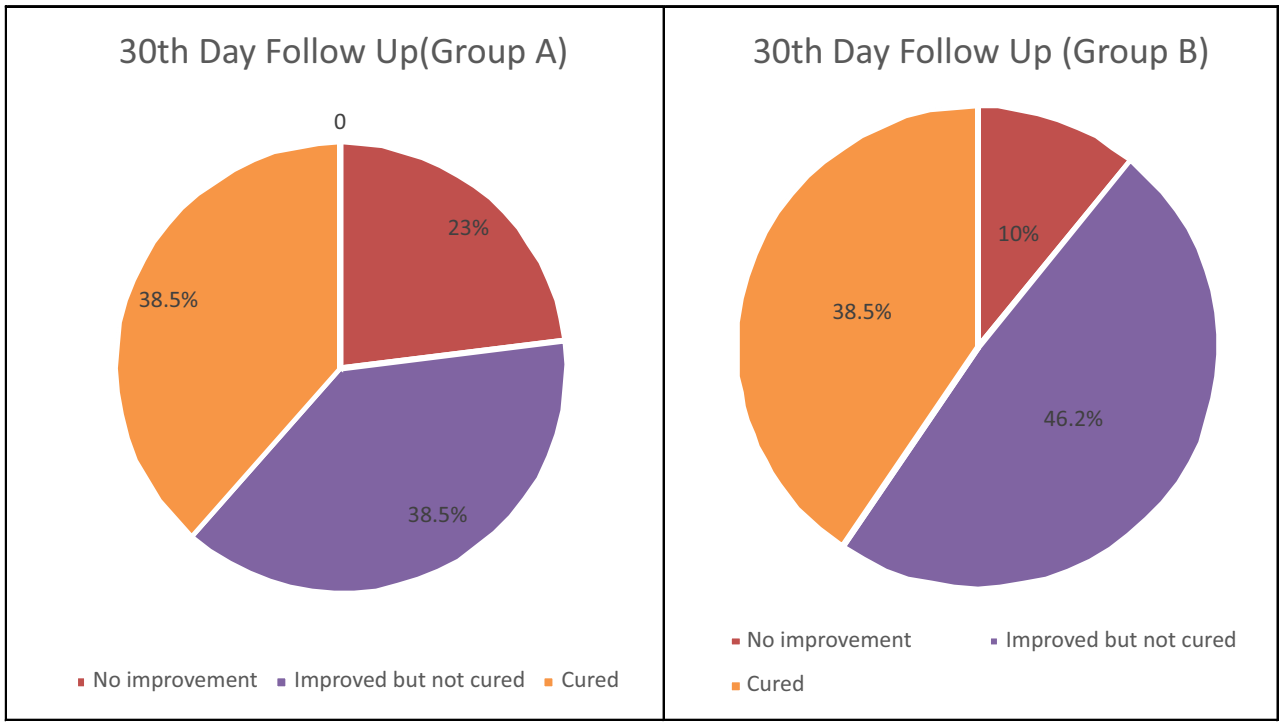

Fig:2 30-days Analysis

10(15.4%), while 30(46.2%) patients reported that they had some improvement but symptoms still persisted. Out of total 65 patients, 25(38.5%) patients were symptom free after one month of treatment.

DISCUSSION:

Nocturnal Enuresis is an uncomfortable condition for the affected children and their parents. Various methods that have been used and studied for treatment of NE are behavioral interventions, that includes parents' education, bladder exercises/retraining, motivation(star charts, encouragement by appreciation and rewards, alarm therapy and pharmacotherapy.

Multiple studies have described different behavioral interventions. A study done by Maxwell[12] included 250 patients with NE showed that combination therapy (Imipramine + simple behavioral therapy) decreased wet nights as compared to placebo with behavioral therapy (MD -0.80, 95% CI -1.33 to -0.27 ; participants= 250). Star charts were used in this study and when combined with Imipramine there was slight improvement in the outcome. However Kumazawa[13] studied a group of patients and concluded that there were no significant differences in the results on follow up of patients treated with Imipramine + behavioral therapy and those treated with placebo and behavioral therapy. (MD -1.13, 95% CI -2.84 to 0.58; participants=20). In this study he used motivation and bladder training exercises as behavioral modalities. The difference in results of both studies may be subjected to different behavioral modalities used, meaning thereby that various behavioral interventions have variable efficacy, difference in sample size and possible variations in patient compliance/bias.

A study conducted by Bhatia [14] on small number of patients revealed that there was no difference in outcomes of combination therapy (Imipramine + behavioral therapy) versus only Imipramine therapy (RR 0.25, 95% CI 0.06 to 1.03; participants=40), However another study by Bhatia suggested better results with combination therapy (Imipramine + behavioral therapy) as compared to other group that was treated with placebo+ behavioral therapy (RR 0.13, 95% CI 0.03 to 0.47; participants=40). In both these studies the behavioral methods used were fluid restriction and avoidance of

punishment. These studies compared behavioral therapy and Imipramine, both in combination and individually. The results of first study points towards Imipramine being the main active component of treatment, however, later study results are similar to our current study and it justifies that behavioral therapy does have a role in itself although a more effective treatment approach involves combining both modalities together.

Fournier[15] also compared Imipramine with behavioral therapy and gave the results that there were 3.3 mean nights per week in behavioral therapy groups compared to 1.9 mean wet nights in Imipramine group. This is also consistent with the results found in our study.

We included the behavioral measures which didn't require any additional training/ knowledge by the parents or any financial strain on family. This was done keeping in view that most of the patients included in our study belonged to lower middle and middle class where both the parents' education and family resources, were limited. On the same grounds, due to its availability in hospital pharmacy the drug used in this study was Imipramine although Desmopressin is preferred now in the treatment of NE because of comparatively less serious side effects[16,17] .

CONCLUSION:

Both behavioral therapy and combination therapy are effective for the management of Nocturnal Enuresis. However, combination therapy shows more rapid and better results when compared to behavioral therapy alone.

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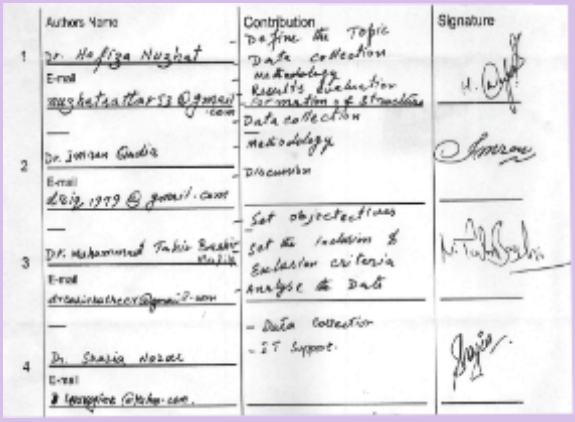

VALUE OF A MAN DEPENDS UPON HIS COURAGE; HIS VERACITY DEPENDS UPON HIS SELF-RESPECT AND HIS CHASTITY DEPENDS UPON HIS SENSE OF HONOR

Hazrat Ali (Karmulha Wajhay)