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COMPARATIVE EFFICACY OF OXYBUTYNIN AND IMIPRAMINE FOR THE TREATMENT OF PRIMARY NOCTURNAL ENURESIS IN A TERTIARY CARE HOSPITAL OF ABBOTTABAD

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Nadia Amin[1], Amjad Iqbal[1], Aziz Ullah[2], Ali Bashir[2], Murad Ali[3]

[1] Combined Military Hospital, Abbottabad

[2] Ayub Teaching Hospital, Abbottabad

[3] Khyber Teaching Hospital, Peshawar

CORRESPONDING AUTHOR: DR AMJAD IQBAL, PROFESSOR OF PAEDIATRICS, COMBINED MILITARY HOSPITAL, ABBOTTABAD

ABSTRACT:

BACKGROUND: Primary nocturnal enuresis (PNE), a common pediatric disease, requires drug therapy when behavioral treatments are ineffective. Although imipramine, a tricyclic antidepressant, and oxybutynin, an anticholinergic drug, are both well-established medications, there is a dearth of direct comparative evidence about their safety profiles, relapse rates, and effectiveness.

AIM: The aim of this study is to evaluate oxybutynin and imipramine's treatment effectiveness, relapse rate, and side effects in children with primary nocturnal enuresis.

METHODS: For a predetermined treatment period, 78 children with PNE diagnoses were recruited and randomized to receive either imipramine (n = 39) or oxybutynin (n = 39) at the Department of Pediatric of

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Combined Military Hospital, Abbottabad from August to November 2025. SPSS 26 was used to examine data on side effects, relapse, treatment response, and demographic characteristics. Mann-Whitney U test, chi square test and t-test was used to compare the variables between the two groups.

RESULTS: The median age was similar between groups. The response rate for oxybutynin was significantly higher (76.9%) than that of imipramine (41.0%) ($p = 0.001$). 10.3% of the oxybutynin group experienced relapse, compared to 28.2% of the imipramine group ($p = 0.044$). Rates of anxiety, sleeplessness, and nausea were similar ($p > 0.05$ for all), but dry mouth was more common with oxybutynin ($p = 0.008$).

CONCLUSION: With a manageable side effect profile, oxybutynin outperformed imipramine in terms of efficacy and relapse rates. For primary nocturnal enuresis, it can be the recommended first-line pharmacologic treatment. In order to confirm these results and evaluate long-term effects, larger multicenter trials are necessary.

KEYWORDS: Primary nocturnal enuresis, Oxybutynin, Imipramine, Comparative study ,Pediatric urology, Therapeutic efficacy , Anticholinergic agents , Tricyclic antidepressants.

INTRODUCTION:

Primary nocturnal enuresis (PNE) represents an issue frequently faced by kids as well as their families. At the young age of five, 15% of children still exhibit insufficient urinary continence, with most cases presenting as isolated nocturnal enuresis (1). The enuresis as the frequent involuntary urination while sleeping occurring at least twice a week among children aged 5 or older for a duration of at least 3 months or enuresis that marks in clinically significant distress or impairment in social as well as academic areas. Enuresis symbolizes the most common urologic issue encountered in pediatric patients within both primary care and specialized medical environments. The condition has a considerable effect on both child as well as the family unit (2–4).

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Healthcare professionals categorize enuresis into two types: monosymptomatic (MNE) as well as non-monosymptomatic (NMNE). MNE is observed in children with no accompanying symptoms of the lower urinary tract and absence of bladder dysfunction (5). Children exhibiting simultaneous lower urinary tract signs are diagnosed with NMNE. The NMNE subtype typically necessitates an extensive evaluation to determine the underlying causes (6).

Imipramine is an antidepressant that has been utilized for a long time. The substance exhibits anticholinergic properties, changes the mechanisms of sleep as well as arousal, along with enhances nocturnal production of antidiuretic hormone (7). The medication may present several side effects, including anxiety, tremor, tachycardia, postural hypotension, allergic skin reactions, as well as elevated intraocular pressure, among others. Oxybutynin functions as an anticholinergic as well as antispasmodic agent, effectively reducing unrestrained bladder contractions (8). It acts as a competitive antagonist of the muscarinic acetylcholine receptors. The substance exhibits direct spasmolytic impacts on the smooth muscle of the bladder, functioning as a calcium antagonist. Oxybutynin being effectively utilized in the management of urologic conditions, including incontinence from urges and neurogenic bladder (9,10). A study compared oxybutynin vs. imipramine in managing PNE in terms of relapse (45%, and 47.8%), and response (40%, and 46.7%) (11).

Oxybutynin is classified as an anticholinergic agent, and imipramine is a tricyclic antidepressant that exhibits both anticholinergic and antidiuretic properties have been utilized separately in the management of PNE. However, their comparative efficacy and possible synergistic effects have not been thoroughly investigated at our local level, therefore the aim of this study is to compare efficacy of oxybutynin and imipramine in treating PNE in a tertiary care hospital of Abbottabad. The findings of this study will be helpful in providing evidence that could guide clinicians in optimizing individualized treatment plans and improving patient outcomes in this common yet challenging condition.

MATERIALS AND METHODS:

This is a randomized controlled trial conducted to compare the efficacy of oxybutynin and imipramine in children with PNE. The study was conducted at the pediatric department of Combined Military Hospital,

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Abbottabad from August to November 2025. Ethical approval was obtained from the Institutional Review Board, and written informed consent was secured from all participants. A total of 78 participants were enrolled in this study.

The participants aged 6-12 years, male or female and who had complaints of repeated urination into bed (nocturnal enuresis) during the sleep minimum of twice a week for at least the period of 3 consecutive months, were included in this study. The children with neurological defects, organic urinary tract diseases, obstructive sleep apnea and renal disease were excluded from this study.

DATA COLLECTION PROCEDURE:

Demographic details like age, gender, weight, financial status, and residence were recorded. Children identified with PNE were randomly allocated in two equal groups (A, and B) by blocked randomization technique. Patients in Group A were treated with oxybutynin tablet with the dosage of 5mg twice daily for 3 months. Patients in Group B were treated with imipramine with the dosage of 25mg 30 minutes before bed time. Efficacy was measured in both groups by recording relapse and response rate. The entire assessment was conducted under the supervision of a consultant with five years of post-fellowship experience.

DATA ANALYSIS PROCEDURE:

Analysis of the data was done using SPSS 26. Mean $\pm$ SD/Median (IQR) were calculated for numerical data i.e. age, and weight after checking the data normality by Shapiro Wilk test. Frequencies and percentages were calculated for categorical data i.e. gender, efficacy, side effect, financial status, and residence. Efficacy was compared in both groups using the chi-square/fisher's exact test. As age was not normally distributed, it was compared using Mann-Whitney U test. p-value $\leq$ 0.05 was considered significant.

RESULTS:

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A total of 78 children were analyzed, with 39 subjects in each of the oxybutynin and imipramine groups. Both groups were similar at baseline for age and weight. The median age of the patients was 9 years; (IQR 8–10) in the oxybutynin group and (IQR 9–10) in the imipramine group. Among the 78 participants, 38 (48.7%) were male. 37 (47.4%) participants were from urban residence and 18 (23.1%) belonged to low income class (Table 1).

Variable	**Oxybutynin (n=39)**	**Imipramine (n=39)**
Age, years, median (IQR)	9 (8–10)	9 (9–10)
Weight, kg, mean ± SD	31.0 ± 3.1	29.5 ± 2.7
Gender		
Male, n (%)	19 (48.7%)	19 (48.7%)
Female, n (%)	20 (51.3%)	20 (51.3%)
Residence		
Urban, n (%)	19 (48.7%)	18 (46.2%)
Rural, n (%)	20 (51.3%)	21 (53.8%)
Socioeconomic status		
Low, n (%)	9 (23.1%)	9 (23.1%)
Middle, n (%)	15 (38.5%)	13 (33.3%)
High, n (%)	15 (38.5%)	17 (43.6%)

Table 1: Demographic characteristics of participants (n=78).

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The intergroup difference in age was statistically significant ($p = 0.041$), but the absolute difference was clinically insignificant. The mean body weight was 31.0 ± 3.1 kg in the oxybutynin group and 29.5 ± 2.7 kg in the imipramine group, showing a statistically significant difference ($p = 0.021$). There were no statistically significant differences between groups regarding residence, or socioeconomic status ($p > 0.05$).

A significantly greater proportion of participants responded to oxybutynin treatment (76.9%) than with imipramine (41.0%) ($p = 0.001$). Relapse after initial improvement was less common in the oxybutynin group (10.3%) than in the imipramine group (28.2%) ($p = 0.044$).

Dry mouth was the most frequent side effect and was significantly more common in children treated with oxybutynin (46.2%) than with imipramine (17.9%) ($p = 0.008$). The prevalence of anxiety (10.3% vs. 23.1%), insomnia (5.1% vs. 17.9%), and nausea (2.6% vs. 10.3%) was not significantly different between the two groups ($p > 0.05$ for all) as shown in Table 2. Both drugs overall were well tolerated.

Adverse Effect	**Oxybutynin (n = 39)**	**Imipramine (n = 39)**	**p-value**
Dry mouth, n (%)	18 (46.2)	7 (17.9)	0.008*
Anxiety, n (%)	4 (10.3)	9 (23.1)	0.129
Insomnia, n (%)	2 (5.1)	7 (17.9)	0.154
Nausea, n (%)	1 (2.6)	4 (10.3)	0.358

Table 2: Frequency and Comparison of Adverse Effects between Oxybutynin and Imipramine Groups

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Multilogistic regression showed that oxybutynin was 4 times higher odds of treatment response compared to imipramine (OR=4.01, 95% CI 1.41-11.39; p= 0.009). Age, gender and weight were not significant predictors for treatment response (Table 3).

Variable	Odds ratio (OR)	95% CI	p-value
Treatment group (Oxybutynin vs Imipramine)	4.01	1.41 – 11.39	0.009
Age (years)	0.66	0.37 – 1.16	0.154
Male sex	0.5	0.18 – 1.34	0.175
Weight (kg)	1.06	0.89 – 1.26	0.512

Table 3: Multivariable Logistic Regression Analysis for Treatment Response.

DISCUSSION:

In this comparative randomized trial, we discovered that oxybutynin yielded significantly greater response rates (76.9%) compared with imipramine (41.0%), with the difference being statistically significant. Furthermore, relapse was less common in the oxybutynin. These findings, combined with tolerability results, indicate that oxybutynin has greater efficacy and long-term benefit than imipramine in PNE children.

Our results are in line with the existing evidence. Osman et al. (12) reported that imipramine is superior to a placebo, although there is a high rate of relapse following therapy withdrawal. However, fewer direct comparison studies are available where imipramine is compared with oxybutynin. Some of the older studies presented better effects on anticholinergics in certain phenotypes, like bladder overactivity with the concomitant condition or small functional bladder capacity (13). For instance, in a double-blind trial

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in children with primary enuresis, oxybutynin was superior to placebo, particularly in those with daytime bladder symptoms (14). These findings add new evidence that, even in a pure nocturnal sample, oxybutynin could be superior to imipramine.

Some combination trials (oxybutynin + desmopressin) imply synergistic efficacy, particularly in refractory patients or mixed-mechanism patients (nocturnal polyuria + bladder hyperactivity) (10). Although those studies are centered on combination therapy, they support the mechanistic likelihood that anticholinergic action (through oxybutynin) can enhance nocturnal detrusor control and decrease wet nights more efficaciously. Our findings, limited to monotherapy, indicate that anticholinergic mechanism of oxybutynin may be adequate in the majority of patients.

The superior performance of oxybutynin can be attributed to its direct action on bladder smooth muscle, decreasing the detrusor overactivity and intravesical pressure at night and enhancing functional bladder capacity. The mechanism of imipramine, on the other hand, is more indirect and may consist of central noradrenergic modulation and anticholinergic side effects. According to the literature (15), anticholinergics are particularly effective if nocturnal enuresis is complicated by intrinsic bladder instability or reduced bladder volume. Considering the heterogeneity of enuresis phenotypes, our patient population could have had children whose pathophysiology predisposed them to respond to anticholinergic therapy. In addition, relapse is a recognized drawback of both treatments. In previous trials, imipramine frequently demonstrates relapse rates of over 30–60% once treatment is discontinued (16,17). Our oxybutynin group's lower relapse indicates that its action may be more long-lasting, or at least that tolerance does not develop as quickly. This might represent more long-lasting modulation of bladder function or reduced central desensitization.

Dry mouth was also much more common in the oxybutynin group, as would be expected based on known anticholinergic side effects. Other side effects—anxiety, insomnia, nausea—did not vary significantly between the groups. This result is consistent with the fairly mild safety profile of oxybutynin noted in previous pediatric series (18). Imipramine has more central actions and, in earlier references, cardiac and anticholinergic hazards; in clinical practice, this usually restricts its application, especially in children

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with cardiovascular risk (19). In our population, CNS side effects were low in both groups, and it appears that, with proper monitoring, either drug can be tolerated. Since dry mouth is usually controllable (e.g., by hydration or modification of dose), the compromise seems to be worthwhile in view of the greater efficacy of oxybutynin. The side effect will result in noncompliance in some patients, so parents should be advised accordingly.

Our data are consistent with the idea that oxybutynin should be included as a potential first-line monotherapy agent in pediatric nocturnal enuresis, particularly where imipramine is utilized. In monotherapy failures, combination therapies (e.g., oxybutynin plus desmopressin) are still useful and have been demonstrated to increase response rates in earlier studies (20). Notably, phenotyping patients (e.g., determining nocturnal polyuria, bladder capacity, frequency pattern) may optimize therapy by allowing identification of those most likely to respond to anticholinergic treatment. In settings where resources are scarce or safety monitoring is difficult, the balance between efficacy and limited side effects of oxybutynin might be better than imipramine's, which calls for greater vigilance. Our 6-month relapse data also reinforce this.

Certain limitations must be recognized. First, our sample size is small; larger multicenter trials will be necessary to validate these results. Second, our follow-up was only for relapse over several months; longer-term results and durability after one year are unknown. Third, we did not stratify patients according to enuretic phenotype (e.g. nocturnal polyuria, bladder capacity), which might affect response to treatment. Fourth, while the side effect profile was good, full quality-of-life or adherence measures were not included.

CONCLUSION:

In this study, oxybutynin showed better therapeutic success and fewer relapses than imipramine in children with PNE. Although oxybutynin caused greater dry mouth, other side effects such anxiety, sleeplessness, and nausea happened at comparable rates in both group, suggesting that the medication was generally well tolerated. According to these results, oxybutynin might be a better first-line medication for treating juvenile enuresis, especially in individuals who exhibit signs of detrusor hyperactivity or who are

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likely to relapse following tricyclic treatment. To validate long-term efficacy, relapse patterns, and safety results, bigger, multicenter trials with longer observation are necessary, as shown by the study's small sample size and scant follow-up.

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