Section: Pharmacology

Original Research Article

COMPARATIVE EVALUATION OF EFFICACY AND COGNITIVE IMPACT OF ANTICHOLINERGIC AGENTS IN THE MANAGEMENT OF OVERACTIVE BLADDER: A RANDOMIZED, OPEN-LABEL STUDY

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ABSTRACT

Background: Overactive bladder (OAB) is a prevalent urological disorder characterized by urinary urgency, frequency, and urge incontinence, and it significantly impairs quality of life. Anticholinergic agents remain the mainstay of pharmacological management for OAB due to their proven efficacy in reducing detrusor overactivity. Among these, tolterodine and oxybutynin are commonly prescribed. However, anticholinergic medications differ in their ability to cross the blood–brain barrier and interact with central muscarinic receptors, leading to variability in cognitive adverse effects. The purpose of this study was to compare the cognitive effects and effectiveness of tolterodine and oxybutynin in OAB patients. **Materials and Methods:** This was an 8-week, randomized, open-label, parallel-group clinical trial conducted among 100 patients with clinically diagnosed OAB. Participants were randomly allocated into two equal groups. One group received tolterodine at a dose of 2 mg twice daily, while the other group received oxybutynin at a dose of 5 mg twice daily. Cognitive function was assessed at baseline and at the end of the study using the Montreal Cognitive Assessment (MoCA), a validated screening tool for mild cognitive impairment. Treatment efficacy was evaluated by documenting changes in the number of urgency episodes and incontinence events per day, as recorded in bladder diaries. Statistical analysis was performed to compare within-group and between-group changes, with a p value <0.05 considered statistically significant. **Result:** Both treatment groups demonstrated a statistically significant reduction in urgency and incontinence episodes over the 8-week period ($p<0.001$), confirming the effectiveness of both tolterodine and oxybutynin in the management of OAB symptoms. Patients treated with tolterodine did not show any significant decline in MoCA scores from baseline, indicating preservation of cognitive function. In contrast, the oxybutynin group exhibited a modest but statistically significant reduction in MoCA scores (mean decrease of 1.8 points; $p=0.03$), suggesting a negative impact on cognition. **Conclusion:** While both tolterodine and oxybutynin are effective in alleviating OAB symptoms, tolterodine demonstrates a superior cognitive safety profile. These findings suggest that tolterodine may be a more suitable option, particularly for patients in whom cognitive preservation is a priority.

INTRODUCTION

Overactive bladder (OAB) is a chronic and distressing clinical condition characterized by urinary urgency, increased frequency, nocturia, and urge urinary incontinence.[1] It affects an estimated 12–17% of the adult population worldwide, with prevalence increasing progressively with advancing age. OAB exerts a substantial negative impact on quality of life, leading to social embarrassment, sleep disturbance, reduced work productivity, and psychological stress.[2] The International Continence Society defines OAB as a symptom complex rather than a single disease entity, emphasizing the heterogeneity of its underlying mechanisms and the importance of individualized therapeutic approaches.[3]

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Pharmacological management remains a cornerstone of OAB treatment, with anticholinergic agents widely regarded as first-line therapy.[4] These drugs exert their therapeutic effect primarily by antagonizing muscarinic receptors, particularly the M2 and M3 subtypes, located on detrusor smooth muscle.[5] Inhibition of these receptors reduces involuntary detrusor contractions, thereby decreasing episodes of urgency, frequency, and urge incontinence.[6]

Muscarinic receptors are widely distributed throughout the body, including the salivary glands, gastrointestinal tract, and central nervous system (CNS).[7] Consequently, anticholinergic therapy is often associated with adverse effects such as dry mouth, constipation, blurred vision, and, more importantly, cognitive dysfunction. Cognitive adverse effects are of particular concern in older adults, who are more susceptible to central anticholinergic burden and may already have age-related cognitive vulnerability.[8]

Oxybutynin is a commonly prescribed antimuscarinic agent for OAB and is known for its non-selective muscarinic receptor antagonism and high lipophilicity. These properties facilitate its penetration across the blood–brain barrier, increasing the likelihood of central nervous system effects, including impaired attention, memory deficits, and reduced executive function.[9,10] In contrast, tolterodine has been developed with greater functional selectivity for bladder muscarinic receptors and demonstrates relatively limited CNS penetration, suggesting a potentially more favorable cognitive safety profile.[11]

Given the widespread use of both medications in routine clinical practice, a direct comparison of their therapeutic efficacy and cognitive effects is clinically relevant. This study was therefore designed to evaluate and compare oxybutynin and tolterodine with respect to symptom control and cognitive outcomes in patients with overactive bladder.

The novelty of this study lies in its simultaneous evaluation of symptom relief and objective cognitive performance using standardized cognitive assessment tools, thereby providing clinically meaningful evidence to guide rational drug selection in OAB management with a focus on cognitive safety.

Aims and Objectives: To compare the therapeutic efficacy and cognitive effects of tolterodine and oxybutynin in patients with overactive bladder.

MATERIALS AND METHODS

Study Design: This study was conducted as a prospective, randomized, open-label, parallel-group clinical trial over a period of 8 weeks in the Departments of Pharmacology and Urology.

Study Population and Sample Size: A total of 50 patients aged between 40 and 75 years, diagnosed with overactive bladder (OAB) according to the International Continence Society (ICS) criteria, were enrolled in the study.

Inclusion Criteria

Patients aged 40–75 years with a clinical diagnosis of OAB, experiencing at least three episodes of urinary urgency per day, and willing to provide informed consent and comply with study procedures were included.

Exclusion Criteria

Patients with known neurodegenerative disorders, narrow-angle glaucoma, urinary retention, or those receiving concurrent central nervous system–active medications were excluded. Individuals with a baseline Montreal Cognitive Assessment (MoCA) score below 24 were also excluded to avoid confounding due to pre-existing cognitive impairment.

Intervention: Eligible participants were randomly allocated into two treatment groups. Group A received oxybutynin at a dose of 5 mg twice daily, while Group B received tolterodine at a dose of 2 mg twice daily, for a duration of 8 weeks.

Outcome Measures: The primary outcome measure was the reduction in the number of daily urgency episodes, as recorded in patient bladder diaries. Secondary outcome measures included changes in cognitive function assessed using the Montreal Cognitive Assessment (MoCA) score from baseline to the end of the study period. Adverse events were actively monitored and recorded throughout the study duration.

Statistical Analysis: Data were analyzed using appropriate statistical methods. Within-group comparisons were performed using the paired t-test, while between-group differences were assessed using analysis of variance (ANOVA). A p value of less than 0.05 was considered statistically significant.

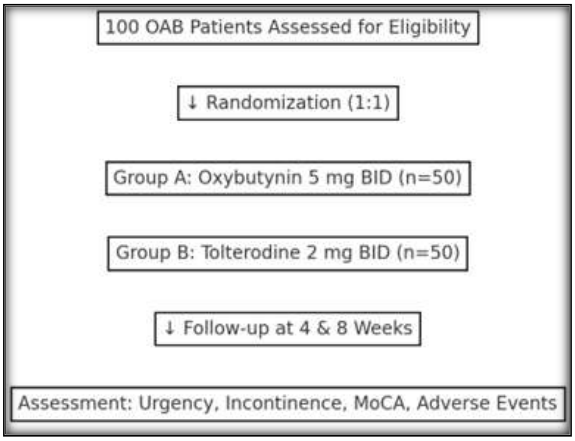

Figure 1: Study Design Flowchart

RESULTS

A total of 100 patients were included in the analysis, with 50 patients each in the oxybutynin and tolterodine groups. As shown in Table 1, both groups were comparable with respect to baseline demographic and clinical characteristics. The mean age of patients in the oxybutynin group was 59.4 ± 8.6 years, while that of the tolterodine group was 58.7

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± 9.1 years, with no statistically significant difference (p = 0.73). Gender distribution was similar between the two groups, with a near-equal male-to-female ratio (28:22 in the oxybutynin group and 27:23 in the tolterodine group; p = 0.85).

Baseline cognitive function, assessed using the Montreal Cognitive Assessment (MoCA), was comparable in both groups (26.2 ± 1.8 vs 26.4 ± 1.6; p = 0.71). The baseline severity of OAB symptoms was also similar, with mean urgency episodes per day of 7.1 ± 1.3 in the oxybutynin group and 7.0 ± 1.2 in the tolterodine group (p = 0.68).

Table 1: Demographic and Baseline Characteristics

Parameter	Oxybutynin (n=50)	Tolterodine (n=50)	p-value
Age (years), mean ± SD	59.4 ± 8.6	58.7 ± 9.1	0.73
Sex (M:F)	28:22	27:23	0.85
Baseline MoCA, mean ± SD	26.2 ± 1.8	26.4 ± 1.6	0.71
Baseline urgency/day, mean ± SD	7.1 ± 1.3	7.0 ± 1.2	0.68

Both treatment groups demonstrated a statistically significant reduction in urgency episodes from baseline (p < 0.001). The mean reduction was 4.5 episodes per day in the oxybutynin group and 4.2 episodes per day in the tolterodine group. The near-overlapping bars illustrate comparable therapeutic efficacy between the two agents, visually confirming substantial symptom improvement with no significant inter-group difference. [Figure 2]

Both oxybutynin and tolterodine produced a significant reduction in urgency episodes after 8 weeks (p < 0.001), with comparable mean decreases of 4.5 and 4.2 episodes per day, respectively, indicating similar therapeutic efficacy. [Table 2]

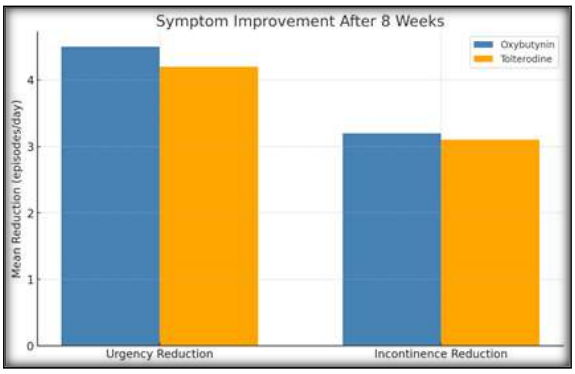

Figure 2: Comparison of Symptom Reduction Between Groups.

Table 2: Efficacy Outcomes (Symptom Improvement After 8 Weeks)

Variable	Drug	Baseline (mean ± SD)	8 Weeks (mean ± SD)	Mean Change ± SD / p-value
Urgency episodes/day	Oxybutynin	7.1 ± 1.3	2.6 ± 1.0	−4.5 ± 1.2; p<0.001
Urgency episodes/day	Tolterodine	7.0 ± 1.2	2.8 ± 1.1	−4.2 ± 1.1; p<0.001

The most common adverse effects observed were dry mouth and constipation, occurring slightly more frequently with oxybutynin (36% and 20%, respectively) than with tolterodine (28% and 16%). This pattern suggests a higher anticholinergic burden with oxybutynin. All adverse events were mild, and no patients discontinued therapy. [Table 3]

Table 3: Frequency of Adverse Effects

Adverse Effect	Oxybutynin n (%)	Tolterodine n (%)
Dry mouth	18 (36%)	14 (28%)
Constipation	10 (20%)	8 (16%)

Oxybutynin was associated with a significant decline in MoCA scores (−1.8; p = 0.03), whereas tolterodine showed no significant cognitive change (−0.3; p = 0.18), demonstrating a superior cognitive safety profile for tolterodine. [Table 4, Figure 3]

Table 4: Cognitive Function (MoCA Scores)

Drug	Baseline MoCA	8 Weeks MoCA	Δ Score	p-value
Oxybutynin	26.2 ± 1.8	24.4 ± 2.0	−1.8	0.03
Tolterodine	26.4 ± 1.6	26.1 ± 1.7	−0.3	0.18

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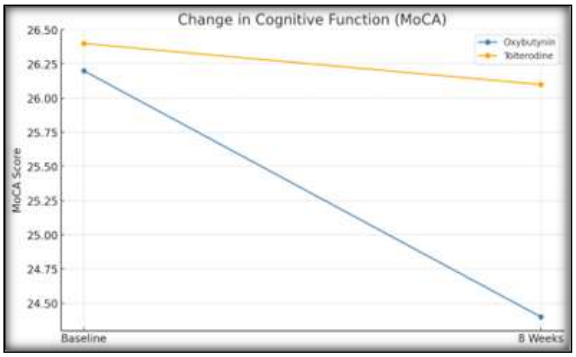

Figure 3: Change in Cognitive Function Measured by MoCA

DISCUSSION

Both oxybutynin and tolterodine demonstrated comparable efficacy in reducing urgency and incontinence episodes among patients with OAB. However, a statistically significant cognitive decline was observed with oxybutynin, likely due to its high lipid solubility and central muscarinic receptor blockade. Tolterodine, due to lower CNS penetration, maintained cognitive stability while achieving similar bladder control.

These findings were in agreement with previous studies (Wagg et al Kay et al),[12,13] which reported a higher risk of cognitive impairment with oxybutynin compared to other anticholinergics. Clinically, this supports the preferential use of tolterodine in elderly or cognitively vulnerable patients. The development of newer therapeutic agents, such as mirabegron and selective M3 antagonists, provides additional alternatives with reduced CNS adverse effects.

The observed cognitive decline with oxybutynin can be explained by its high lipophilicity and non-selective muscarinic antagonism, facilitating CNS penetration, particularly in older adults. Tolterodine, while also a non-selective antagonist, demonstrates functional bladder selectivity, achieving therapeutic benefit with fewer off-target CNS effects. This supports the established concept that M1 receptor antagonism is strongly associated with cognitive impairment, accounting for oxybutynin's higher cognitive burden. Additionally, differential P-glycoprotein interactions may influence CNS accumulation of anticholinergic drugs, contributing to the observed disparities in cognitive outcomes.

Harvey MA et al,[14] reported that oxybutynin was slightly more effective than tolterodine in reducing 24-hour incontinent episodes (weighted mean difference 0.41; 95% CI, 0.04–0.77) and increasing mean voided volume per micturition (8.24 mL; 95% CI, 3.38–14.19). However, tolterodine was associated with a lower incidence of dry mouth (relative risk 0.54; 95% CI, 0.48–0.61) and fewer withdrawals due to adverse effects (relative risk 0.63; 95% CI, 0.46–0.88), indicating better tolerability despite comparable overall efficacy.

Sand PK et al,[15] found that daily extended-release oxybutynin chloride (10 mg) provided greater improvement in urge and total incontinence compared to tolterodine tartrate (2 mg BID), while the incidence of dry mouth, central nervous system events, and other adverse effects was similar between the two drugs.

Welk B et al,[16] observed that anticholinergic use for OAB was not associated with significant cognitive changes in individuals with normal or impaired baseline cognition. They emphasized the need for further research to determine whether oxybutynin and tolterodine carry a differential risk of cognitive decline.

Given the comparable efficacy of both drugs, tolerability—particularly cognitive safety—becomes a key determinant in treatment selection. Tolterodine is therefore a more practical option for older OAB patients. Cognitive monitoring using tools such as the MoCA or MMSE is recommended when prescribing oxybutynin to patients over 55–60 years, especially those with comorbidities.

The study also underscores the importance of minimizing polypharmacy, as cumulative anticholinergic burden from other medications can exacerbate cognitive decline. Early recognition of common anticholinergic adverse effects, such as dry mouth, constipation, and dizziness, allows clinicians to implement timely dose adjustments or switch to alternative therapies, optimizing both safety and treatment outcomes.

Limitations

1. Short study duration (8 weeks).
2. Open-label design with potential bias.
3. No inclusion of newer OAB drugs such as mirabegron.
4. Cognitive testing limited to MoCA; detailed neuropsychological assessments were not performed.

CONCLUSION

Both oxybutynin and tolterodine effectively alleviate overactive bladder symptoms, but tolterodine shows superior cognitive safety. Its lower central nervous system penetration minimizes cognitive impairment, making it the preferred choice for older adults or patients at risk of cognitive decline, while maintaining comparable efficacy in symptom control.

REFERENCES

1. Shaw C, Wagg A. Overactive bladder in frail older adults. Drugs & Aging. 2020 Aug;37(8):559-65.
2. Gomes CM, Averbeck MA, Koyama M, Soler R. Impact of OAB symptoms on work, quality of life and treatment-seeking behavior in Brazil. Current medical research and opinion. 2020 Aug 2;36(8):1403-15.
3. Sekido N, Omae K, Kubota Y, Mitsui T, Masumori N, Haga N et al. Underactive bladder as defined by the international continence society in the 2023 Japan community health survey. International Journal of Urology. 2025 Jan;32(1):51-9.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

4. Welk B, Richardson K, Panicker JN. The cognitive effect of anticholinergics for patients with overactive bladder. Nature Reviews Urology. 2021 Nov;18(11):686-700.
5. Hsu FC, Weeks CE, Selph SS, Blazina I, Holmes RS, McDonagh MS. Updating the evidence on drugs to treat overactive bladder: a systematic review. International urogynecology journal. 2019 Oct;30(10):1603-17.
6. Yudiati Y, Hasanah H. Management of Overactive Bladder. The International Journal of Medical Science and Health Research. 2024 Oct 27;5(8):44-58.
7. Reza KH, Das PP, Hossain CM, Shaharyar MA, Pal S, Ali SZ et al. Mechanism of action of cholinergic drugs. InHow Synthetic Drugs Work 2023 Jan 1 (pp. 27-46). Academic Press.
8. Ochoa DC, Bouchard B, Abrams P. A historical perspective on anticholinergics in overactive bladder (OAB) treatment:"Foundations, current practices, and future prospects". Continence. 2024 Dec 1;12:101707.
9. Lin J, Bu G, Unge J, Gonen T. An updated structure of oxybutynin hydrochloride. Advanced Science. 2024 Oct;11(40):2406494.
10. Alghamdi MM, Ko KJ, Lee KS. An update on the cognitive safety of antimuscarinics in the treatment of overactive bladder. Expert Opinion on Drug Safety. 2024 Oct 2;23(10):1227-36.
11. Hoshi N, Ehlert F. Muscarinic Antagonists and Their Clinical Uses. Brody's Human Pharmacology-E-Book: Brody's Human Pharmacology-E-Book. 2024 Feb 2;79.
12. Wagg A, Gibson W. OAB and cognition in the elderly: review and future directions. Drugs Aging. 2019;36(10):897–906.
13. Kay GG. Cognitive effects of anticholinergic medications in older adults. J Am Geriatr Soc. 2016.
14. Harvey MA, Baker K, Wells GA. Tolterodine versus oxybutynin in the treatment of urge urinary incontinence: a meta-analysis. American journal of obstetrics and gynecology. 2001 Jul 1;185(1):56-61.
15. Sand PK, Miklos J, Ritter H, Appell R. A comparison of extended-release oxybutynin and tolterodine for treatment of overactive bladder in women. International Urogynecology Journal. 2004 Aug;15(4):243-8.
16. Welk B, McClure JA. The impact of anticholinergic use for overactive bladder on cognitive changes in adults with normal cognition, mild cognitive impairment, or dementia. European Urology Open Science. 2022 Dec 1;46:22-9.

ISSN (O): 2687-5365; ISSN (P): 2753-6556