Anticholinergic drugs and risk of Cognitive Impairment or Dementia in patients with Overactive Bladder Syndrome: A Systematic Review and Meta-Analysis

534

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Introduction

Overactive bladder syndrome (OAB) is one of the most common medical conditions referred to Urologists (1).

Anticholinergic medications are commonly used as to treat such patients (2).

The relationship between cognitive impairment or dementia and anticholinergic medications remains uncertain.

There has been an ongoing debate regarding the relationship between the adverse events of these drugs and Central Nervous system (CNS) impairment in these patients.

The aim of our study is to evaluate the reported relationship between using anticholinergic drugs for patients with OAB and the risk of cognitive impairment or dementia as an adverse event.

Methods

A literature search was conducted using PubMed, Scopus, Web of science, and Science Direct to identify relevant studies published until December 2018.

Studies included were randomized controlled trials (RCTs) and cohort studies in patients with OAB, which used the mean change of Mini-Mental State Examination (MMSE) as a scale for assessment of the cognitive status, comparing anticholinergic agents with placebo or other active treatments in relation to deterioration in the MMSE score, as a primary outcome, and CNS adverse events, as a secondary outcome.

Data were pooled as risk ratio (RR) or mean difference (MD) between the two compared groups in a random effects meta-analysis model. Subgroup and sensitivity analysis were conducted.

Results

Three cohort studies and six RCTs with a total of 2,594 participants (mean age 70.7 ± 9.4 years) were included in the analysis.

The RCTs consisted of a total 1,626 participant with OAB of which 949 participants were using anticholinergic drugs. This included Fesoterodine (41.4%), Darifenacin (3.0%), Trospium (2.0%), Oxybutynin (7.5%) or Placebo (46.1%).

The cohort studies consisted of 968 participants with OAB using Solifenacin (82.5%), Darifenacin (5.2%), Oxybutynin (4.4%), Trospium (2.7%), Tolterodine (2.2%) or other drugs including Placebo (3.0%).

The longest follow up duration was 6 months. Meta-analysis of the primary outcome showed that Darifenacin was slightly more significant in lowering MMSE Score compared to Trospium (MD= -1.60, 95% CI [-3.10, -010], p=0.04).

This is the only study that showed dementia as a side effect (11.9%). There was no significant difference in MMSE between Oxybutynin Extended and Immediate Release.

The pooled estimate of two studies did not favor either Fesoterodine or Placebo to reducing MMSE Score (MD= -0.01, 95% CI [-0.25, 0.27], p=0.94).

No significant differences were observed between other anticholinergic drugs when compared to each other or to Placebo.
With regards to the secondary outcomes, Fesoteridine had higher risk of Dizziness than Placebo (RR= 2.82, 95% CI [1.12,7.09], p=0.03).

No significant difference was observed in term of Serious Side Effects between Fesoteridine and Placebo (RR= 1.45, 95% CI [0.76, 2.78], p=0.26)

Figures

Fig.1. Effect of Anticholinergic agents on Cognitive impairment using MMSE Assessment between Oxybutynin Extended and Immediate Release. *(Randomized Controlled Trials)*

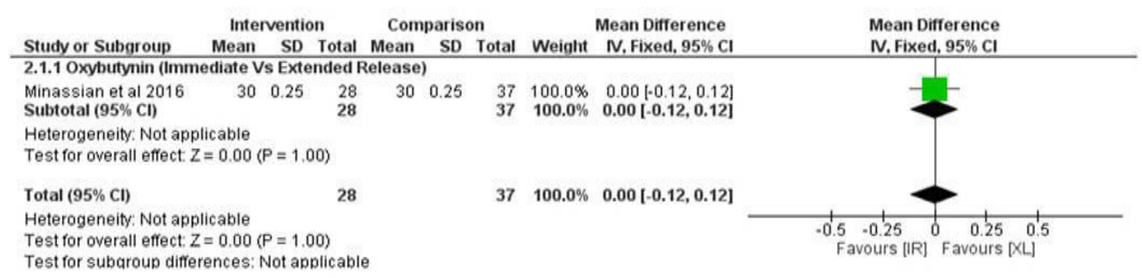


Fig.2. Effect of Anticholinergic agents on Cognitive impairment using MMSE Assessment Comparing Anticholinergics agents to Placebo. *(Randomized Controlled Trials)*

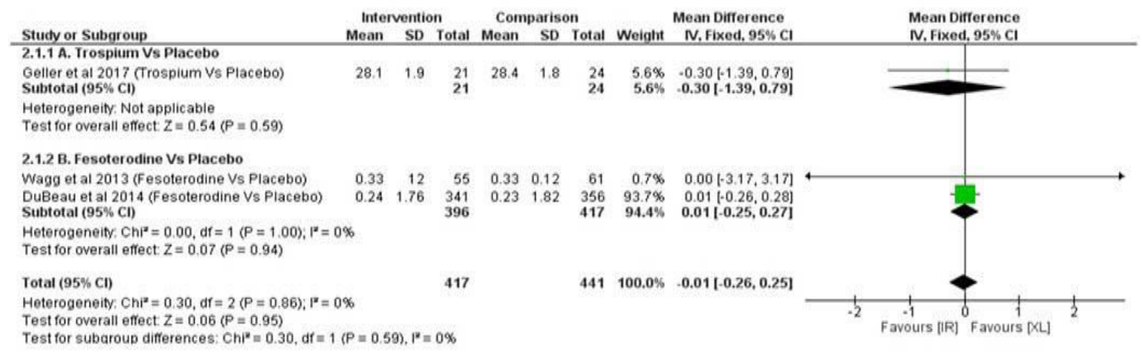


Fig.4. Forest plot of Serious Adverse events: Comparing Anticholinergics to Placebo

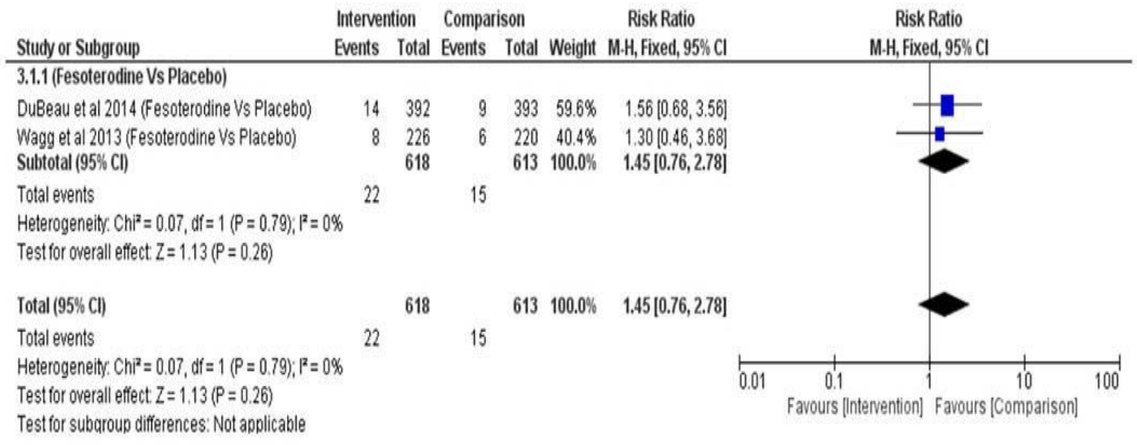
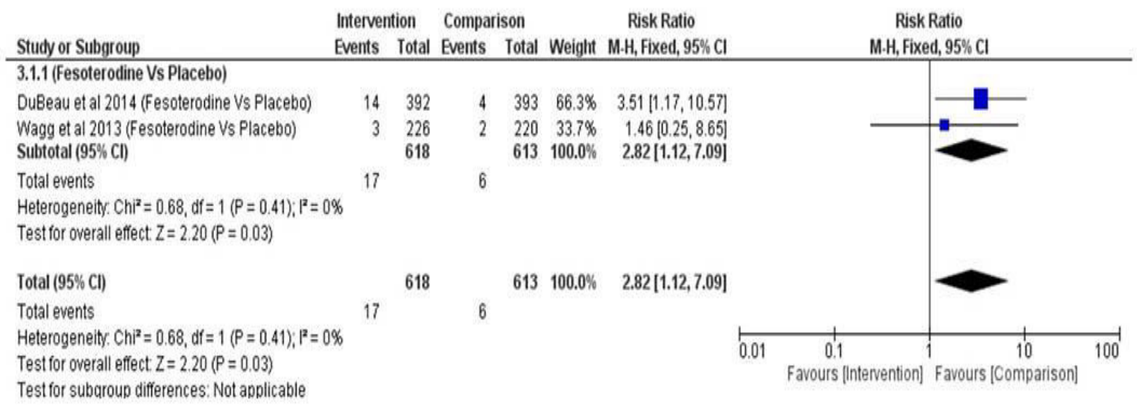


Fig.5. Forest plot of Dizziness Side Effect: Comparing Anticholinergics to Placebo



Interpretation of Results

From our review study, we can see that there were a few studies that discussed the effects of anticholinergic medication on cognitive impairment, using the Mini Mental State Examination as a standard scale for cognition and dementia.

However, none of the RCTs discussed the direct effect on dementia except for one cohort study that showed dementia as side effect but was not significant.

Conclusions

The present meta-analysis of RCTs and cohort studies with short term follow up duration of up to 6 months has demonstrated that anticholinergic medications do not impair cognitive functions according to the Mini Mental State Examination scores in patients with OAB.

Further RCTs with larger number of patients and longer follow up period with MMSE assessment are needed to confirm our findings.

References

1.Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R, Hunt TL, Wein AJ. Prevalence and burden of over-active bladder in the United States. World J Urol. 2003;20:327–336
2.Schroder A, Thuroff JW (2010) New strategies for medical management of overactive bladder in children. Curr Opin Urol 20(4):313–317.