Systematic Review and Meta-Analysis

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Systematic review and meta-analysis of the efficacy and safety of vibegron vs antimuscarinic monotherapy for overactive bladder

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Abstract

Background: Vibegron is a new β3-adrenergic receptor agonist which has been demonstrated for the treatment of overactive bladder (OAB). We carried out meta-analysis to evaluate the efficiency of vibegron vs antimuscarinic monotherapy for treating OAB.

Methods: Randomized controlled trials (RCTs) of Vibegron vs antimuscarinic monotherapy for OAB were searched systematically by using EMBASE, MEDLINE, and the Cochrane Controlled Trials Register. The RevMan version 5.3.0. was used to analysis the data.

Results: Three RCTs involving a total of 1751 patients were studied in the Systematic review and Meta-analysis. Efficacy end points: the mean number of micturitions episodes/d ($P = .16$); the mean number of urgency episodes/d ($P = .05$); mean number of urgency incontinence episodes/d ($P = .11$) and mean number of incontinence episodes/d ($P = .14$) indicated that vibegron and antimuscarinic had no significant differences in terms of OAB treatment. Mean volume voided/micturition showed a distinct difference in the two groups ($P = .009$). With regard to dry mouth and drug related treatment-emergent adverse event (TEAE), vibegron showed better tolerance than antimuscarinic. Serious adverse event (SAE) and discontinuations due to adverse event (AE) did not show a significant difference between the two groups.

Conclusions: The therapeutic effect of vibegron is similar to that of antimuscarinic, but vibegron does not increase the risk of AE.

Abbreviations: AE = Adverse event, BPH = Benign prostatic hyperplasia, CI = Confidence interval, KHQ = King's Health Questionnaire, LUTS = Lower urinary tract syndrome, MD = Mean difference, OAB = Overactive bladder, OR = odds ratio, RCT = randomized controlled trial, SAE = serious adverse event, TEAE = treatment-emergent adverse event.

Keywords: vibegron, antimuscarinic, overactive bladder, randomized controlled trials, systematic review and meta-analysis

1. Introduction

Overactive bladder (OAB) is characterized by urinary urgency with or without urgent urinary incontinence and usually accompanied by frequent micturition and nocturia, but absence of a urinary-tract infection or other underlying disease.[1] It is a multifactorial and common health disorder associated with detrimental effects on quality of life and huge economic burden and the prevalence in adults is 10% to 20% all over the world.[2,3] The first-line treatment of OAB is antimuscarinic agents (e.g., solifenacin, imidafenacin, fesoterodine, oxybutynin, and tolterodine).[4] Nevertheless, antimuscarinic drugs have short-term persistence due to inadequate efficacy or adverse events (AEs), including blurred vision, constipation, and dry mouth.[5]

Several clinical trials have demonstrated that 12-week treatment with vibegron is effective and well tolerated in patients with OAB.[6] Besides, Shi et al[7] conducted a systematic review and pooled analysis demonstrating that compared with placebo, vibegron 75 mg or 100 mg/d statistically significant improved OAB symptoms.

However, there were few articles focusing on the advantages and disadvantages of vibegron vs antimuscarinic agents. Comparison of the different roles of vibegron and antimuscarinic agents in OAB treatment is important. Therefore, we conducted a Systematic review and Meta-analysis to access the efficiency and safeness of vibegron and antimuscarinic agents in treating OAB patients, aiming to aid process of choosing medicine for OAB patients.

2. Materials and methods

2.1. Search strategy

We searched relevant randomized controlled trials (RCTs) referred to the efficacy and safety of vibegron vs antimuscarinic monotherapy for OAB to March 2020 on MEDLINE, EMBASE, and Cochrane Controlled Trials Register databases. The search

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The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the present study are available from the corresponding author on reasonable request.

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terms includes "vibegron," "antimuscarinic," "OAB," and "RCTs." Two authors completed the whole screening process independently, and if there was any dispute, articles would be sent to another author for evaluation. Relevant reference articles were also included.

2.2. Inclusion and exclusion criteria

All of the included RCTs meet the following criteria:

1. vibegron vs antimuscarinic (tolterodine or imidafenacin) in treating OAB which was analyzed at least 12-week,
2. According to the King's Health Questionnaire (KHQ),[8] the study provided effective and accurate data, these indicators were considered to be better reflect the symptom and treatment effect of OAB, such as: the number of OAB patients, the mean number of micturitions episodes/d, the mean number of urgency episodes/d, mean number of urgency incontinence episodes/d, mean number of incontinence episodes/d, mean volume voided/micturition, dry mouth, drug related TEAE (treatment-emergent adverse event) (diarrhea, cystitis nasopharyngitisan, and others), SAE (serious adverse event) (deaths, back pain, pyelonephritis, colon cancer, and so on) and discontinuations due to AE (adverse event), and
3. full text available.

These studies are excluded as follow:

1. The data was incomplete;
2. The type of study was abstract, review, comment, case–control, and cohort studies;
3. Patients had a daily average urine volume output of >3000 mL.

2.3. Quality assessment

We evaluated the quality of included RCTs by using the Jadad Scale.[9] Furthermore, the quality of each study was evaluated on the basis of method of patient allocation, concealment of allocation, blinding method, and number of lost to follow up. Based on the guidelines published in the Cochrane Handbook for Systematic Reviews of Interventions V.5.1.0,[10] the quality of each study is graded into three degrees: quality degree "A," the study met all quality criteria and had a low-risk of bias; quality degree "B," the study met most quality criteria and had a moderate risk of bias; and quality degree "C," the study met few quality criteria and had a high risk of bias. All authors participated in the evaluation process and reach consensus on the final results.

2.4. Data extraction

The patients came from all over the world, and there were no repetition of the crowd among the studies. From included studies, we obtained the following information:

1. Published time;
2. The first author' name;

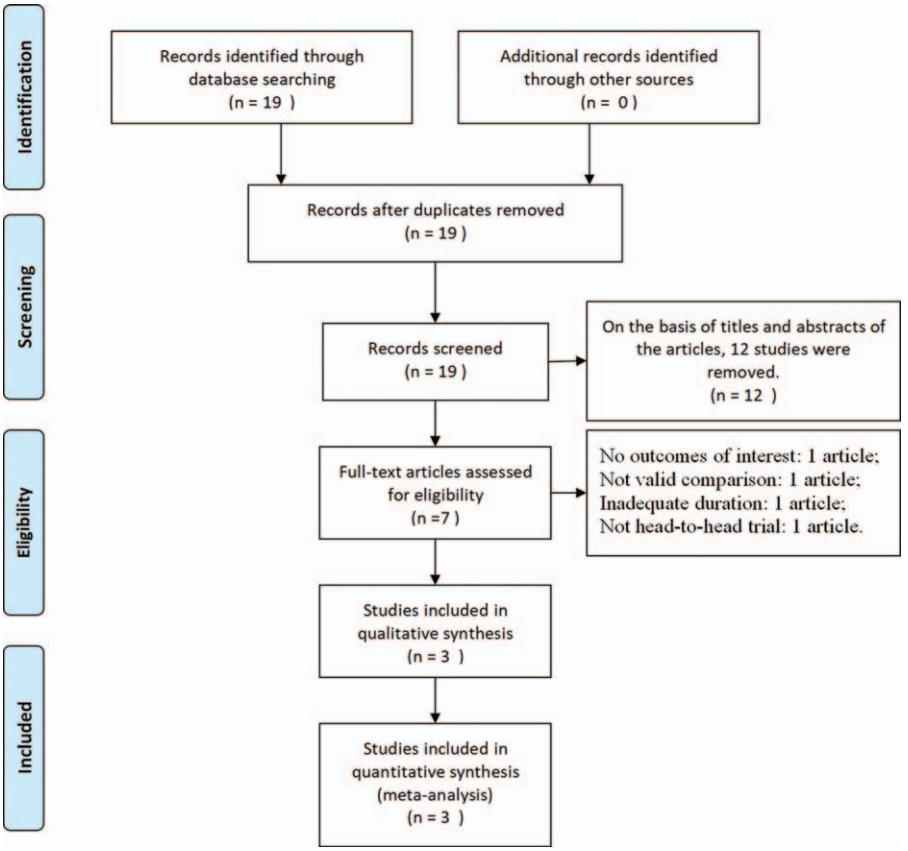

Figure 1. A flow diagram of the study selection process.

3. Patient's received therapy;
4. Sample size of each group;
5. Differences in the following indicators: the mean number of micturitions episodes/d, the mean number of urgency episodes/d, mean number of urgency incontinence episodes/d, mean number of incontinence episodes/d, mean volume voided/micturition, dry mouth, drug related TEAE, SAE and discontinuations due to AE.

A noteworthy fact is that as the dose of tolterodine was different in 2 RCTs, some indicators of cardiovascular system could not be analyzed in this meta-analysis due to the half-baked data.

2.5. Statistical analysis and meta-analysis

The abstracted data (Table 3) were analyzed with Review Manager 5.1.0 (The Cochrane Collaboration, London, UK).[9] The publication bias were assess by Egger's test and Begg's funnel plot. The mean difference (MD) with 95% confidence interval (CI) was utilized to analyze the continuous data and the odds ratio (OR) with 95% CI was applied to analyze the dichotomous data among the different groups.[11] The chi-square based Q statistic was performed to check the heterogeneity among the studies, and result was recognized as significant at $P < .05$. When the $I^2 < 50\%$, indicated that there was no significant heterogeneity and the fixed-effects model (Mantel–Haenszel method) would be used. And we performed the random-effects model (DerSimonian and Laird method) when the heterogeneity of the data could not be explained ($P < .05$, $I^2 > 50\%$).

3. Results

3.1. Study selection process, search results and characteristics of studies

Based on retrieval terms, we found 19 articles in database. According to the aforementioned inclusion and exclusion criteria, 12 studies were removed after reviewing the titles and abstracts of the articles. And in the rest of 7 articles, 4 studies were excluded for lack of useful data (No outcomes of interest: 1 article; not valid comparison: 1 article. inadequate duration: 1 article; not head-to-head trial: 1 article). Finally, three RCTs[12–14] involving 1751 patients were included in the analysis (detail in Fig. 1). Table 1 listed characteristics of the included studies.

3.2. Quality of the individual studies

All of the included studies in the Systematic review and Meta-analysis were high quality RCTs. All articles had a appropriate number of participants to analyze, and no study showed intention-to-treat analysis (Table 2). Finally, the quality level

Table 1

Study and patient characteristics.

Study	Therapy in experimental group	Therapy in control group	Country	Sample size/dosage		Administration method	Duration of treatment	Inclusion population	Pre-treatment methods
				experimental	Control				
Yoshida 2018	Vibegron	Imidafenacin	Japan	372/100 mg once-daily	117/0.1 mg twice daily	Oral	12 week	Men and women ≥18 year of age with symptoms of OAB for ≥6 mouth	2-week placebo run-in phase. Two tablets of vibegron placebo and one tablet of imidafenacin placebo in the morning and one tablet of imidafenacin placebo in the evening.
Mitcheson 2019	Vibegron	Tolterodine	USA	149/100 mg once-daily	135/4 mg once-daily	Oral	12 week	Men and women ≥18 year of age with symptoms of OAB for ≥3 mouth	8-week placebo run-in phase
Staskin 2020	Vibegron	Tolterodine	USA	547/75 mg once-daily	431/4 mg twice-daily	Oral	12 week	Patients ≥18 year of age with symptoms of OAB for ≥3 mouth	1- to 5-week screening period, 28-day washout; 2-week single-blind (patient) placebo run-in.

OAB = overactive bladder.

Table 2

Quality assessment of individual study.

Study	Allocation sequence generation	Allocation concealment	Blinding	Discontinued	Calculation of sample size	Statistical analysis	Level of quality
Yoshida 2018	A	A	A	28	YES	Chi-square test	A
Mitcheson 2019	A	A	A	17	YES	The full analysis set	A
Staskin 2020	A	A	A	99	YES	The full analysis set	A

A = all quality criteria met (adequate): low risk of bias.
B = one or more of the quality criteria only partly met (unclear): moderate risk of bias.
C = one or more criteria not met (inadequate or not used): high risk of bias.

Table 3

Pre- and post-treatment measures for different indicators, the period of follow-up, different adverse events and secondary treatment.

Study	the mean number of micturitions episodes/d				the mean number of urgency episodes/d				mean number of urgency incontinence episodes/d				mean number of incontinence episodes/d				mean volume voided/micturition			
	Vibegron (SD)		Antimuscarinic (SD)		Vibegron (SD)		Antimuscarinic (SD)		Vibegron (SD)		Antimuscarinic (SD)		Vibegron (SD)		Antimuscarinic (SD)		Vibegron (SD)		Antimuscarinic (SD)	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Yoshida 2018	11.08 (2.25)	9.05 (2.25)	11.21 (2.17)	9.15 (2.17)	3.77 (2.25)	1.33 (2.25)	3.54 (1.91)	1.39 (1.91)	1.86 (1.31)	0.39 (1.31)	2.15 (1.44)	1.00 (1.44)	2.04 (1.54)	0.51 (1.54)	2.43 (1.79)	0.96 (1.79)	157.08 (45.74)	187.86 (45.74)	158.86 (53.07)	179.66 (53.01)
Mitcheson 2019	11.15 (2.32)	9.02 (2.59)	11.00 (2.17)	9.24 (2.11)	7.34 (4.14)	4.22 (4.36)	6.39 (3.78)	3.91 (3.65)	2.69 (2.42)	0.84 (1.34)	2.80 (2.13)	1.15 (2.18)	3.43 (2.83)	1.12 (2.08)	3.08 (2.39)	1.32 (2.38)	NA	NA	NA	NA
Staskin 2020	10.43 (3.57)	8.63 (3.65)	10.67 (3.37)	9.07 (3.50)	7.75 (6.12)	5.05 (4.15	8.00 (5.47)	5.50 (4.1)	2.00 (2.85)	0.00 (2.1)	2.00 (2.57)	0.20 (2.05)	NA	NA	NA	NA	150 (80.6)	173.5 (60.5)	143.3 (73.5)	158.80 (62.5)

Study	Period of follow-up	Different adverse events										Secondary treatment
		Dry mouth		Drug related TEAE		SAE		Discontinuations due to AE				
		Vibegron (SD)	Antimuscarinic (SD)	Vibegron (SD)	Antimuscarinic (SD)	Vibegron (SD)	Vibegron (SD)	Vibegron (SD)	Antimuscarinic (SD)			
Yoshida 2018	12 weeks	2	9	20	12	1	1	3	1			NA
Mitcheson 2019	12 weeks	4	22	31	42	2	3	5	4			NA
Staskin 2020	12 weeks	9	28	36	38	8	10	9	14			NA

AE = adverse event; NA = not available; SAE = serious adverse event; SD = standard deviation; TEAE = treatment-emergent adverse event.

Figure 2. Funnel plot of the studies represented in our analysis. MD = mean difference, SE = standard error.

of individual studies was high with the Jadad scores rating A. Figure 2 demonstrated that the plot was highly symmetrical and no evidence of bias was found (Table 3).

3.3. Efficacy

The mean number of micturitions episodes/d, the meannumber of urgency episodes/d, the mean number of urgency incontinence episodes/d, the mean number of incontinence episodes/d and the mean volume voided/micturition.

The changed indicators before and after treatment (the mean number of micturitions episodes/d, the mean number of urgency episodes/d, the mean number of urgency incontinence episodes/d, the mean number of incontinence episodes/d, and the mean volume voided/micturition) were used to assess the efficacy of vibegron and antimuscarinic in treating OAB. There are 3 studies including 1751 patients compared the indicator the mean number of micturitions episodes/d, the mean number of urgency episodes/d, the mean number of urgency incontinence episodes/d and 2 RCTs compared the mean number of incontinence episodes/d and the mean volume voided/micturition between the two groups that treated with vibegron or antimuscarinic, respectively. According to the analysis, the mean number of micturitions episodes/d (MD = −0.19, 95%CI = −0.45 to 0.07, $P = .16$; Fig. 3A); the mean number of urgency episodes/d (MD = −0.30, 95%CI = −0.59 to −0.01, $P = .05$; Fig. 3B), mean number of urgency incontinence episodes/d (MD = −0.15, 95%CI = −0.32 to 0.03, $P = .11$; Fig. 3C) and the mean number of incontinence episodes/d (MD = −0.21, 95%CI = −0.50 to 0.07, $P = .14$; Fig. 3D) indicated that vibegron and antimuscarinic had no significant differences in terms of OAB treatment. As to the mean volume voided/micturition (MD = 8.40, 95%CI = 2.11–14.69, $P = 0.009$; Fig. 3E), patients who treated with vibegron had significantly increased the urination volume compared with antimuscarinic.

3.4. Safety

3.4.1. Dry mouth, drug related TEAE, SAE, and discontinuations due to AE. Dose of tolterodine was different in 2 RCTs. Some indicators of cardiovascular system could not be analyzed in this meta-analysis due to the half-baked data. Safety indicator mainly included dry mouth, drug related TEAE, SAE, and discontinuations due to AE. Dry mouth (OR 0.17; 95% CI 0.10–

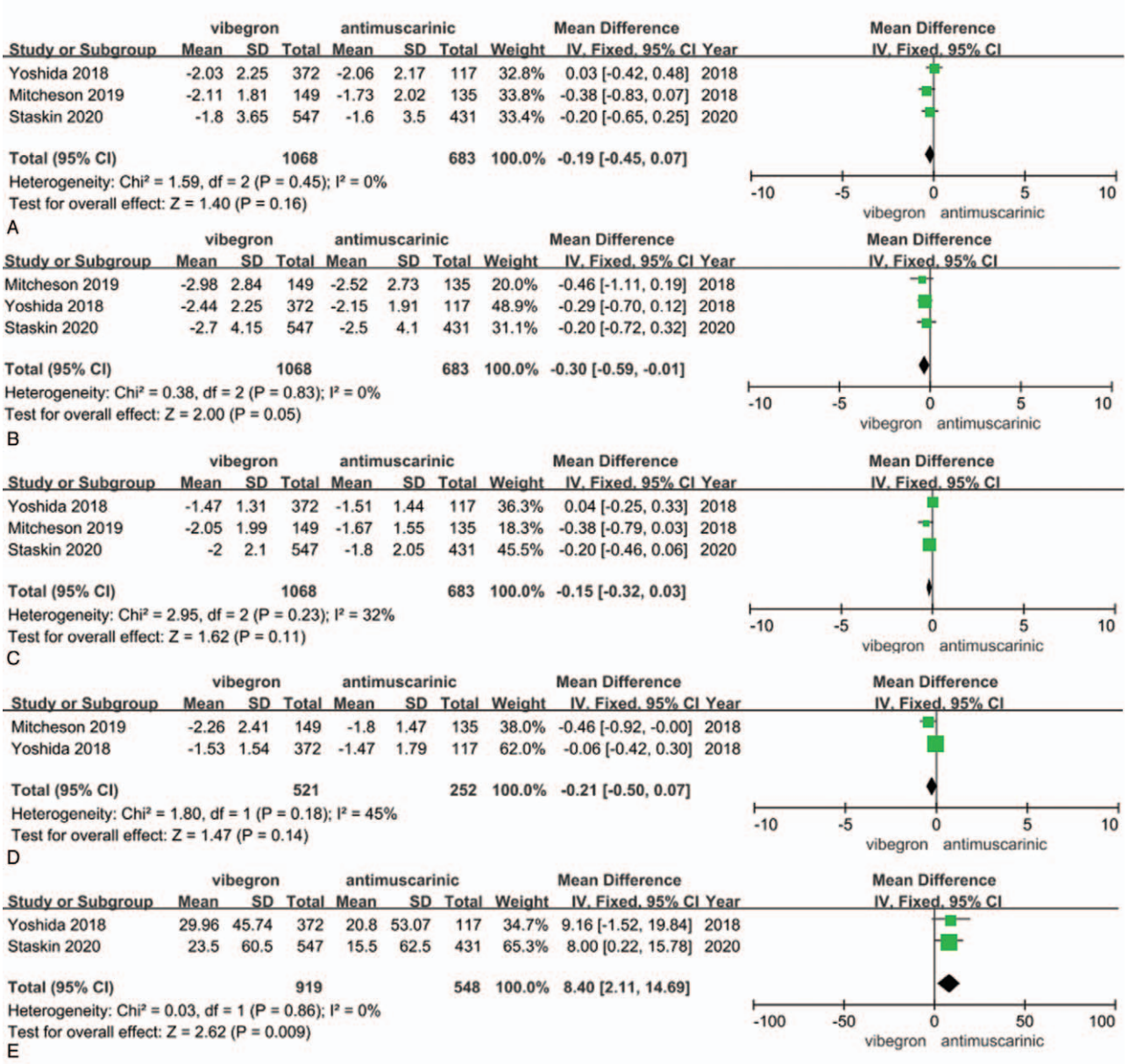

Figure 3. Forest plots showing changes in (A) the mean number of micturitions episodes/d, (B) the mean number of urgency episodes/d, (C) mean number of urgency incontinence episodes/d, (D) mean number of incontinence episodes/d, (E) mean volume voided/micturition. CI = confidence interval, IV = inverse variance, SD = standard deviation.

0.52; $P < .00001$; Fig. 4A) and drug related TEAE (OR 0.63; 95% CI 0.46–0.87; $P = .005$; Fig. 4B) were more common among those patients treated with antimuscarinic compared with those treated with vibegron. However, there was no significant difference in SAE (OR 0.59; 95% CI 0.27–1.31; $P = .19$; Fig. 4C) and discontinuations due to AE (OR 0.65; 95% CI 0.33–1.28; $P = .21$; Fig. 4D) between the two groups.

4. Discussion

OAB is clinical definitions based on Lower urinary tract syndrome (LUTS) and signs that do not rely on urodynamic criteria.[15] Behavioral and bladder training, pharmacotherapy, botulinum toxin, electrical stimulation, biofeedback, or surgery could be used to treat OAB patients. Antimuscarinic agents are the pharmacotherapeutic treatment options indicated for OAB, such as tolterodine, imidafenacin, fesoterodine, solifencin, and so on. But they have unpredictable side effects, which can result in poor tolerance and a suboptimal response.[16,17] Mirabegron is the first approved β3-adrenergic receptor agonist for the treatment of OAB and the only class of compounds that is currently used in clinical practice world-wide, it is approved for OAB treatment universally as its efficacious and generally well tolerated in several articles.[18] Meanwhile, prior studies have suggested that the therapeutic effect of mirabegron is similar to that of antimuscarinics (solifenacin).[19] Vibegron is a new selective β3-adrenergic receptor agonist belongs to a novel class of agents developed for treating OAB. It could mediate relaxation

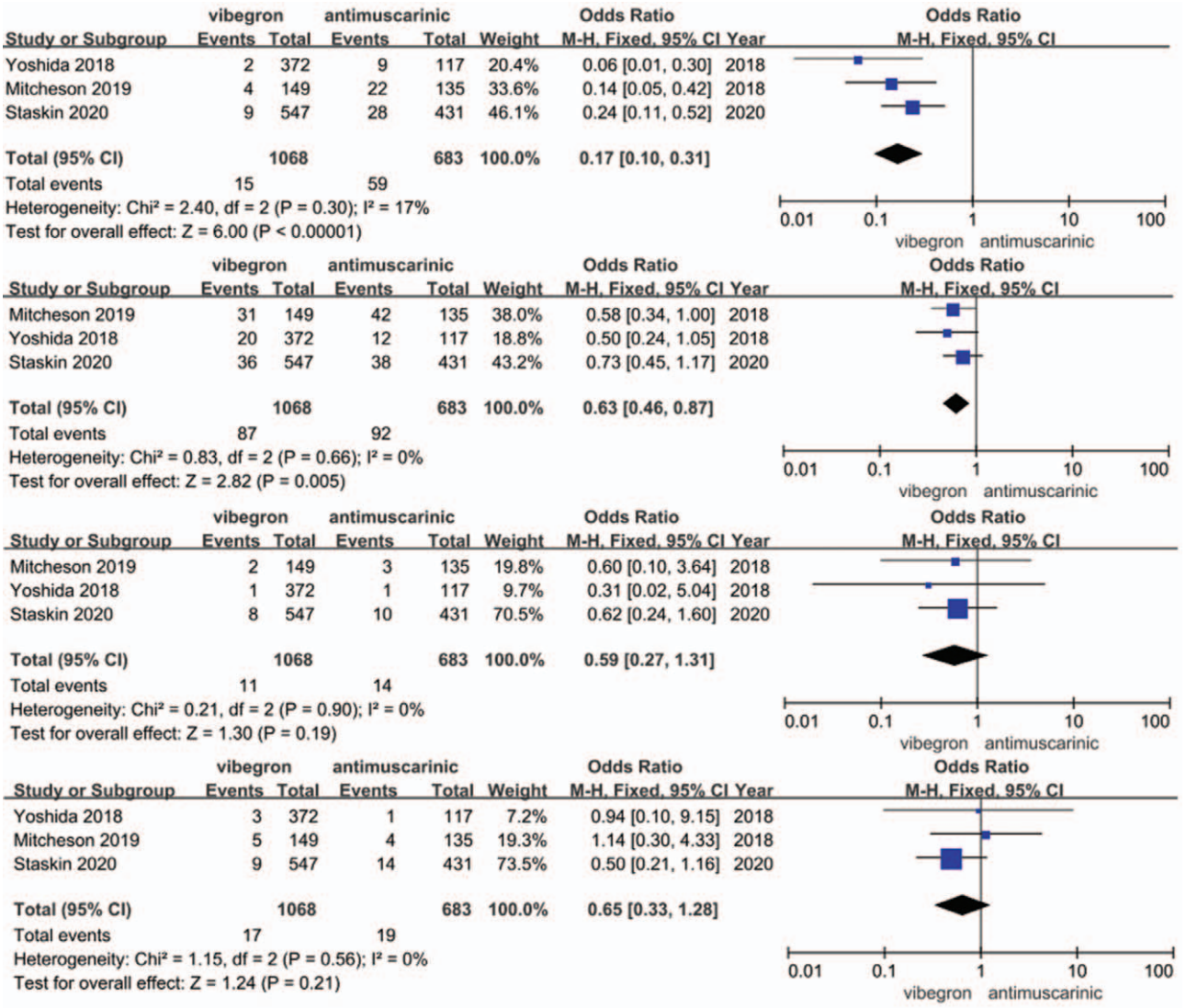

Figure 4. Forest plots showing changes in dry mouth, drug related TEAE, SAE, and discontinuations due to AE. CI = confidence interval, MH = mantel haenszel.

of the detrusor in the course of the storage phase of the micturition cycle, ameliorating bladder storage capacity without impeding bladder voiding.[20,21]

This systematic review and meta-analysis compared the efficacy and safety of vibegron (100 mg once-daily) with antimuscarinic (tolterodine [4 mg once-daily] or imidafenacin [0.1 mg twice-daily]) for OAB patients, and the treatment duration is 12 weeks. We proved no significant differences between the two drugs for reducing the mean number of micturitions episodes/d, the mean number of urgency episodes/d, mean number of urgency incontinence episodes/d and mean number of incontinence episodes/d. In an international phase III trial, micturitions decreased by an adjusted mean of 1.8 episodes/day for vibegron vs 1.6 for tolterodine ($P < .001$). Among incontinent patients, urge-incontinence episodes decreased by an adjusted mean 2.0 episodes/day for vibegron vs 1.8 for tolterodine ($P < .0001$).[14] Besides, Staskin et al[14] proved that across primary (the mean number of micturitions episodes/d and the mean number of urgency incontinence episodes/d) and key secondary endpoints (the mean number of urgency episodes/d, the mean number of incontinence episodes/d and the mean volume voided/micturition), numerical results were consistently greater for vibegron than for tolterodine.

Compared with vibegron, antimuscarinic agents had a greater prevalence of dry mouth and drug related TEAE. As to the mean volume voided/micturition, patients who treated with vibegron had significantly increased the urination volume compared with antimuscarinic. This may be attributed to the different mechanisms between the two kinds of medicine. Vibegron can relax the detrusor muscle by inhibiting β3-adrenoceptors, while antimuscarinic inhibiting muscarinic receptors. Related clinical trials have found that patients treated with antimuscarinic agents frequently suffered from urinary retention. It is more obvious in elderly benign prostatic hyperplasia (BPH) patients. In the present study, SAE and discontinuations due to AE did not show a significant difference between the two groups. Vibegron (100 mg/day) seems to provide a better balance between efficacy and side-effects. Yoshida et al[22] conducted a 1-year, open-label, multicenter, noncontrolled study reporting that the incidence of drug-related AE was 11.8% in vibegron 100 mg group. As for

the incidences of the adverse events, the most common AE were nasopharyngitis, dry mouth, cystitis, and constipation. Due to vibegron's drawbacks, the treatment must be "tailored" to patient status and ability to tolerate the drug. The final decision on the appropriate treatment option for OAB refractory to drug therapy should be discussed with the patient fully informed of long-term efficacy results and risks.[23]

The Systematic review and Meta-analysis included articles which are all findings from high quality RCTs. Basing on the quality-assessment scale that we designed, the quality of the individual articles in the meta-analysis was conforming. The results of the meta-analysis acquire great importance in the everyday clinical practice but also from scientific standpoint. However, this study also has some limitations. The number of included articles was not many. We were unable to clarify what happened for patients after discontinuation of the medication (secondary treatment). Dose of tolterodine was different in 2 RCTs. Some indicators of cardiovascular system could not be analyzed in this meta-analysis due to the half-baked data. The longer-term efficacy, safety, and persistence of vibegron and antimuscarinic agents could not be extrapolated from this meta-analysis. In addition, this article did not include the unpublished studies' data. These factors may lead to a bias. More high-quality trials are proposed to learn more about the efficacy and safety of vibegron vs antimuscarinic monotherapy for OAB.

5. Conclusions

The therapeutic effect of vibegron is similar to that of antimuscarinic, but vibegron does not increase the risk of AE.

Author contributions

Conceptualization: Shunye Su.
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Funding acquisition: Yuan Gao.
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Methodology: Liqin Liang.
Project administration: Liqin Liang, Zhipeng Chen.
Resources: Jinlei Lin.
Software: Jinlei Lin.
Supervision: Jinlei Lin.
Validation: Ludong Liu.
Visualization: Ludong Liu, Zhipeng Chen.
Writing – original draft: Shunye Su.
Writing – review & editing: Yuan Gao.

References

[1] Xing D, Wang YH, Wen YB, et al. Prevalence and risk factors of overactive bladder in Chinese children: a population-based study. Neurourol Urodyn 2020;39:688–94.
[2] Burgio KL, Kraus SR, Johnson TN, et al. Effectiveness of combined behavioral and drug therapy for overactive bladder symptoms in men: a randomized clinical trial. JAMA Intern Med 2020;180:411–9.
[3] Al HAAB, Al HAO, Lee R, et al. Overactive bladder: clinical updates in women's health care primary and preventive care review. Obstet Gynecol 2020;135:253.
[4] Gratzke C, Chapple C, Mueller ER, et al. Efficacy and safety of combination pharmacotherapy for patients with overactive bladder: a rapid evidence assessment. Eur Urol 2019;76:767–79.
[5] El-Zawahry A, Rizk D. Combination pharmacotherapy for the treatment of the overactive bladder syndrome: a new solution for an old problem? Int Urogynecol J 2019;31:855–6.
[6] Di Salvo J, Nagabukuro H, Wickham LA, et al. Pharmacological characterization of a novel beta 3 adrenergic agonist, Vibegron: evaluation of antimuscarinic receptor selectivity for combination therapy for overactive bladder. J Pharmacol Exp Ther 2017;360:346–55.
[7] Shi H, Chen H, Zhang Y, et al. The efficacy and safety of Vibegron in treating overactive bladder: a systematic review and pooled analysis of randomized controlled trials. Neurourol Urodyn 2020;doi:10.1002/nau.24387.
[8] Luz R, Pereira I, Henriques A, et al. King's Health Questionnaire to assess subjective outcomes after surgical treatment for urinary incontinence: can it be useful? Int Urogynecol J 2017;28:139–45.
[9] Jadad AR. Randomised Controlled Trials. London, UK: BMJ Publishing Group; 1998.
[10] Jonathan J. Shuster. Review: cochrane handbook for systematic reviews for interventions, version 5.1.0, published 3/2011. julian p.t. higgins and sally green, editors.Research Synthesis Methods, 2, 126-130.
[11] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88.
[12] Yoshida M, Takeda M, Gotoh M, et al. Vibegron, a novel potent and selective beta3-adrenoreceptor agonist, for the treatment of patients with overactive bladder: a randomized, double-blind, placebo-controlled phase 3 study. Eur Urol 2018;73:783–90.
[13] Mitcheson HD, Samanta S, Muldowney K, et al. Vibegron (RVT-901/MK-4618/KRP-114V) administered once daily as monotherapy or concomitantly with tolterodine in patients with an overactive bladder: a multicenter, phase IIb, randomized, double-blind. Control Trial Eur Urol 2019;75:274–82.
[14] Staskin D, Frankel J, Varano S, et al. International phase III, randomized, double-blind, placebo-and active-controlled study to evaluate the safety and efficacy of vibegron in patients with symptoms of overactive bladder: EMPOWUR. J Urol 2020;101097JU0000000000000807.
[15] Mancini V, Tarcan T, Serati M, et al. Is coexistent overactive-underactive bladder (with or without detrusor overactivity and underactivity) a real clinical syndrome? ICI-RS 2019. Neurourol Urodyn 2020;39(Suppl 3):S50–9.
[16] Kasman A, Stave C, Elliott CS. Combination therapy in overactive bladder-untapped research opportunities: a systematic review of the literature. Neurourol Urodyn 2019;38:2083–92.
[17] Huang AJ, Grady D, Mendes WB, et al. A randomized controlled trial of device Guidedm, slow-paced respiration in women with overactive bladder syndrome. J Urol 2019;202:787–94.
[18] Cui Y, Zong H, Yang C, et al. The efficacy and safety of mirabegron in treating OAB: a systematic review and meta-analysis of phase III trials. Int Urol Nephrol 2014;46:275–84.
[19] Wang J, Zhou Z, Cui Y, et al. Meta-analysis of the efficacy and safety of mirabegron and solifenacin monotherapy for overactive bladder. Neurourol Urodyn 2019;38:22–30.
[20] Keam SJ, Vibegron: . First global approval. Drugs 2018;78:1835–9.
[21] Edmondson SD, Zhu C, Kar NF, et al. Discovery of Vibegron: a potent and selective beta3 adrenergic receptor agonist for the treatment of overactive bladder. J Med Chem 2016;59:609–23.
[22] Yoshida M, Kakizaki H, Takahashi S, et al. Long-term safety and efficacy of the novel beta3-adrenoreceptoragonist vibegron in Japanese patients with overactive bladder: a phase III prospective study. Int J Urol 2018;25:668–75.
[23] Chermansky C, Schurch B, Rahnama'i MS, et al. How can we better manage drug-resistant OAB/DO? ICI-RS 2018. Neurourol Urodyn 2019;38(Suppl 5):S46–55.