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ORIGINAL ARTICLE

Pooled analysis of the efficacy and safety of intraoperative dexmedetomidine on postoperative catheter-related bladder discomfort

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Abstract

Objectives: The goal of the pooled analysis was to demonstrate the efficacy and safety of intraoperative dexmedetomidine in postoperative catheter-related bladder discomfort (CRBD).

Methods: MEDLINE, the Cochrane Central Register of Controlled Trials, and the Excerpta Medica Database (Embase) were used to pick out randomized controlled trials (RCTs) that used intraoperative dexmedetomidine in postoperative CRBD. This study was carried out using the preferred reporting items for systematic reviews and pooled analysis. We used RevMan version 5.3.0. to analyze the data.

Results: Seven RCTs involving 607 patients were brought into in the analysis. The incidence of CRBD and the incidence of moderate to severe CRBD were assessed at 0 hours, 0.5 or 1 hour, 2 or 3 hours, 6 hours, and 12 or 24 hours postoperatively. The analysis proved that both the incidence of CRBD ($P < .00001$) and the incidence of moderate to severe CRBD had a statistically significant reduction at 0 hours, 0.5 or 1 hours, 2 or 3 hours, and 6 hours postoperatively ($P < .00001$, $P < .00001$, $P < .00001$, $P = .003$, respectively). The postoperative pain score was lower in the dexmedetomidine group at 0 hours ($P < .00001$) and 1 hour ($P = .002$). Safety assessments indicated that there were no statistical differences between dexmedetomidine and control for side effects, mainly including dry mouth ($P = .99$) and postoperative vomiting and nausea ($P = .77$).

Hongbin Shi and Huaping Zhang contributed equally to this study as co-first authors.

Conclusions: The pooled analysis demonstrates that intraoperative dexmedetomidine administration decreases the rate and severity of early postoperative CRBD without causing significant side effects.

KEYWORDS

dexmedetomidine, pooled analysis, randomized controlled trials, catheter-related bladder discomfort

1 | INTRODUCTION

The indwelling Foley catheter is extensively needed during surgery, while the Foley catheter is inserted temporarily to facilitate urination and measure urine output during the perioperative period. However, patients with Foley catheter after numerous kinds of operations often suffer from catheter-related bladder discomfort (CRBD) during the early postoperative period.[1]

CRBD is similar to an overactive bladder (OAB), including urinary urgency and urinary frequency with or without urge incontinence, in addition to discomfort in the suprapubic region.[2] CRBD is one of the most distressing complications, which may increase the incidence of postoperative pain and reduces the quality of recovery.[3] Currently, the exact pathophysiology of CRBD is not clear. However, its symptoms are similar to the symptoms of OAB, caused by involuntary contractions of the bladder mediated by muscarinic receptors located in the urothelium and efferent nerves.[4] Multiple medicines have been developed to treat CRBD, with varying degrees of success, including tolterodine, solifenacin, tramadol, dexmedetomidine, ketamine, and so on.[5] Muscarinic antagonists are recommended for treating CRBD.[4,5] However, they are only preoperatively administered orally and may cause side effects.

Dexmedetomidine is identified as a selective α_2-adrenoceptor agonist with analgesic, sedative properties and sedative sympatholytic, and it has been demonstrated to have a favorable effect in avoiding CRBD by inhibiting the M3 receptor.[6] A number of studies considering intraoperative CRBD have been reported. However, there is still deficient evidence to demonstrate the efficacy and safety of intraoperative dexmedetomidine in postoperative CRBD, limited due to the quality and quantity of previously published articles. Therefore, we conducted a pooled analysis to evaluate the efficacy and safety of intraoperative dexmedetomidine in patients with an indwelling urinary catheter.

2 | METHODS

2.1 | Inclusion criteria

Randomized controlled trials (RCTs) were included according to the following criteria: (a) The effect of intraoperative dexmedetomidine on postoperative CRBD was studied; (b) the articles provided sufficient data for analysis, mainly including the number of patients with CRBD symptoms, the incidence of moderate to severe CRBD, postoperative pain scores, and the rate of adverse events such as dry mouth and postoperative nausea and vomiting (PONV); and (c) full text was available. Articles would be excluded from the pooled analysis if the above inclusion criteria were not met.

2.2 | Search strategy

We performed a systematic search of MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials databases and the reference lists of the retrieved literature for studies referring to the efficacy and safety of intraoperative dexmedetomidine in postoperative CRBD before October 2019. The following search terms were applied for the search: RCT, dexmedetomidine, and CRBD.

2.3 | Trial selection

All authors independently identified relevant studies according to the inclusion criteria. Any discrepancies were noted, debated, and settled in a negotiated manner. If the research was reported by several articles, the latest article would be included in our study. At the same time, if a group of patients was involved in two or more studies, each study was analyzed in the pooled analysis.

2.4 | Quality assessment

We evaluated the quality of individual studies by the Jadad scale.[7] Each RCT was assessed in terms of the concealment of allocation procedures, sequence generation, blinding, selective outcome reporting, incomplete outcome data, and other sources of bias. We classified the studies qualitatively following the protocol released in the *Cochrane Handbook for Systematic Reviews of Interventions* version 5.1.0.[8] According to the quality evaluation criteria, each article was appraised and assigned to one of the following three

quality classes: (A) a low probability of bias, (B) a secondary probability of bias, or (C) a high probability of bias was considered to exist in this study. All authors took part in the process of quality assessment. Differences were settled by discussion among the authors, and all authors agreed with the results of the assessment.

2.5 | Data extraction

We drew the following data by reading the studies: (a) the first author's name and publication year, (b) therapy that patients received, (c) design types of the study, (d) types of the catheters, (e) the number of patients, and (f) methods of the operation.

2.6 | Statistical analysis

The abstracted data was analyzed with the Review Manager 5.3.0 (The Cochrane Collaboration, London, UK).[8] 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.[9] The chi-square-based Q statistic was performed to check the heterogeneity among the studies, and the result was recognized as significant at $P < .05$. When an $I^2 < 50\%$ indicated that there was no significant heterogeneity, the fixed-effects model (Mantel-Haenszel method) would be used. We used 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, our study found 158 articles in the databases. Scrutinizing the abstracts and titles, 119 articles were ruled out, and from the remaining 39 articles, 32 studies were removed owing to a lack of effective indicators. Finally, seven RCTs[10-16] involving 607 patients were included in the analysis. Table S1 lists characteristics of the included studies.

3.2 | Quality of individual studies

All of the included studies in the pooled analysis were RCTs. All articles had an appropriate number of participants to analyze, and no study showed intention-to-treat analysis (Table S2). Finally, the quality level of the individual studies was high with Jadad score rating A. Figure 1 demonstrates that the plot was highly symmetrical and no evidence of bias was found.

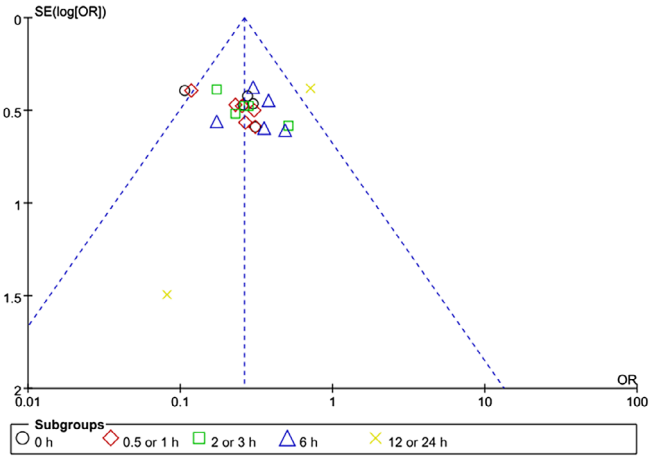

FIGURE 1 Funnel plot of the studies included in our meta-analysis. OR, odds ratio; SE, standard error [Color figure can be viewed at wileyonlinelibrary.com]

3.3 | Dexmedetomidine vs placebo on the incidence of CRBD

Seven studies involving 607 participants (303 in the dexmedetomidine group and 304 in the control group) were enrolled in the analysis to assess the impact of dexmedetomidine on the incidence of CRBD.

Participants treated with dexmedetomidine showed a lower incidence of CRBD than those treated with placebo at 0 hours (OR 0.22; 95% CI, 0.15-0.33; $P < .00001$), 0.5 or 1 hour (OR 0.22; 95% CI, 0.15-0.32; $P < .00001$), 2 or 3 hours (OR 0.25; 95% CI, 0.17 to 0.38; $P < .00001$), and 6 hours (OR 0.32; 95% CI, 0.21-to 0.49; $P < .00001$) postoperatively, while there was no significant difference between the two groups in the incidence of CRBD at 12 or 24 hours postoperatively (OR 0.56; 95% CI, 0.28-1.12; $P = .10$) (Figure 2).

3.4 | Dexmedetomidine vs placebo on the incidence of moderate to severe CRBD

Five studies including 497 participants (198 in the dexmedetomidine group and 199 in the control group) were enrolled in the analysis in order to determine the impact of dexmedetomidine on the incidence of moderate to severe CRBD.

Patients treated with dexmedetomidine showed a lower incidence of CRBD than those treated with placebo at 0 hours (OR 0.19; 95% CI, 0.11-0.31; $P < .00001$); 1 hour (OR 0.19; 95% CI, 0.10-0.33; $P < .00001$), 2 or 3 hours (OR 0.25; 95% CI, 0.14-0.48; $P < .0001$), and 6 hours (OR 0.29; 95% CI, 0.12-0.66; $P = .003$) postoperatively. In contrast, no meaningful difference was discovered between the two sets in the incidence of moderate to severe CRBD at 12 or 24 hours postoperatively (OR 0.67; 95% CI, 0.11-4.08; $P = .66$) (Figure 3).

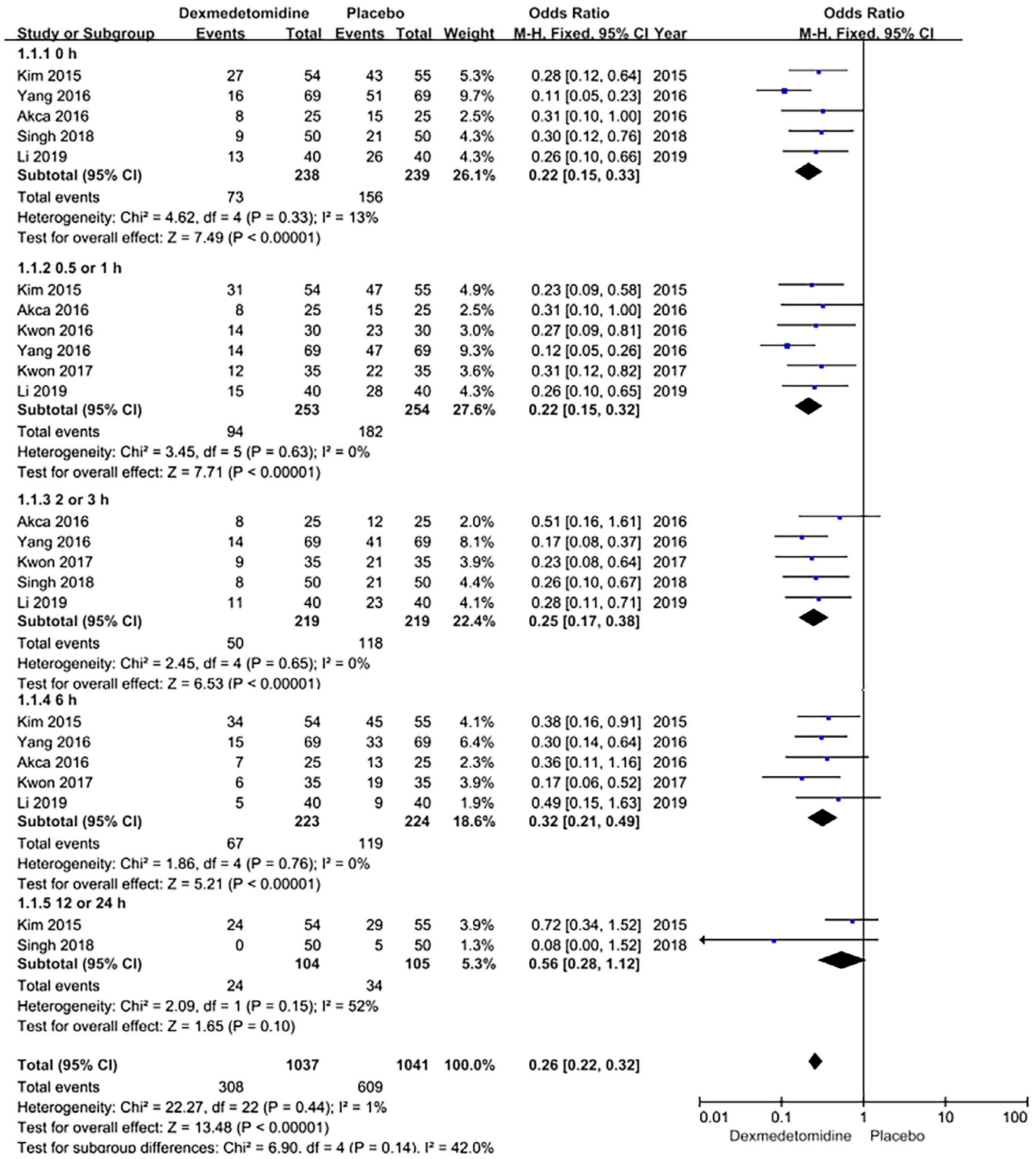

FIGURE 2 Incidence of catheter-related bladder discomfort in dexmedetomidine vs placebo. df, degrees of freedom; M-H, Mantel-Haenszel; OR, odds ratio [Color figure can be viewed at wileyonlinelibrary.com]

3.5 | Dexmedetomidine vs placebo on postoperative pain score

Three studies containing 297 participants (148 in the dexmedetomidine group and 149 in the control group) were included in the analysis to determine the influence of dexmedetomidine on postoperative pain score.

The postoperative pain score was lower in the dexmedetomidine group compared with placebo at 0 hours (MD −0.95; 95% CI, −1.36 to −0.53; $P < .00001$) and 1 h (MD −0.33; 95% CI, −0.60 to −0.06;

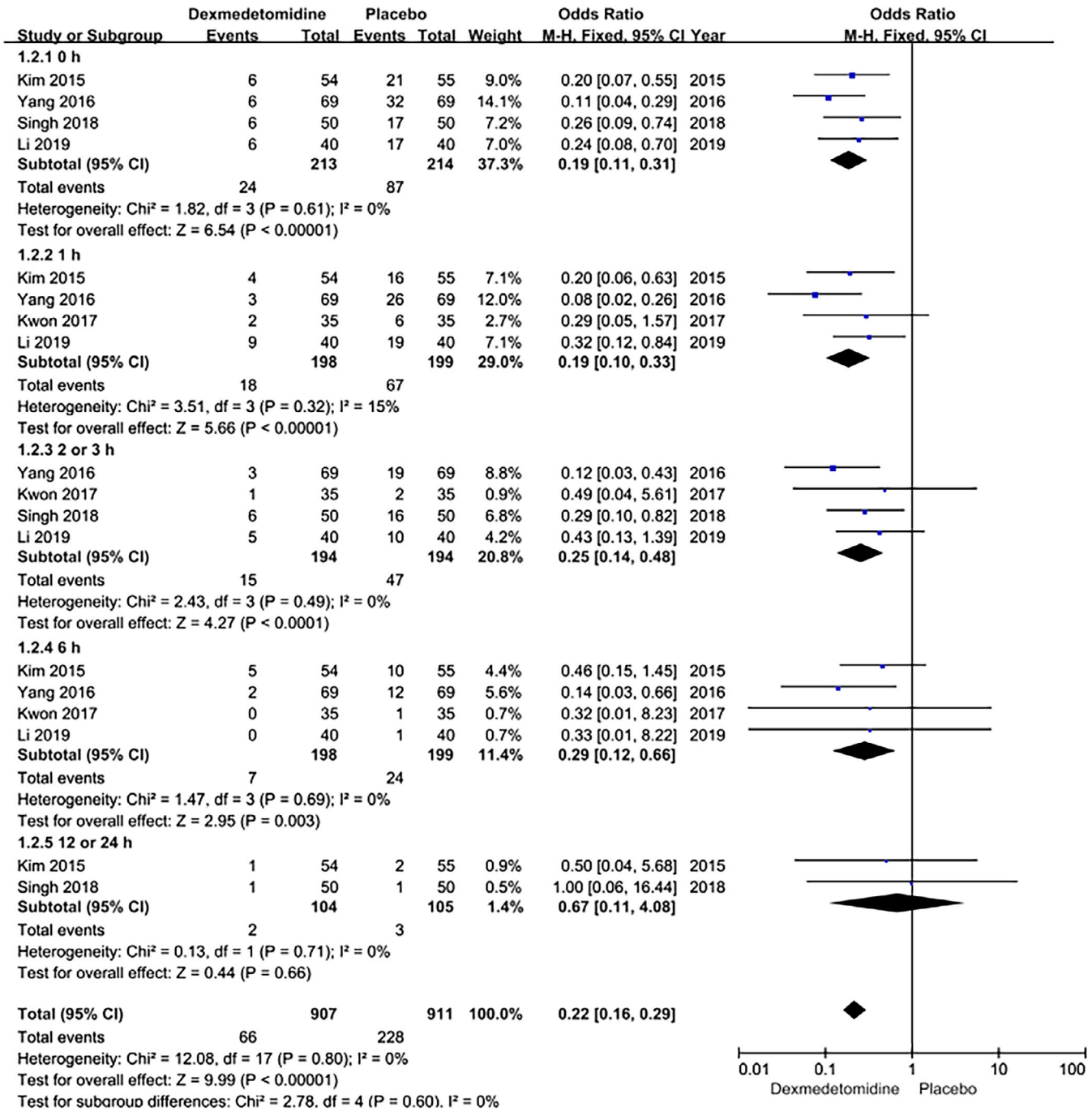

FIGURE 3 Incidence of moderate to severe catheter-related bladder discomfort in dexmedetomidine vs placebo. df, degrees of freedom; M-H, Mantel-Haenszel; OR, odds ratio [Color figure can be viewed at wileyonlinelibrary.com]

P = .02). And there was no meaningful difference between the two sets in the pain score at 6 hours postoperatively (MD 0.00; 95% CI, −0.21 to 0.21; *P* = 1.00).

3.6 | Dexmedetomidine vs placebo on the rate of adverse events

Side effects including dry mouth and PONV could be analyzed through the included RCTs. Our pooled analysis showed that there was no difference in the incidence of side effects between the dexmedetomidine and control groups.

3.6.1 | Dry mouth

Two RCTs involving 179 patients reported the occurrence of dry mouth. Our pooled analysis indicated that dexmedetomidine was not significantly different from placebo in the incidence of dry mouth (OR 1.01; 95% CI, 0.31-3.27; *P* = .99).

3.6.2 | PONV

Six RCTs involving 507 patients reported the occurrence of PONV. No significant difference was shown between the two sets in the incidence of PONV (OR 1.09; 95% CI, 0.63-1.88; $P = .77$).

4 | DISCUSSION

Urinary catheterization frequently causes CRBD during various surgeries in the immediate postoperative period with an incidence ranging from 47% to 90%.[17] Clinically, patients with indwelling urinary catheter are found suffering from a variety of catheter-related symptoms, such as urgency, frequency, urge incontinence, and suprapubic pain.[18] Thus, most patients may have a strong vocal response, flail limbs, and even attempt to pull out the urinary catheter, which may lead to an increased incidence of sever postoperative complications.[19]

We made this pooled analysis from seven high-quality RCTs including 607 participants to compare intraoperative dexmedetomidine administration in postoperative CRBD with placebo. Compared with placebo, patients treated with intraoperative dexmedetomidine had a lower incidence of early postoperative CRBD (0-6 hours), while there was no meaningful difference between the two sets in the incidence of relatively late CRBD at 12 or 24 hours postoperatively. The same is valid for the incidence of moderate to severe CRBD. Besides, the postoperative pain score decreased in the dexmedetomidine group compared with placebo in the early period (0-1 hours), while there was no meaningful difference between the two sets in the pain score at 6 hours postoperatively.

Five of the included RCTs reported that the dexmedetomidine group received a bolus of 0.5 or 1 μg/kg dexmedetomidine infusion before anesthesia induction, followed by an infusion of 0.3 to 0.5 μg/kg/h dexmedetomidine. Removing the other two RCTs, we redid the pooled analysis and found that participants treated with dexmedetomidine showed a lower incidence of CRBD than those treated with placebo, which is consistent with the previous results (OR 0.28; 95% CI, 0.18-0.44; $P < .00001$). According to the types of surgeries, we divided the included studies into two groups for subgroup analyses: urological and nonurological operations. There were no differences between the urological (OR 0.28; 95% CI, 0.16-0.51; $P < .0001$) and nonurological operation (OR 0.22; 95% CI, 0.14-0.33; $P < .00001$) groups regarding the changes of the incidence of CRBD.

As for adverse events, only dry mouth and PONV could be analyzed through the included RCTs. This pooled analysis could only prove that patients treated with intraoperative dexmedetomidine had no significant difference in the incidence of dry mouth or PONV compared with placebo. Although dexmedetomidine has certain effects on the cardiovascular system, as Kwon et al[14] reported that the incidence of bradycardia was higher in the dexmedetomidine group, bradycardia that affects hemodynamic stability was not observed. Several patients suffered from episodes of transient hypotension or hypertension and were stabilized quickly by treatment with ephedrine or nitroglycerin. Besides, Zhao et al[12] demonstrated that no statistically significant differences were found between the two groups with respect to side effects including bradycardia, hypotension, or hypertension. Kim et al[10] found that the two groups did not differ in changes in Ramsay Sedation Score over time. Also, the postoperative application of rescue analgesics seems different between groups statistically. The number of patients who needed rescue analgesics postoperatively was less in the dexmedetomidine group compared with placebo, which again reflected that the drug has a considerable effect in relieving CRBD.

The indwelling Foley catheter may trigger the afferent nerve of the cyst, causing acetylcholine release resulting in muscarinic receptor-mediated involuntary contraction of the bladder detrusor muscle.[20] Dexmedetomidine inhibits the activity of the sympathetic nervous system and decreases bladder tension, thereby reducing the transmission of afferent impulses.[21] Dexmedetomidine may also reduce the generation of excitatory signals from the bladder, thereby preventing the pontine micturition center and cerebrum from initiating the impulse to urinate.

As far as we know, this is the first study to elucidate the efficacy and safety of dexmedetomidine vs placebo in relieving CRBD symptoms. Through an extensive analysis of all data, our pooled analysis manifests the significant superiority of dexmedetomidine in mitigating CRBD symptoms compared to placebo.

This pooled analysis enrolled articles where all findings are from RCTs. Albeit the high quality of all included studies, our study involves several limitations. First, this meta-analysis only enrolled seven studies with sample sizes that are not large for the limited quantity of relevant original studies. Second, the baseline characteristics of the patients are not uniform. Third, patients included in the analysis underwent various types of surgeries, and the incidence of CRBD was high among patients with urological surgeries. In addition, different sizes of catheters and different doses of medications may have led to bias. When heterogeneity among articles is considered, this meta-analysis remains important for evaluating the efficacy of dexmedetomidine vs placebo for prevention or treatment of CRBD symptoms. Thus, further high-quality RCTs are necessary for better understanding about dexmedetomidine for the treatment of CRBD symptoms.

5 | CONCLUSION

The pooled analysis demonstrates that intraoperative dexmedetomidine administration mitigates the frequency and severity of early postoperative CRBD without causing evident side effects.

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None.

DISCLOSURE

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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