Efficacy of dexmedetomidine with spinal block to prolong sedation in elderly patients undergoing transurethral resection of prostate - Meta Analysis

Abhilash Sadhankar [1], Ajit Kumar [1a], Manasa Kantha [1], Sukhdeo Gupta [2], Sridhar M [2], Karthik Pandian [2], Pradeep Atter [3]

[1a] -Professor and In charge, Division of Pain Medicine and OncoAnesthesia, Department of Anesthesiology, All India Institute of Medical Sciences RISHIKESH, India.
[1,2,3]- Senior resident, Division of Pain Medicine, Department of Anesthesiology, All India Institute of Medical Sciences RISHIKESH, India.

Corresponding Author
Prof.Dr Ajit kumar
Department of Anesthesiology, All India Institute of Medical Sciences, RISHIKESH, India
***Email**: ajitdr.ajit@gmail.com*

Statements and Declarations:
***Conflicts of Interest:** The authors declare no conflict of interest.*
***Funding**: None to declare.*
***Ethical Approval:** Not applicable.*
***Registration:** Registered via PROSPERO with identification number of CRD42025640177*

KEYWORDS
dexmedetomidine; spinal anaesthesia; saline; Transurethral resection of the prostate

ABSTRACT

Objective: To evaluate the effectiveness of dexmedetomidine in conjunction with spinal anesthesia on the duration of sensory and motor block, hemodynamic parameters, side effects, time to first analgesia, length of stay in the PACU, and excessive sedation in patients undergoing transurethral resection of the prostate (TURP).

Methods: A systematic search was conducted in PubMed, Scopus, the Cochrane Library, and Google Scholar for randomized controlled trials (RCTs) comparing dexmedetomidine with saline in TURP patients. The RoB 2 tool was used to evaluate the quality of the studies, while RevMan was used for statistical analysis.

Results: Five RCTs involving 260 participants met the inclusion criteria. Dexmedetomidine significantly prolonged the duration of sensory block (SMD = 1.05, 95% CI: 0.60 to 1.51, P < 0.00001). It was also associated with the lowest intraoperative heart rate (HR) (SMD = -0.50, 95% CI: -0.86 to -0.15, P = 0.005), lowest systolic blood pressure (SBP) (SMD = -0.61, 95% CI: -1.06 to -0.15, P = 0.009), and lowest mean blood pressure (MBP) (SMD = -0.46, 95% CI: -0.92 to -0.01, P = 0.04). Additionally, dexmedetomidine significantly delayed the time to first analgesia (RR 2.19, 95% CI 1.69–2.70, P < 0.00001). However, no significant differences were observed in the duration of motor block, adverse events (hypotension, bradycardia, and nausea), PACU stay, or excessive sedation.

Conclusion: Dexmedetomidine prolongs sensory block and time to initial analgesia, thereby increasing the effectiveness of spinal anesthesia. It does not lengthen the duration of motor block, increase the frequency of adverse events, or lengthen PACU stay or excessive sedation.

1. Introduction

Benign prostate hyperplasia is the most common disease in the older population, affecting 60% of men by the age of 60 annually (1). The average age is approximately 60-80 years, which is often associated with other comorbid conditions such as diabetes and hypertension (2). Transurethral resection of the prostate (TURP) is a surgical procedure commonly performed under spinal anesthesia to treat BPH. As the population is mostly geriatric, bupivacaine is often used for spinal anesthesia because of its minimal impact on hemodynamics during surgery (3). However, due to its shorter duration of action, it is usually inadequate when used alone to compensate for the surgical time, which can lead to the emergence of postoperative pain (3). To account for this problem, spinal anesthesia is now administered along with an adjunct to prolong the duration of the block. Several combinations of morphine, fentanyl, or clonidine are used in various surgical populations to assess the impact of adjuncts on the prolongation of spinal anesthesia (4).

Among these adjuncts, dexmedetomidine has gained significant attention in recent years (3). Dexmedetomidine is an α2-adrenoceptor agonist that has analgesic and sedative properties (5). Studies have shown that its use as an adjunct to spinal anesthesia is associated with a better postoperative profile in terms of pain scores and prolongation of anesthesia (6). Although its impact has been studied in various populations, such as those undergoing caesarean sections (7,8), little is known about its impact on the elderly population undergoing transurethral resection of the prostate (TURP). To the best of our knowledge, this is the first meta-analysis to assess the effects of dexmedetomidine and spinal anesthesia on the duration of anesthesia and safety profile of patients undergoing TURP.

2. Methods:

The Preferred Reporting Items for Systematic Review and Meta-Analysis" (PRISMA) guidelines (9) were followed.

2.1 Data sources and search strategy

A literature search was performed in four databases: (i) PubMed/MEDLINE, (ii) Cochrane Library, (iii) Scopus, and (iv) Google Scholar using keywords such as "dexmedetomidine," "transurethral resection of the prostate," and "spinal anaesthesia" spinal anesthesia spinal anesthesia. The search strategy was constructed for each database, and results were retrieved from inception to November 20, 2024. A detailed search strategy for each database is presented in ***Table S1.*** The review was registered with PROSPERO (CRD 42025640177**).**

Table S1: Search Strategy Used for Databases

Search Strategy (searched on 20 November 2024)	Database	Results
("dexmedetomidine"[MeSH Terms] OR "dexmedetomidine"[All Fields] OR "dexmedetomidines"[All Fields]) AND ("transurethral resection of prostate"[MeSH Terms] OR ("transurethral"[All Fields] AND "resection"[All Fields] AND "prostate"[All Fields]) OR "transurethral resection of prostate"[All Fields] OR ("transurethral resection of prostate"[MeSH Terms] OR ("transurethral"[All Fields] AND "resection"[All Fields] AND "prostate"[All Fields]) OR "transurethral resection of prostate"[All Fields] OR "turp"[All Fields]))	PUBMED	15
(Dexmedetomidine) AND (transurethral resection of prostate OR TURP)	COCHRANE LIBRARY	51
(Dexmedetomidine) AND (transurethral resection of prostate OR TURP)	GOOGLE SCHOLAR	1040
(Dexmedetomidine) AND (transurethral resection of prostate OR TURP)	SCOPUS	69

2.2 Eligibility criteria:

The following criteria were used to select studies for our systematic review and meta-analysis: (a) RCTs; (b) inclusion of patients undergoing TURP; (c) intervention with dexmedetomidine with spinal anesthesia in one arm of the study; (d) use of normal saline in the comparison arm; and (e) reporting of efficacy outcomes such as duration of sensory and motor block, hemodynamic changes, and adverse effects. Studies were excluded if (a) they included patients who underwent surgery other than TURP, (b) intervention other than dexmedetomidine, (c) did not use spinal anesthesia, (d) consisted of non-human trials, (e) had inadequate data, and (f) were observational and cohort studies, letters and editorials, case reports, case series, and reviews

2.3 Data extraction:

A third reviewer (MK) addressed any discrepancies after the two independent reviewers completed the data extraction. The year of publication, length of study, country, drug route and dose, number of patients in each arm, mean age, and duration of surgery were extracted. The specific features of every study are shown in ***Table 1***

First Author	Year	Study duration	Country	Route of administeration	Intervention	Comparator	Age (years)		No . of Participant		Preloading	Anaesthesia given at level	Position for spinal anesthesia	Anaesthesia given	Peak Block level	
							I	C	I	C					I	C
Sangkum et al	2024	11 Months	Thailand	IV[†]	Dex/0.4 µg/kg,	NS[‡]	69.28± 6.54	71.88± 6.29	18	16	-	L3 - L4	lateral position	0.5% bupivacaine	T7 (T6 – T8)	T10 (T7 – T10)
Park et al	2014	NM	Korea	IV	Dex/0.5µg/kg	NS	71.9 ± 8.0	73.9 ± 7.3	13	14	500 ml lactated Ringer's solution	L3-L4.	-	bupivacaine 6 mg	T8.6 ± 2.1	T9.4 ± 1.7
Kim et al	2013	NM	korea	IV	Dex/3µg	NS	66.6±6.2	68.8±6.3	27	27	300mL of 0.9% sodium chloride solution	L3-4 or L4-5	lateral decubitus position.	bupivacaine 6mg	T10 [T6 – T12]	T10 [T7 – L1]
Hong et al	2012	3 months	korea	IV	Dex/1.0 mg/kg	NS	75.1 ± 7.2	73.7 ± 7.0	26	25	500 ml of lactated Ringer's solution	L3–4	lateral decubitus position.	bupivacaine, 5 mg/ml	T10 (T11– T7)	T10 (T12– T8)
Kaya et al	2010	NM[§]	NM	IV	Dex/0.5 ug kg-1	NS	56.6 ± 8.5	57.2 ± 5.2	25	25	500 mL of	L3–5	lateral positio	Bupivacaine	(T 4.6	(T 6.4

											lactated Ringer's solution		n	0.5%	± 0.6)	± 0.8)

Table. 1: Baseline characteristics of included studies
† Intravenous
‡Normal Saline
§ Not mentioned
Dex; Dexmedetomidine

2.4 Quality assessment:

Two reviewers (AS,AK) performed quality assessments of the included studies. The Cochrane Risk of Bias Tool for Randomized Controlled Trials (RoB-2) (10) was used to assess the quality of the included studies. Quality was assessed based on the following domains: (i) randomization of participants, (ii) deviations from the intended interventions, (iii) missing outcome data, (iv) measurement of outcomes, and (v) selection bias in the reported results. In cases of discrepancies between the two independent reviewers, a third reviewer (MK)was invited to reach a consensus.

2.5 Statistical Analysis

Statistical analyses were performed using Review Manager (RevMan v5.4.1) to analyze the data. Risk ratios (RRs) with their corresponding 95% confidence intervals (CIs) were used for outcomes with dichotomous data using the Mantel-Haenszel method, and standard mean differences (SMD) with CIs were calculated using the inverse variance method for continuous outcomes. A random-effects model was used for the data synthesis. A p-value of less than or equal to 0.05 was regarded as significant in every setting. Statistical heterogeneity within studies was estimated using Higgins I2 statistics (11), with values <50%, 55-75%, and >75% representing low, moderate, and high degrees of heterogeneity, respectively. A sensitivity analysis using the leave-one-out method was performed for outcomes with moderate-to-high heterogeneity.

3. Result:

3.1 Study screening:

The initial literature search yielded 1,175 results. Of these, 11 duplicates were excluded. The studies were thoroughly reviewed based on their title and abstract. An additional 1,049 studies were removed based on the predefined inclusion and exclusion criteria. Finally, after a full-text review, five studies (Study Id-3,12–15) were included in our review, as shown in the PRISMA flow chart ***in Fig. 1***.

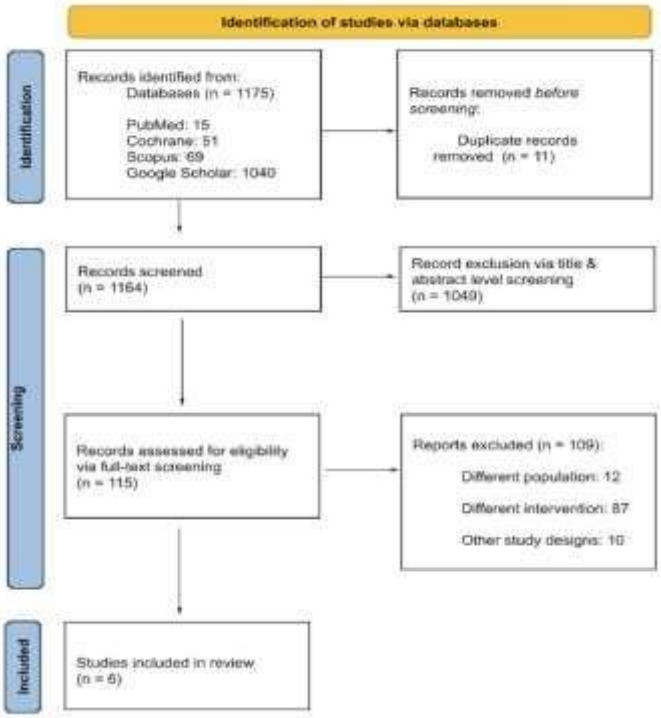

Figure 1: **Prisma flow chart of included studies**

3.2 Study characteristics

A total of 260 participants were included in the study; 131 were in the dexmedetomidine group and 129 were in the normal saline group. The mean age of the participants was 50–81 y. All study participants were administered preloading solutions ranging from 300 to 500 ml, except for Sangkum et al. (3). All studies were performed using spinal blocks between levels L2-L5**.** The detailed characteristics of the included studies are presented in ***Table 1.***

3.3 Bias Assessment:

The risk of bias was assessed using the RoB2 tool. All studies reported random sequence generation. Both patients and caregivers were blinded to the intervention, and the outcome assessors were unaware of the treatment groups, minimizing detection bias. Furthermore, no selective reporting of results was identified any in of the studies. Overall, the studies were deemed to have a low risk of bias, as detailed in ***Fig. 2.***

Figure 2. **Risk of bias assessment of included studies**

3.4 Meta Analysis of Outcomes

3.4.1 Duration of sensory block

All studies (3,12–15) compared the duration of the sensory block between the dexmedetomidine and normal saline groups. Dexmedetomidine showed significantly longer duration of sensory block when combined with spinal anaesthesia in comparison to normal saline (SMD = 1.05, 95% CI: 0.60 to 1.51, P<0.00001) (***Fig. 3***).

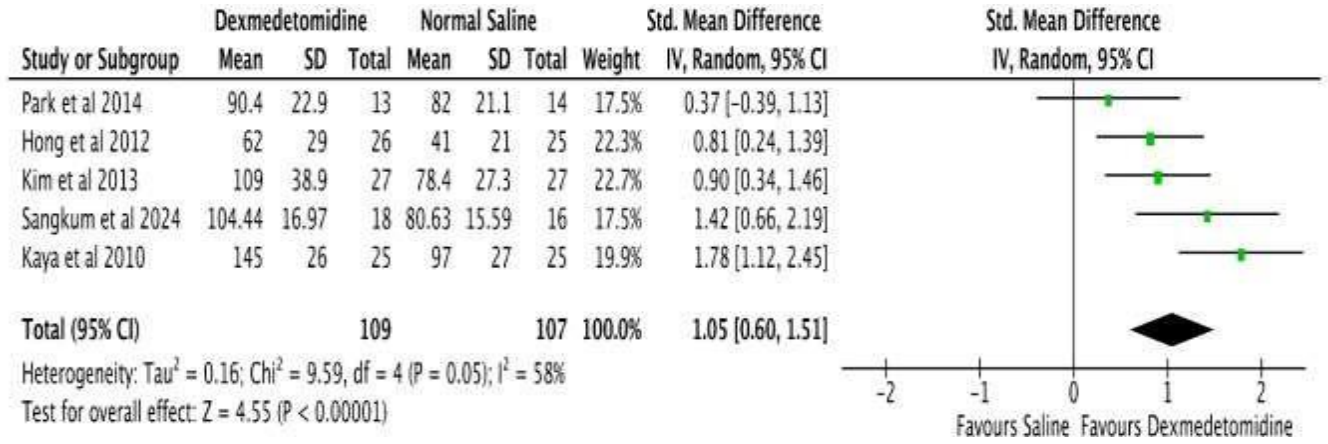

Figure 3 Forest plot of duration of sensory block comparing dexmedetomidine with saline

Significant heterogeneity was observed (I = 58%). Sensitivity analysis was performed using the leave-one-out method. By removing Kaya et al., heterogeneity significantly decreased (I = 19%) (***Fig. S1)***.

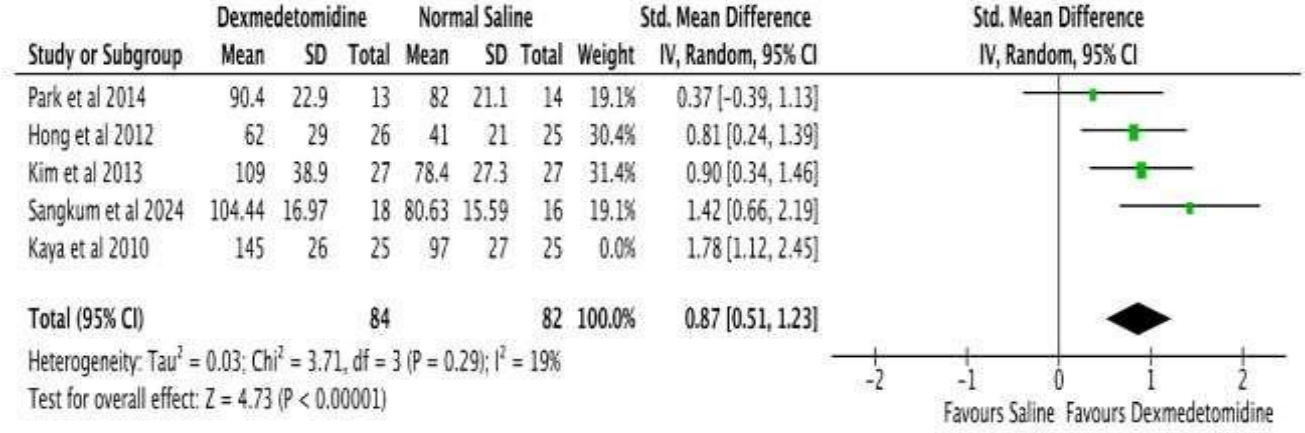

Figure.S1 Sensitivity analysis of duration of sensory block

3.4.2 Duration of motor block

Three studies (12,14,15) reported the duration of the motor block. Pooled analysis showed no significant difference between the dexmedetomidine and saline groups when administered with spinal anesthesia(SMD = 1.50, 95% CI -0.28 to 3.29, P = 0.10) ***(Fig. 4).***

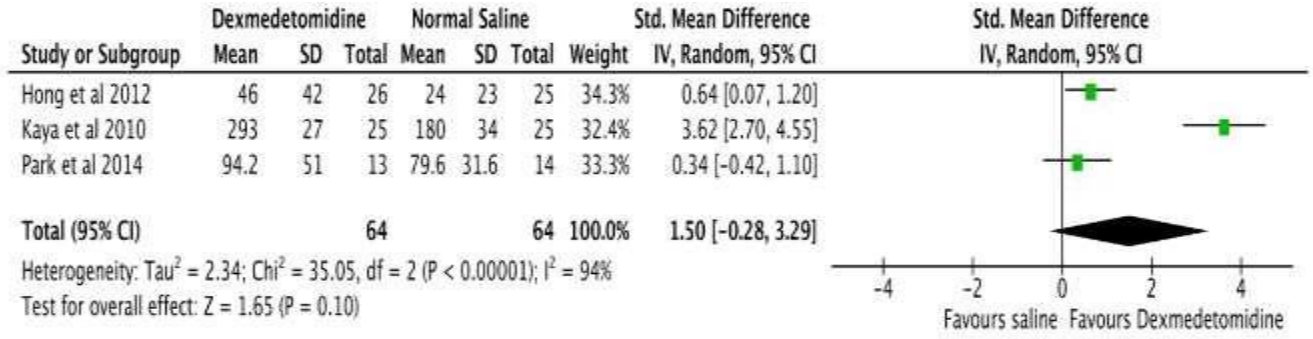

Figure.4 Forest plot of duration of motor block comparing dexmedetomidine with saline

Significant heterogeneity was observed (I=94%). By removing Kaya et al., the heterogeneity was significantly decreased (I = 0%) and also changed the significance of the result (P = 0.02) ***(Fig: S2)***

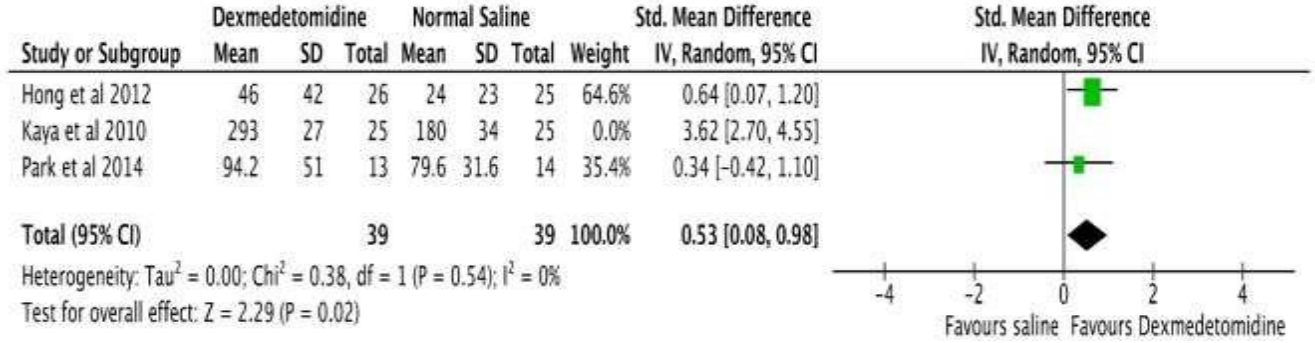

Figure.S2 Sensitivity analysis of duration of motor block

3.4.3 Hemodynamic changes

The lowest hemodynamic changes, such as HR, SBP, and MBP, were analyzed. Three studies (12,14,15) reported the lowest HR after spinal block, which was significantly lower in the dexmedetomidine group than in the saline group (SMD -0.50, 95% CI -0.86 to -0.15, P = 0.005, I = 0%) ***(Fig. 5)***.

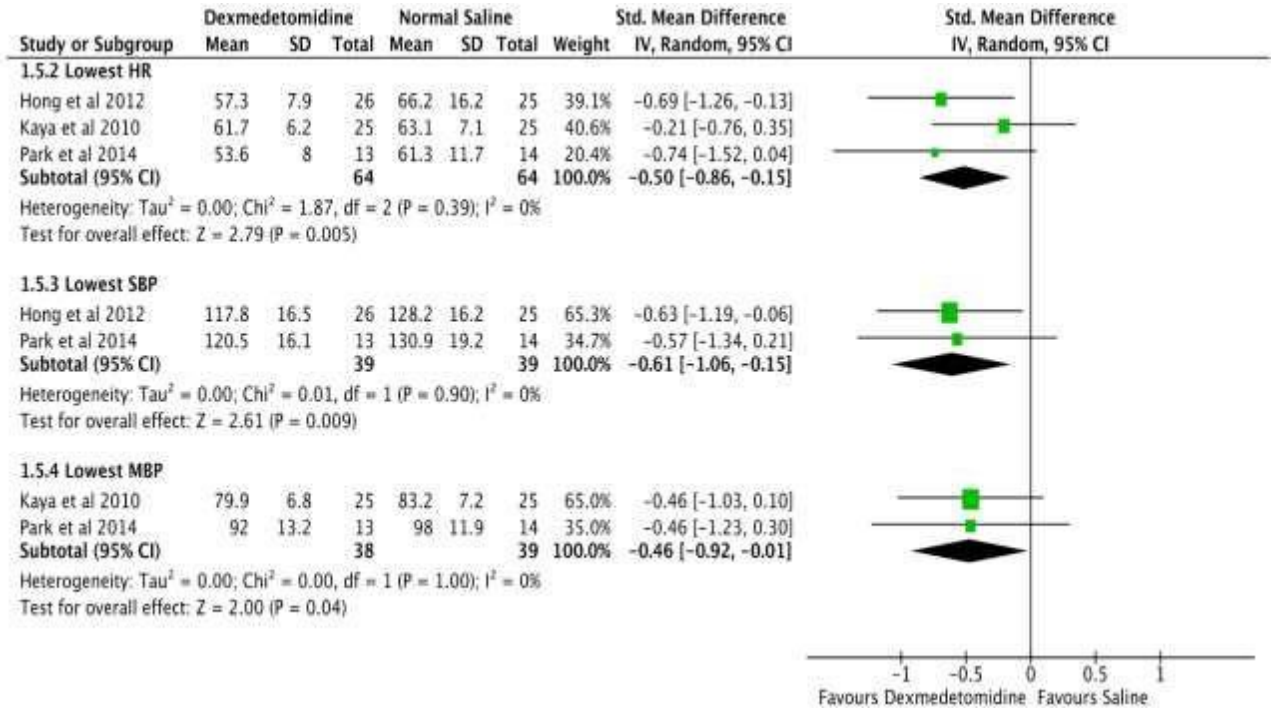

Figure.5 Forest plot of the duration of hemodynamic changes comparing dexmedetomidine with saline.

Two studies (12,14) reported the lowest SBP after spinal block, which was significantly lower in the dexmedetomidine group than in the saline group (SMD -0.61, 95% CI -1.06 to -0.15, P = 0.009, I=0%) ***(Fig. 5)***. Similarly, the lowest MBP reported by two studies (12,15) was also significantly lower in the dexmedetomidine group (SMD= -0.46, 95% CI -0.92 to -0.01, P = 0.04, I = 0%) %) ***(Fig. 5)***

3.4.4 Adverse effects

Adverse events, such as hypotension, bradycardia, and nausea, were also analyzed. Four studies (3,12,13,15) reported the incidence of hypotension intraoperatively. There was no significant difference between the dexmedetomidine and saline groups (RR 1.09, 95% CI 0.40–3.02, P = 0.86, I = 0%) ***(Fig. 6)***.

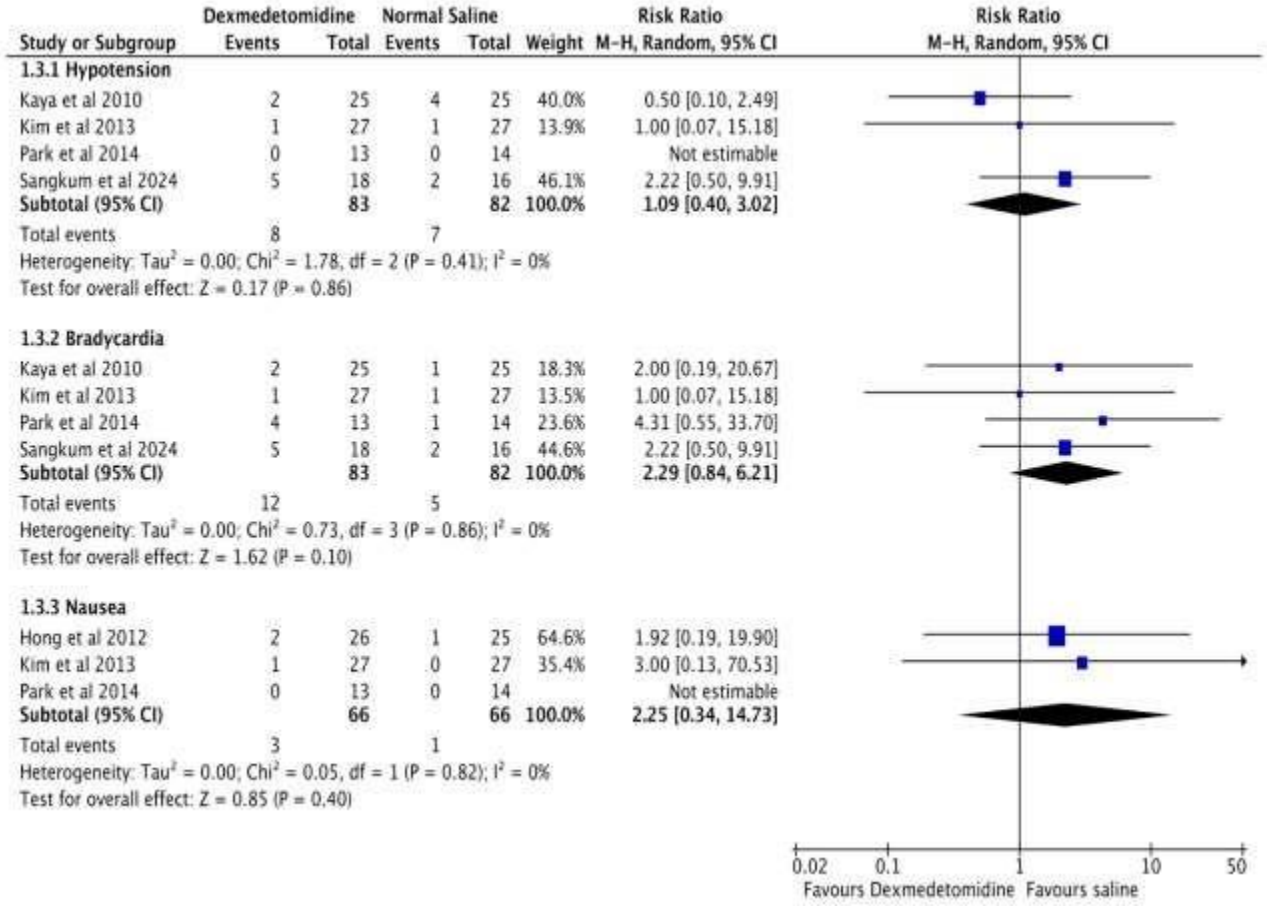

Figure.6 Forest plot of adverse effects including hypotension, bradycardia and nausea between dexmedetomidine and saline.

Four studies (3,12,13,15) reported the incidence of intraoperative bradycardia. No significant difference was found between the dexmedetomidine and saline groups (RR 2.29, 95% CI 0.84–6.21, P = 0.10, I = 0%) ***(Fig. 6).*** Three studies (12–14) reported the incidence of nausea. There was no significant difference between the dexmedetomidine and saline groups (RR = 2.25, 95% CI 0.34 to 14.73, P = 0.40, I = 0%) ***(Fig. 6)***.

3.4.5 Time to first analgesia

Two studies (14,15) reported the time to the first postoperative analgesia. The time to first analgesia was significantly longer in the dexmedetomidine group than in the saline group (RR 2.19, 95% CI 1.69 to 2.70, P<0.00001, I=0%) ***(Fig. S3)***

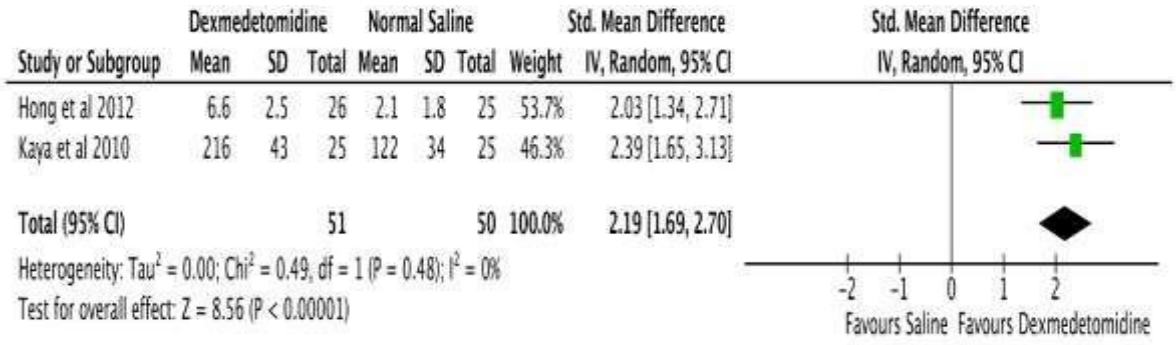

Figure.S3 Forest plot of time to first analgesia comparing dexmedetomidine with saline

3.4.6 PACU stay

Two studies (12,14) reported PACU stay duration. No significant difference was found between the dexmedetomidine and saline groups (RR=0.42, 95% CI -1.02 to 1.85, P=0.57, I=89%) ***(Fig. S4)***. Significant heterogeneity was found between the two studies.

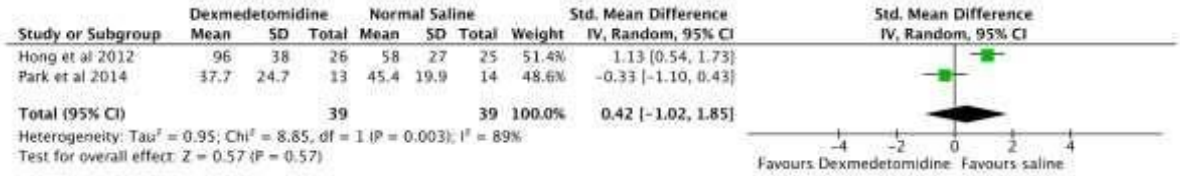

Figure.S4 Forest plot of PACU stay comparing dexmedetomidine with saline
PACU: post-anesthesia care unit.

3.4.7 Excessive sedation

Two studies (12,15) reported excessive sedation. However, no significant difference was found between the two groups (RR 0.25, 95% CI -0.16 to 0.67, P = 0.23, I = 87%) ***(Fig. S5).*** Significant heterogeneity was found between the two studies.

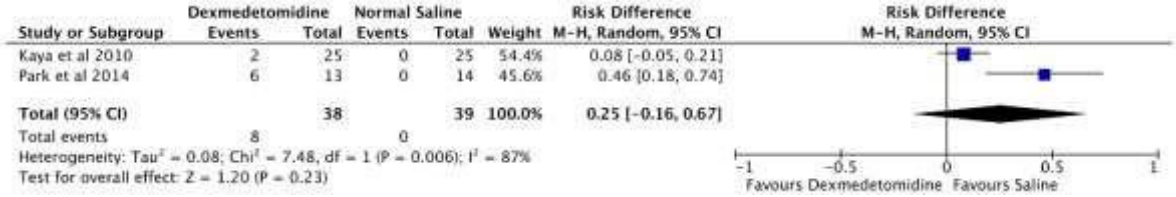

Figure.S5 Forest plot of excessive sedation comparing dexmedetomidine with saline

4. Discussion:

Our meta-analysis included five RCTs comparing dexmedetomidine and normal saline as an adjunct to spinal anesthesia in patients undergoing TURP. The analysis showed that dexmedetomidine was associated with a longer duration of sensory block, longer time to first analgesia, and the lowest hemodynamic changes intraoperatively. Although no significant results were detected for the duration of motor block, PACU stay, excessive sedation, and adverse events such as nausea, hypotension, and bradycardia.

Dexmedetomidine, an alpha-2 adrenergic agonist, is known to increase the duration of sensory blockade. This prolonged effect is due to its mechanism of action, where it binds to presynaptic C fibers, depressing the release of C-fiber neurotransmitters, and hyperpolarizing postsynaptic dorsal horn neurons. This enhances the efficacy of local anesthetics, such as bupivacaine, by prolonging

sensory blockade (16). Sangkum et al. (3) reported similar findings, with the 2-dermatome regression time being considerably longer in the dexmedetomidine group.
The results were also significant for the lowest hemodynamic measures intraoperatively, including HR, SBP, and MBP. This is primarily due to dexmedetomidine's ability to decrease sympathetic tone by reducing plasma norepinephrine concentrations (17). Activation of α2-adrenoceptors in the brain and spinal cord inhibits neuronal firing, leading to sedation, analgesia, and a pronounced sympatholytic effect, which reduces HR, SBP, and MBP during surgical stimuli (18). Furthermore, dexmedetomidine lowers HR by diminishing the tonic levels of sympathetic outflow and enhancing cardiac vagal activity (19).
Notably, while dexmedetomidine significantly reduced the lowest hemodynamic parameters, there was no observable difference in the incidence of adverse effects, such as bradycardia and hypotension, between dexmedetomidine and saline. This may result from physiological changes associated with aging; the body exhibits a diminished response to parasympathetic inhibition and beta-adrenergic stimulation. (20), which may mitigate the impact of dexmedetomidine on bradycardia. Ahn et al. indicated that bradycardia during spinal anesthesia with dexmedetomidine occurs in approximately 13–30% of patients, with variations contingent upon the loading dose administered (20).

The incidence of nausea was not significantly different between the two groups in our study. A meta-analysis of 82 trials involving 6,480 patients demonstrated that dexmedetomidine significantly reduced postoperative nausea and vomiting (PONV) compared to saline, with a risk ratio of 0.61 (95% CI: 0.50–0.73) (21). However, the effect of dexmedetomidine on PONV prevention appears to be dose-dependent. Studies have shown that lower doses of dexmedetomidine (e.g., 0.4 μg/kg/h) effectively reduce PONV, whereas higher doses may not provide additional benefits. For example, in a study evaluating dexmedetomidine at 0.2 μg/kg/h and 0.5 μg/kg/h, both doses significantly reduced the severity of nausea and vomiting compared to the control, but no difference was observed between the two doses (22).
Research indicates that pairing dexmedetomidine with ropivacaine can lead to pain relief after surgery compared to ropivacaine alone (23). When administered intrathecally, dexmedetomidine outperformed intravenous delivery in delaying the need for analgesics during the initial 24 h following spinal anesthesia (24). This spinal approach targets α2-adrenergic receptors in the spinal cord and blocks the ERK1/2 pathway, resulting in stronger pain relief without affecting the patient’s motor function (25). By addressing pain through these dual mechanisms, the patient is not only comfortable during surgery but also reduces their reliance on postoperative painkillers.

Our analysis showed no notable differences in the duration of PACU stay or excessive sedation. These results align with a large review of 33 studies (2,676 patients), which found PACU stays differed by less than a minute on average which is too small to be clinically meaningful (95% CI: -1.42 to 2.81) (26). However, sedation outcomes varied between studies, likely due to differences in patient demographics and dosing strategies. For example, Park et al. (12) noted higher sedation rates in groups with an average age of 70 years or older, which may be due to the fact that older adults often metabolize drugs more slowly and have weaker physiological reserves, making them prone to stronger sedative effects and blood pressure drops from dexmedetomidine. Seto et al. (27) supported this, recommending cutting the initial dose by half for patients over 75 to avoid over-sedation and hypotension. Standardized dosing strategies and age-adjusted protocols are crucial

for reducing variability in outcomes and ensuring the safe and effective use of dexmedetomidine in diverse patient populations.

This study had several limitations that warrant consideration. First, elderly patients, who constitute a significant proportion of the study population, may have comorbidities, such as diabetes mellitus (DM) and hypertension (HTN), that can influence the outcomes. However, most of the studies included did not report the presence of such comorbidities, limiting the generalizability of the findings to patients with multimorbidity. Second, many of the included RCTs had small sample sizes, which limited the robustness of the conclusions. To enhance the reliability and generalizability of these findings, future studies should incorporate larger, well-designed RCTs with detailed reporting of patient comorbidities and other relevant baseline characteristics of the patients.
Dexmedetomidine enhances the spinal anesthesia effects by prolonging the sensory block and delaying the timing of first analgesia. It did not affect the incidence of adverse events, PACU stay, or sedation scores.

Conclusion

A meta-analysis has shown that dexmedetomidine is a safe and effective adjunct to spinal anesthesia in elderly patients undergoing transurethral resection of the prostate (TURP). It prolongs the sensory block duration and delays the need for the first analgesia, enhancing the overall effectiveness of spinal anesthesia without compromising patient safety. Dexmedetomidine is associated with lower intraoperative heart rate, systolic blood pressure, and mean blood pressure, reflecting its sympatholytic properties. No significant differences were observed in motor block duration, PACU stay, excessive sedation, or adverse events. However, large-scale, high-quality randomized controlled trials are needed to strengthen these findings and refine the dosing strategies. Overall, dexmedetomidine is a valuable adjunct to spinal anesthesia in TURP, providing prolonged analgesia and hemodynamic stability without increasing postoperative risks.

Abbreviations:

1. Transurethral resection of the prostate (TURP).
2. Randomized controlled trials = (RCTs)
3. Heart rate = (HR)
4. Systolic blood pressure = (SBP)
5. Mean blood pressure = (MBP)
6. Preferred Reporting Items for Systematic Review and Meta-Analysis = (PRISMA)
7. Postoperative nausea and vomiting = (PONV)
8. Diabetes mellitus =(DM)
9. Hypertension = (HTN)

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