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Review Article

Effect of intravenous dexmedetomidine as an adjuvant to brachial plexus block in upper limb orthopedic surgeries – A systemic review and meta-analysis

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ABSTRACT

Brachial plexus block for upper limb orthopedic surgeries has been widely used for surgical anesthesia and post operative analgesia. Various adjuvants are used to prolong the duration of the nerve block. Systemic dexmedetomidine as an adjuvant to local anesthetics has been shown to prolong the duration of the nerve block in some randomized controlled trials (RCTs) but is far from unanimous in its efficacy. Hence, an updated meta-analysis was planned to assess the efficacy and safety of systemic dexmedetomidine as an adjuvant to local anesthetics in brachial plexus nerve block (BPNB). Objective of the study is to assess the duration of analgesia in patients undergoing upper limb orthopaedic procedures with BPNB and intravenous dexmedetomidine as an adjuvant. Data sources were PubMed, Cochrane, and Google Scholar were systematically searched till July 2023. The meta-analysis included all published studies that investigated the effect of systemic dexmedetomidine on duration of analgesia following BPNB. The data extraction was guided by a predetermined checklist. Analysis was done Using RevMan_5 software, the mean difference for duration of analgesia between the two groups and odds ratio was calculated from the selected studies. The fixed-effects model was used to compare the difference in the duration of analgesia between the two groups. The outcome was prolonged duration of analgesia in patients undergoing upper limb orthopedic procedure where intravenous dexmedetomidine was used as an adjuvant to peripheral nerve blocks. Our meta-analysis currently generates the evidence that intravenous dexmedetomidine administration offers advantages over other drugs in terms of prolonged duration of analgesia.

Keywords: Local anesthesia, Dexmedetomidine, Brachial plexus, Analgesia, Nerve block

INTRODUCTION

Brachial plexus nerve block (BPNB) for the upper limb orthopedic surgeries has been widely used for surgical anesthesia and post-operative analgesia.[1] Various techniques such as continuous perineural catheters, intravenous or perineural dexamethasone, clonidine, midazolam, dexmedetomidine (intravenous and perineural), and adrenaline had been tried to prolong the duration of analgesia postoperatively.[2-5] Perineural administration of adjuvants carries the risk of neurotoxicity and safety is not proven. Dexmedetomidine, a highly selective alpha 2-adrenergic receptor agonist, is widely used perioperatively for its sedative, anxiolytic, and analgesic properties. Systemic dexmedetomidine as an adjuvant to local anesthetics has been shown to

prolong the duration of the nerve block in some randomized controlled trials (RCTs) but are far from unanimous in the efficacy.[6-10] Hence, an updated meta-analysis was planned to assess the efficacy and safety of systemic dexmedetomidine as an adjuvant to local anesthetics in BPNB.

MATERIAL AND METHODS

This study protocol was prospectively registered with PROSPERO and conducted with the requirements of the reporting rules in the "Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines"[11] and strictly complied with its specifications. Since this work is a systematic review, the heterogeneity was present within the acceptable range, meta-analysis was performed.

Eligibility criteria

Criteria for included studies were defined as patients undergoing upper limb orthopedic procedure under brachial plexus block. The criteria for the inclusion included,

- Patients undergoing upper limb orthopedic procedure under brachial plexus block
- RCTs
- Studies assessed the duration of analgesia
- Studies compared with other drugs or placebo.

Search strategy

The electronic retrieval methods were adopted for the literature retrieval. A comprehensive and systematic research review using combination of Medical Subject Headings (MeSH), controlled vocabulary, and keywords was conducted through various databases, include PubMed, Cochrane, and Google Scholar for studies till 2023. Furthermore, a manual search of reference list of primary trials was conducted from the selected topics and relevant articles were included in the review and analysis.

Study selection

The search results were uploaded into the online systematic review program Rayyan to conduct the study selection.[12] A two-stage screening process were conducted for study selection. Two independent authors (S.R, P.J) performed the literature search and screened the title, abstract, and keywords of all the studies. Screening of abstract and full text was done independently by two authors (S.R, P.J) to select the studies that satisfy the eligibility criteria of our review. Any disagreements or discordances present during the entire selection process were resolved either through consensus or consultation with third author (R.M).

Data extraction and management

The relevant study characteristics for the review were extracted by the first and coauthor independently related to outcome measures from the included studies. Data extraction was guided by a predetermined checklist with the first author's last name, published year, total sample size, type of surgery, type of nerve block, dose of drug, study design, duration of analgesia, and type of control (placebo or other drugs) [Table 1].

Second author (P.J) transferred the obtained data into the software Review Manager (RevMan_5.3, Copenhagen: The Nordic Cochrane Center, the Cochrane Collaboration, 2014).[13] Data entry was double-checked for correct entry by the second author (P.J) through comparison of data presented in the review and included the reports.

Outcome measure for the study

The outcome was to assess the duration of analgesia with intravenous dexmedetomidine in patients undergoing upper limb orthopedic procedure.

Quality assessment

Risk of bias by Cochrane was used to assess the risk of bias of the selected articles and the quality review process was monitored. Each article was categorized as follows: "low-risk," "moderate-risk," or "high-risk" of bias.

Statistical analysis

A comprehensive qualitative analysis was made. For quantitative meta-analysis, the binomial data were performed using RevMan_5.3. When studies reported multiple arms in single trial, only the relevant arms were included for the analysis. Due to heterogeneity among studies, a logistic-normal-fixed-effect model was conducted. The 95% confidence interval (CI) was performed for study-specific and overall pooled prevalence, respectively. To assess the heterogeny, I^2 statistics was used. Significant heterogeny was considered if $P < 0.05$ or $I^2 > 50\%$ among the studies. Study specific and pooled estimates were graphically represented through forest plot. Sensitivity analysis was done to assess the reliability of the estimate obtained in the meta-analysis.

RESULTS

Study selection and characteristics

A total of 2460 studies were initially retrieved following the removal of duplicates. Of those, five studies met the inclusion criteria. These five articles were ultimately included for the qualitative and quantitative analysis. [Table 1] Of the five

Table 1: Characteristics of study participants.

Study	Year	Number of participants IV group/ control group	Type of surgery	Nerve block	Local anesthetic drug and dose	Dexmedetomidine IV dose	Control group	Outcome	Duration of analgesia in IV dexmed group (h)	Duration of analgesia in control group
Abdallah *et al.*[9]	2016	34/32	Shoulder arthroscopy	Interscalene block	15 mL ropivacaine 0.5% with adrenaline 1 in 200000	0.5 μg/kg	IV saline	Duration of analgesia	10	7
Bao *et al.*[8]	2022	20/20	Hand surgery	Mid forearm ulnar radial median nerve block	0.75% ropivacaine 3 ml each for ulnar radial median nerve	0.5 μg/kg	IV saline	Duration of analgesia	11	10
Hong *et al.*[7]	2018	49/47	Forearm fracture	Supraclavicular block	25 mL of 1:1 mixture of 1% lidocaine and 0.75% ropivacaine	Loading dose 1 μg/kg Maintenance dose 0.6 μg/kg	IV midazolam 2 mg	Duration of analgesia	10	7
Kang *et al.*[10]	2018	18/18	Shoulder arthroscopy	Interscalene block	15 mL ropivacaine 0.5% with adrenaline 1 in 200000	0.5 μg/kg	IV saline	Duration of analgesia	11	11
Rodrigues *et al.*[6]	2020	65/65	Shoulder surgery	Interscalene block	30 mL 0.5% bupivacaine	50 μg	IV dexamethasone 4 mg	Duration of analgesia	16	24

articles, three articles compared with saline and one with Midazolam and one with Dexamethasone.[8-10] The PRISMA flowchart for the study selection is available in Figure 1. When using ROB by Cochrane, all five articles had moderate risk of bias [Figures 2 and 3].

Characteristics of the patient

From all five studies included, a total of 186 patients were in the intervention group and 182 patients in the control group who underwent upper limb orthopedic procedure with BPNB. Among them, 186 patients in the intervention group received intravenous dexmedetomidine. Of them, 70 patients in the control group received Intravenous saline, whereas remaining 112 patients received other drugs.[6-10] Overall, the duration of the analgesia ranged between 10 and 16 h in the intervention group and 7 and 24 h in the control group.

Methodological quality of the included studies

The included five studies of the final review were all RCT with other drugs or placebo as control. These articles were published between 2016 and 2020 done in the hospital setting. Among these, one study was triple blinded, and four studies were double blinded.[6-10] [Table 1].

Effect of the intravenous dexmedetomidine

A meta-analysis of five eligible comparative studies to assess the duration of analgesia following peripheral nerve block involving 186 subjects who were exposed to intravenous dexmedetomidine and 182 subjects who were exposed to placebo drug showed an overall significant effect in favor of dexmedetomidine (odds ratio-0.95, 95% CI 0.57–1.58, $P = 0.85$), as shown in Figure 2. A significant Q statistic ($P = 0.35$) indicated the presence of heterogeneity ($I^2 = 9\%$).

DISCUSSION

Intravenous dexmedetomidine is widely used for sedation and analgesia in critical care unit and procedural sedation in the operating room.[14] The described mechanism underlying the intravenous injection of dexmedetomidine is that it can act on the alpha 2-receptor in the nucleus ceruleus of the brainstem to produce its sedative-hypnotic and antianxiety effects and relieve the patient's stress.[15] Furthermore, at the level of peripheral nerves, the possible mechanisms of dexmedetomidine as an analgesic adjuvant may be as follows: first, dexmedetomidine suppresses the production of action potentials by C and Aδ fibers, enhances the inhibition of Na+ channels by local anesthetics, and blocks the conduction of

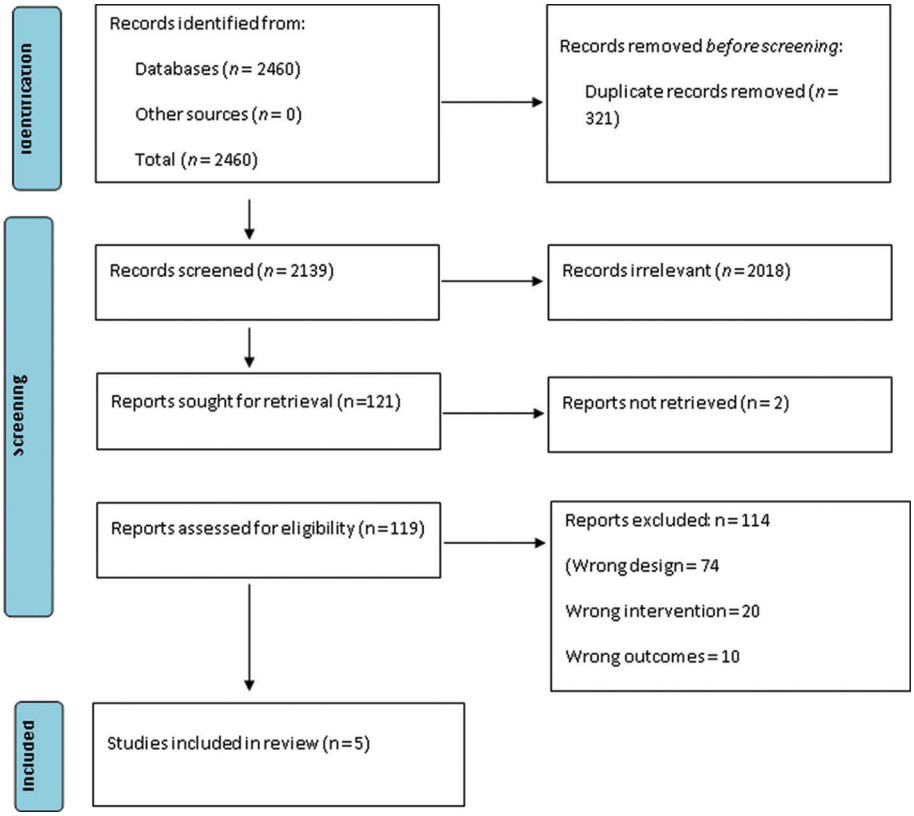

Figure 1: Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) flow diagram of the study selection process.

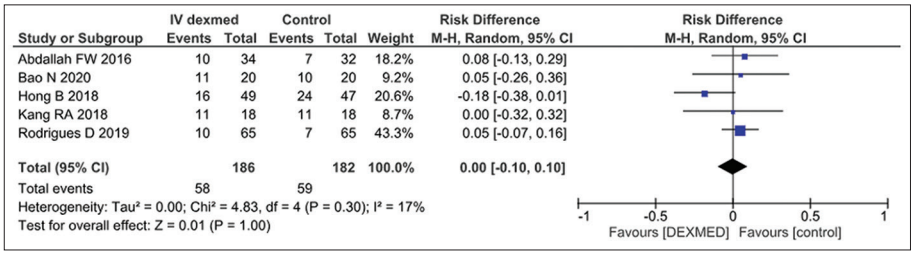

Figure 2: Effect of dexamedotomidine on brachial plexus nerve block in the included studies. CI: Confidence interval, black diamond: pooled effect.

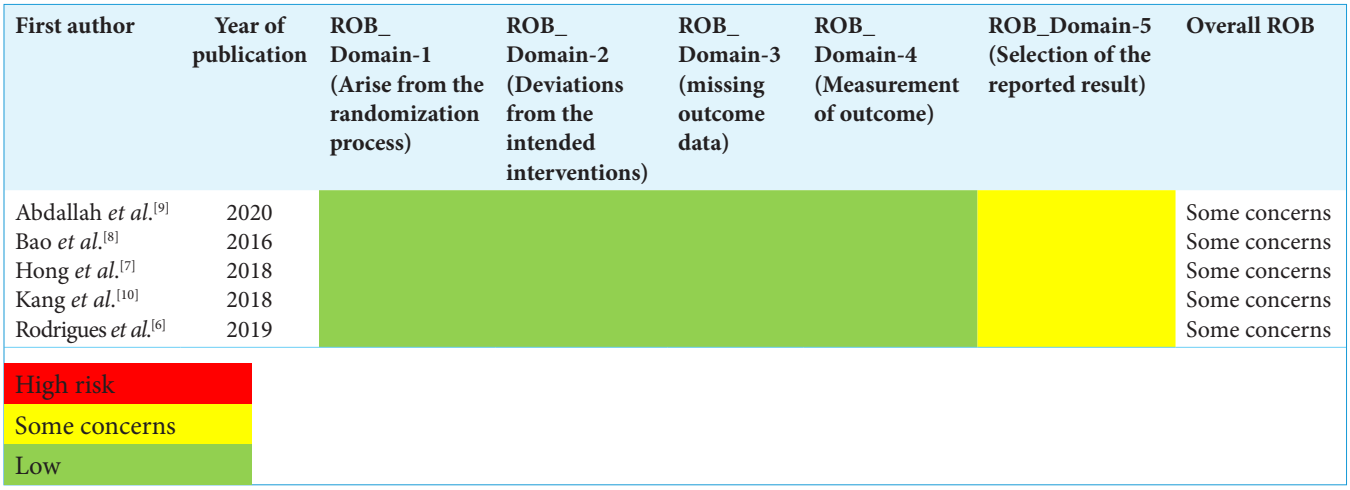

Figure 3: Risk of Bias (ROB) analysis in the included studies.

excitation;[16] and second, both the activation of inwardly rectifying G1-protein-gated potassium channels and the regulation of entry of calcium through N-type voltage-gated calcium channels are independent of cyclic adenosine monophosphate and protein phosphorylation.[17]

Our meta-analysis showed that intravenous dexmedetomidine as a local anesthetic adjuvant significantly prolonged the duration of analgesia and reduced the analgesic consumption, compared with the placebo group. Administration of intravenous dexmedetomidine as procedural sedation can be used while performing BPNB which can prolong the duration of analgesia postoperatively.

Limitations

Our review has a few limitations. A moderate level of heterogeneity was observed in the measured outcome. The method of operating nerve block was not unified, including ultrasound-guided or nerve stimulator. Finally, the strength of evidence remains limited due to the small number of studies. More high-quality studies are needed to confirm our results.

CONCLUSION

Our meta-analysis currently generates evidence that intravenous dexmedetomidine administration offers advantages over other drugs and placebo in terms of prolonged duration of analgesia.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

Dr. P Sanjay, Dr. Reenaa Mohan and Dr. Srinivasan Ramachandran are on the Editorial Board of the Journal.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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