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Intravenous versus Non-intravenous Sedation for Cataract Surgery: A Systematic Review and Meta Analysis

Running Head: IV vs Non-IV Sedation for Cataract Surgery Meta Analysis

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Abstract

Topic: This review assesses the effectiveness of intravenous sedation compared to non-intravenous sedation for routine cataract surgery.

Clinical Relevance: Cataract surgery is a safe and routinely performed surgery. Sedation practices vary, with centers providing either intravenous (IV), oral or no sedation for surgery. Improving sedation practices may have significant implications for patient safety, patient experience and health system efficiency.

Methods: Medline, Embase, Cochrane Library, BIOSIS, Web of Science, and CINAHL were searched from inception to July 2024 for relevant articles containing original data. Randomized controlled trials that compared IV to oral or no sedation and 1) used a validated pain scale to report on pain or 2) reported on perioperative complications were included. A random effects meta-analysis was conducted. Odds ratios, standard mean differences, 95% confidence intervals (CIs), and I^2 statistics were reported. The review was registered in PROSPERO (CRD42024582495) and PRISMA guidelines were followed.

Results: 12 randomized controlled trials including 1130 patients were included in the meta-analysis. IV sedation was associated with significantly decreased pain compared to no sedation (SMD = -0.98, 95% CI -1.68 to -0.29). Comparing IV and oral sedation, however, there was no difference in patient reported pain (SMD = -0.54, 95% CI -1.60 to 0.52). Analysis of intraoperative complications showed that there was no significant difference in complications between patients receiving IV and oral sedation (OR = 0.68, 95% CI 0.27 to 1.73).

Conclusion: For routine cataract surgery, IV sedation was associated with less pain than no sedation, but oral and IV sedation provided comparable pain control. Perioperative complications occur at similar rates regardless of sedation modality. These findings may help to inform sedation practices for cataract surgery.

Introduction

Cataract surgery is one of the most frequently performed surgical procedures worldwide. Over the past decade, tremendous advancements in surgical techniques have greatly improved patient outcomes and safety.[1] The widespread use of phacoemulsification, better surgical microscopes, enhanced phacoemulsification machines with improved irrigation systems, combined with the advent of sutureless incisions and superior intraocular lenses (IOLs), have all contributed to the remarkable improvements in visual acuity and patient safety.[2] As a result, cataract surgery is now considered one of the safest surgeries, with excellent postoperative visual outcomes.[1]

The approach to sedation during routine cataract surgery varies across centers. Some centers rely on intravenous (IV) sedation, while others perform the surgery without sedation or with oral sedation. Improving the quality of care, enhancing patient experiences, and optimizing outcomes remain key priorities in cataract surgery. Furthermore, the use of oral sedation may have significant time and cost saving potential. Modeling from 2001 demonstrated that modifications to anesthetic protocols for cataract surgery could reduce costs by up to $282 USD per case (adjusted to 2001 dollars).[3] The purpose of this systematic review and meta-analysis is to explore and compare patient pain perception and complication rates associated with IV versus no sedation or oral sedation during routine cataract surgery.

Methods

An electronic search strategy was developed in consultation with an experienced medical information specialist (Supplemental Material 1). We used this strategy to search Medline, Embase, Cochrane Library, BIOSIS, Web of Science, and CINAHL until July 2024. The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO 2024, registration number, CRD42024582495). All results were exported to Covidence (Veritas Health Innovation, Melbourne, Australia), where duplicates were removed. For primary study selection, titles and abstracts from the initial search were screened by two independent reviewers using eligibility criteria.

This review included any randomized controlled trial comparing intraoperative complications and/or patient-reported pain between patients receiving IV sedation and those receiving either oral sedation or no sedation during cataract surgery. Included studies must have measured patient reported pain and/or intraoperative complications. Only adult patients undergoing phacoemulsification cataract surgery were included. We excluded non-randomized controlled trials. There were no restrictions for the year of publication.

For secondary study selection, the full texts of selected studies were assessed by two independent reviewers against the same above eligibility criteria. An explanation was provided for the excluded full texts. Any disagreement between the two reviewers regarding the inclusion of a study was resolved through consensus. Data extraction was conducted (see Supplemental Material 2 for data extraction framework) by two independent reviewers and any discrepancies were resolved through consensus. Meta-analysis was conducted using a random-effects model

comparing the intraoperative complications and pain scores for patients undergoing phacoemulsification with intravenous sedation versus no sedation or oral sedation. Pain scores for each study were converted to a score out of 10 and standard mean difference in pain scores was determined. The meta-analysis was performed using Review Manager (RevMan 5.4), where odds ratios (ORs), weighted/standard mean differences, 95% confidence intervals (CIs), and I^2 statistics were synthesized. Subgroup analysis was conducted to compare the intraoperative complications and patient reported pain for the IV versus oral sedation groups and the IV versus no sedation groups.

The risk of bias was assessed by two independent reviewers using the RoB 2.0 revised Cochrane RoB tool.4 The tool assesses the studies in the domains of randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported results. The RoB for each domain and the overall study were judged as either "low," "some concerns," or "high." We evaluated the certainty of evidence of each outcome in our meta-analysis with the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool.5

Results

Included Studies

The search yielded 7464 articles. After deduplication, 4011 articles underwent title/abstract screening, and 537 articles were retrieved for full-text review. Ultimately, 12 articles were included in the review. An overview of the study selection process is presented in a PRISMA flow diagram (Figure 1).

Study Characteristics

This review includes randomized controlled trials from many countries including four from Turkey, two from the United States, two from India, two from Germany, one from Brazil, and one from the United Kingdom. The studies ranged in date between 2002 and 2021. The country and year of publication of each study are reported in Supplementary Table 1.

Patient Characteristics

Across the 12 studies, a total of 1130 patients were included. There were 592 patients included in the IV sedation group, 207 patients received oral sedation and 331 patients received no sedation. In the IV sedation group, the mean age was 69 years, and the percentage female was 57%. In the no sedation group, the mean age was 67 years, and the percentage female was 43%. In the oral sedation group, the mean age was 71 years, and the percentage female was 58%. The mean age and sex for each study is reported in Supplemental Table 2.

Type of Sedation

Eight studies including 702 patients compared IV sedation to no sedation, while four studies including 428 patients compared IV sedation to oral sedation. The specific IV sedation used in each study is reported in Table 1. Drugs used for IV sedation included midazolam (n=301), fentanyl (n=134), remifentanil (n=85), and dexmedetomidine (n=52) and clonidine (n=20). Among the four studies comparing IV sedation to oral sedation, two studies used oral clorazepate dipotassium, one study used oral triazolam and one study used oral diazepam.

Dilation, topical anesthesia and ocular injection

As only randomized controlled trials were included, the type of dilation, topical anesthetic, and ocular injection (if any) between the IV sedation and the non-IV sedation group were identical for all included studies. The specific dilation and topical anesthetic agents used are listed in the Table 1. Across the 12 studies, three studies used a retrobulbar block, and two studies used intracameral lidocaine.

Pain Scales

11 studies reported on pain. The Verbal Pain Scale (VPS) was used by three studies, the Visual Analogue Scale (VAS) was used by three studies, Numerical Pain Rating Scale (NRS) was used by three studies and two studies used a Likert scale. Results for all scales were converted to a score out of ten.

Risk of Bias and Quality Assessments

The risk of bias of each study was assessed using the Cochrane risk of bias tool (Table 2) and the overall quality of the evidence was assessed using the GRADE tool (Supplemental Table 3). The overall risk of bias across the studies was low and the general quality of the evidence was high.

Pain

IV vs No Sedation

Eight studies compared the pain outcomes of patients receiving IV sedation to those receiving no sedation. Patients receiving IV sedation reported significantly less pain compared to those patients receiving no sedation, with a standard mean difference of -0.98 (95% CI -1.68 to -0.29). This can be noted in Figure 2a. The raw and standardized pain scores can be noted in Supplemental Table 4 and 5, respectively.

IV vs Oral Sedation

Three studies reported on the pain outcomes of patients receiving sedation to those receiving oral sedation. There was no significant difference in the pain experienced between those receiving IV sedation compared to those receiving oral sedation with a standard mean difference of -0.54 (95% CI -1.60 to 0.52). This can be noted in Figure 2b.

Complications

IV vs No Sedation

Across the 8 studies comparing patients receiving IV sedation to those receiving no sedation, only one study reported on complications. Inan et al. found that patients receiving no sedation were more like to have intraoperative complications (ie., systemic hypertension) compared to those receiving IV sedation (OR 0.08, 95% CI 0.00 to 1.54).[12] All cases of hypertension were managed with IV antihypertensive medication (enalapril 10 mg).

IV vs Oral Sedation

Three studies compared the rates of intraoperative complications in patients receiving oral sedation to those receiving IV sedation. Synthesis of these results (Figure 3a) show that the odds of intraoperative complications, either ocular or systemic were comparable in both groups (OR 0.68, 95% CI 0.27 to 1.73). Further subgroup analysis (Figure 3b) exploring only studies that reported on ocular intraoperative complications was conducted. Patients receiving IV and oral sedation had comparable rates of ocular complications OR 0.91 (95% CI 0.36 to 2.30). The specific complications that occurred in each group are reported in the Supplementary Table 6.

Discussion

The purpose of this review was to compare patient-reported pain and intraoperative complications during cataract surgery in patients receiving either intravenous sedation, oral sedation, or no sedation. Compared to those receiving IV sedation, patients receiving no sedation were significantly more likely to report pain. The evidence regarding complications associated with cataract surgery under no sedation is limited. Comparing patients receiving oral sedation to those receiving IV sedation, there was no difference in patient pain perception or intraoperative complications.

1130 patients across 12 studies were included in this review. Overall, the quality of the evidence reviewed was high as shown in the GRADE assessment. 10 of the studies were of high quality and the remaining two studies were of moderate quality due to concerns in risk of bias. Some inter-study heterogeneity was present in the meta-analysis, presumably secondary to variability in patient populations as well as diagnostic protocols.

Our meta-analysis showed that IV and oral sedation provided comparable pain control for cataract surgery. These results are similar to those of patients undergoing other intraocular surgeries. A randomized controlled trial studying patients undergoing cornea and glaucoma surgery also showed similar outcomes, with IV and oral sedation providing comparable patient and surgeon satisfaction, as well as adverse events.[18]

Our analysis also showed no difference in complications between IV and oral sedation groups. The most commonly reported intraoperative ocular complication was posterior capsule rupture, which is consistent with previously reported rates ranging from 0.5% to 16%.[19] Intraoperative side effects of intravenous sedation included bradycardia and intraoperative diaphoresis . Conversely, oral sedation was associated with tachycardia. Both types of sedation were associated with cases of postoperative nausea and vomiting. Overall, there was no significant difference in intraoperative complications for patients receiving oral sedation compared to those receiving IV sedation. Our meta-analysis comparing complications between patients who received IV sedation and those receiving oral sedation included 3 studies with 428 participants. Further studies with larger patient cohorts are needed to confirm the safety of oral sedation in cataract surgery and to identify potential differences in the incidence of rare complications.

Currently, IV sedation is used in many institutions worldwide, however, oral sedation is increasingly being used. [20,21] Besides patient satisfaction, recent evidence has shown that surgeon satisfaction was similar regardless if patients underwent IV or oral sedation.[15] Given the evidence supporting a comparable safety profile and equivalent patient reported pain scores for oral and IV sedation, oral sedation may be an increasingly valuable form of sedation for cataract surgery.

A substantial cost in cataract surgery can result from the anesthesia and sedation strategy. When intravenous neuroleptic sedation is included as part of the anesthesia management strategy, it calls for the added personnel cost of anesthesia nurses and anesthesiologists, as well as preoperative, intraoperative and postoperative medications, and several disposable

materials associated with the intravenous therapy. Anesthesia assistants may also be used depending on the model employed. Cataract surgery under oral sedation eliminates the additional personnel and materials needed for IV sedation and may decrease the cost of cataract surgery. Experience from a tertiary care academic center in the United States suggests that replacing IV sedation with oral sedation for cataract surgery—eliminating the need for anesthesiologist monitoring—could reduce costs by $427.05 per 45-minute case.[22] It is, however, unclear if these savings would be offset by costs for unplanned items such as the need for additional pupil manipulation. Previous evidence has shown that patients reported IV cannulation as the worst pain experienced during cataract surgery and that the omission of the placement of an IV was associated with improved patient experience.[23] Furthermore, oral sedation may also be a valuable alternative to IV sedation, improving the surgical experience for the approximately 16% of patients with a fear of needles.[24,25] Another advantage of oral sedation is the elimination of the pre-operative fasting requirement, leading to an improved patient experience.[26]

This meta-analysis following PRISMA methodology included 10 randomized controlled trials of high quality and two of moderate quality. Evidence was included from a variety of settings and studies between 2002 and 2021 were included. A limitation of this study is the variability in anesthetic across the studies. Some of the randomized controlled trials used retrobulbar blocks in both sedation groups while others used intracameral anesthesia for each group. Another important factor that must be explored is the complexity of the cataract surgery. It is unclear whether the included studies considered complex cataract surgeries as well as more routine

cases. Furthermore, the involvement of trainees in surgery is another factor that must be explored further. The health status of patients is another important consideration. Patients with more comorbidities may require more anesthetic support and may thus be ineligible for oral sedation without anesthesiologist oversight. Further research is required to explore which patients may not be good candidates for cataract surgery under oral sedation.

Conclusion

Compared to those receiving IV sedation, patients receiving no sedation were significantly more likely to feel pain during surgery. Patients receiving IV and oral sedation reported similar levels of pain during surgery and had similar rates of complications. The overall quality of evidence supporting these conclusions was high.

Supplemental Material 1 - http://links.lww.com/JRS/B348
Supplemental Material 2 - http://links.lww.com/JRS/B349
Supplementary Tables - http://links.lww.com/JRS/B350

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Figure 1: PRISMA Flow Diagram – Study Selection Process

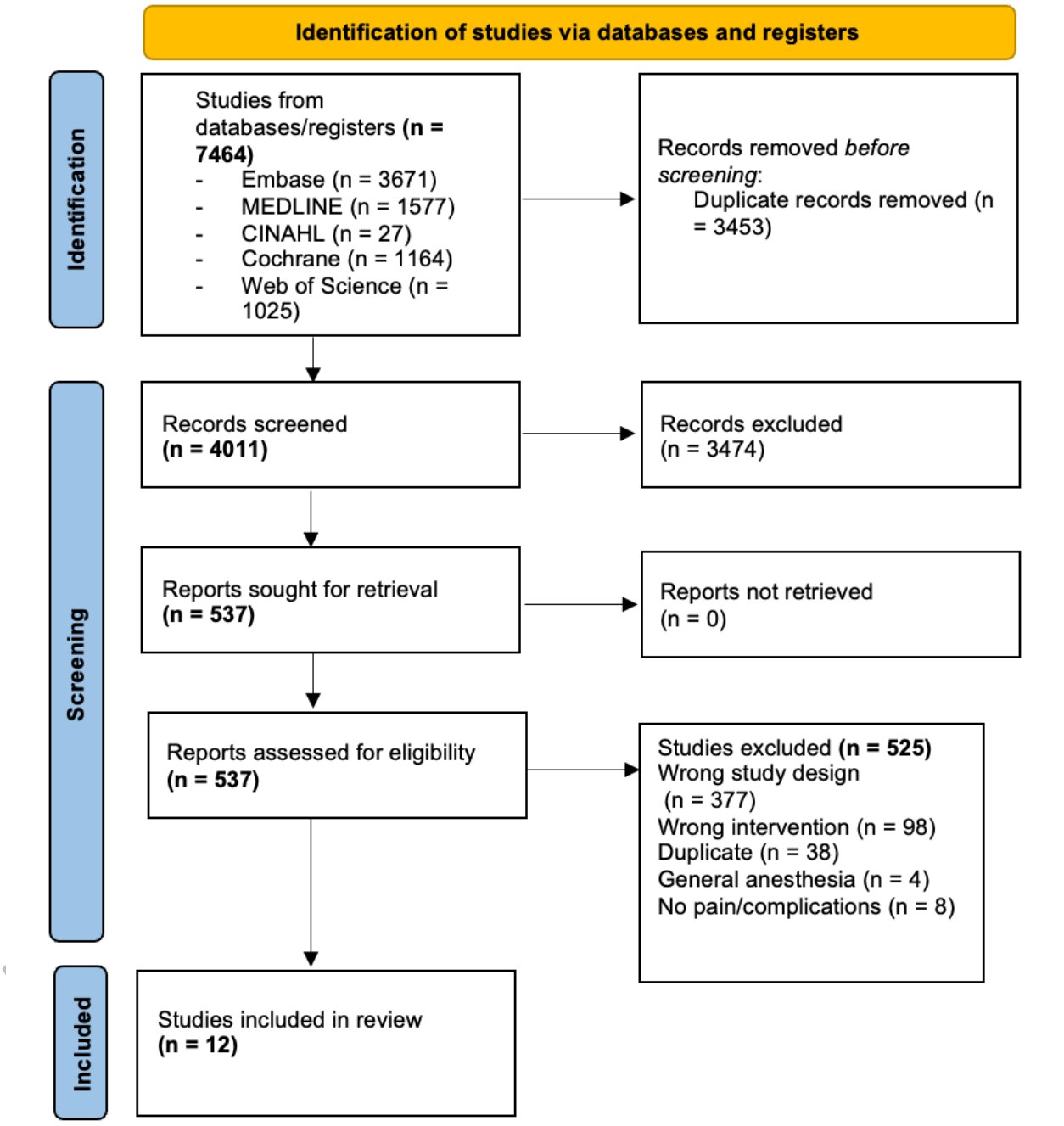
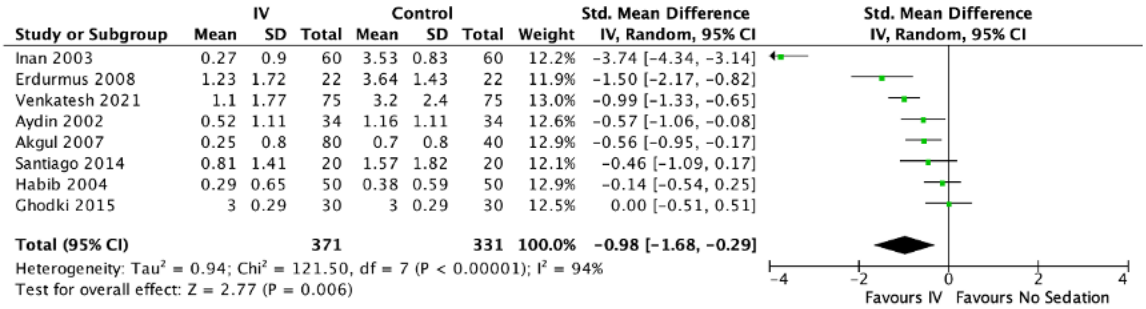


Figure 2: Pain – A) IV versus No sedation and b) IV versus Oral Sedation

A



B

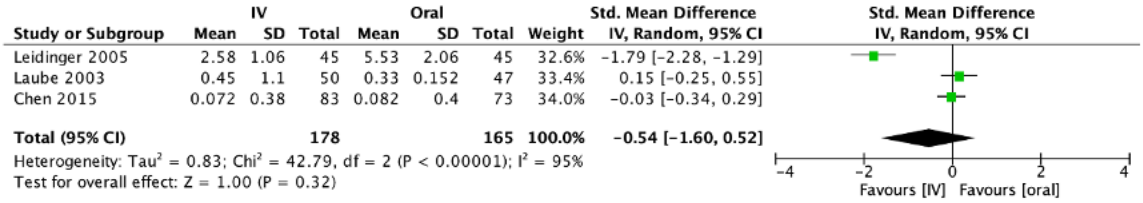
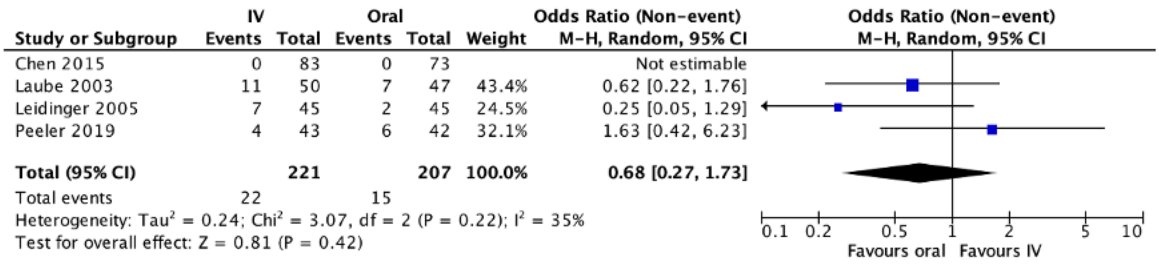


Figure 3: A) Total Complications – IV versus Oral Sedation and B) Ocular Complications – IV versus Oral Sedation

A



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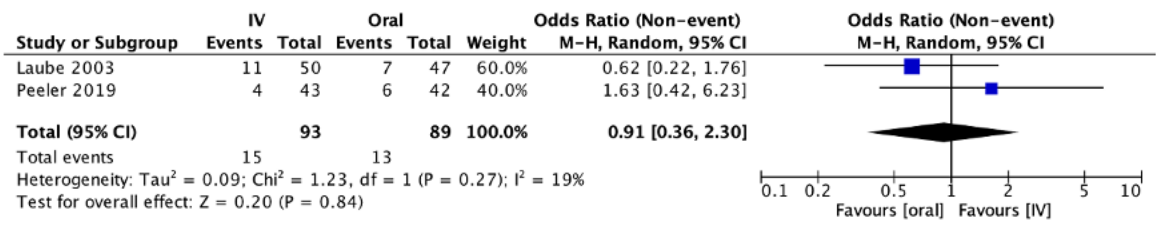

Table 2: Intervention Characteristics of Included Studies

Study	IV Sedation Group	Non-IV Sedation Group	Dilation (both groups)	Topical Anesthetic (both groups)	Ocular injection (both groups)
Akgul 2007[6]	IV fentanyl 0.7 µg/kg PCA OR remifentanil 0.3 µg/kg PCA (Two intervention groups combined for a pairwise comparison)	IV saline	Cyclopentolate hydrochloride 1%, tropicamide 1%, phenylephrine hydrochloride 10%	Oxybuprocaine hydrochloride 0.4% drops, a sponge soaked with lidocaine 2% and bupivacaine 0.5%	None
Aydin 2002[7]	IV fentanyl 0.7 µg/kg	IV balanced salt solution	Cyclopentolate hydrochloride 1%, tropicamide 1%, phenylephrine hydrochloride 10%	Oxybuprocaine hydrochloride 0.4%, sponge soaked with lidocaine 2% and bupivacaine 0.5%	None
Chen 2015[8]	IV midazolam 1.0 mg	Oral diazepam 5.0 mg	Not reported	Tetracaine hydrochloride 1%, lidocaine hydrochloride 2% gel	Intracameral lidocaine hydrochloride 1.0%
Erdurmus 2008[9]	IV dexmedetomidine 1 µg/kg	IV saline	Diclofenac sodium 0.1%, phenylephrine hydrochloride 2.5%,	Proparacaine 0.5% drops	None

			cyclopentolate 1%		
Ghodki 2015[10]	IV dexmedetomidine 1 µg/kg	IV saline	Not reported	Paracaine 0.5%	None
Habib 2004[11]	IV midazolam 0.015 mg/kg	IV cannula inserted	Not reported	Proxymetacaine hydrochloride 0.5% drops	Intracameral 1 to 2 mL preservative free lidocaine 1%
Inan 2003[12]	IV fentanyl 2 µg/kg	IV of 500 cc electrolyte solution	Phenylephrine hydrochloride 2.5%, tropicamide 0.5%, cyclopentolate hydrochloride 1%	Proparacaine hydrochloride	Retrobulbar block mixture of 1 mL (5 mg/mL) bupivacaine and 1.5 mL (20 mg/mL) of lidocaine 2%
Laube 2003[13]	IV midazolam 1 mg	Oral clorazepate dipotassium 10mg	Not reported	Not reported	Retrobulbar block of 6 to 8mL mepivacaine hydrochloride 2% with 75 IE hyaluronidase
Leidinger 2005[14]	IV remifentanil 0.3 µg/kg	IV saline, Oral clorazepate dipotassium	Not reported	Not reported	Retrobulbar block
Peeler 2019[15]	IV midazolam (1.0 mg/ml)	Oral Triazolam	Not reported	Not reported	None

		(BMI below 35kg/m^2: 0.125 mg and BMI above 35kg/m^2: 0.25 mg)			
Santiago 2014[16]	IV clonidine 4µg/kg I	IV Saline	phenylephrine 10%, tropicamide 1%	lidocaine 2% gel	None
Venkatesh 2021[17]	IV midazolam (0.015 mg/kg)	IV Saline	tropicamide 1%	proparacaine hydrochloride 0.5% and ketorolac tromethamine	None

Table 4- Risk of Bias

Study ID	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting	Other Bias
Akgul 2007[6]	🟢	🔴	🟢	🟢	🟢	🟢	🟢
Aydin 2002[7]	🟢	🔴	🟢	🟢	🟢	🟢	🟢
Chen 2015[8]	🟢	🔴	🔴	🟢	🟢	🟢	🟢
Erdurmus 2008[9]	🟡	🟡	🟢	🟢	🟢	🟢	🟢
Ghodki 2015[10]	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Habib 2004[11]	🟢	🟢	🟢	🟢	🟢	🟢	🟢
IInan 2003[12]	🟡	🟡	🔴	🟡	🟢	🟢	🟢
Laube 2003[13]	🔴	🔴	🔴	🟡	🟢	🟢	🟢
Leidinger 2005[14]	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Peeler 2019[15]	🟡	🟢	🟢	🟢	🟢	🟢	🟢
Santiago 2014[16]	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Venkatesh 2021[17]	🟢	🟢	🟢	🟢	🟢	🟢	🟢