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Systematic Review / Meta-analysis

Review of clinical evidence of caudal block for postoperative analgesia in children with ketamine added local anesthetics

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ABSTRACT

Background: Adding ketamine to local anesthetics used for caudal block in children is an emerging clinical practice. This review aims to resolve controversies related to this adjuvant for a caudal block in children who underwent sub-umbilical surgeries.

Methods: Between January 2010 and November 2021, PubMed, Cochrane Review, and Google Scholar were searched for a caudal block with ketamine added local anesthetics for children. After screening for eligibility and removing duplicates, 38,187 articles were found, 13 reviewed.

Discussion: Despite adding ketamine to local anesthetics used for a caudal block, it is a recent technique practiced worldwide. Ketamine showed equi-efficacious as other adjuvants used for the caudal block to control post-operative pain in children.

Conclusion: Ketamine with a 0.5 mg/kg dose is safe and effective to manage postoperative children's pain when used as an adjuvant to local anesthetics used for caudal block.

1. Introduction

Caudal block is a widely used technique of providing analgesia by depositing local anesthetics in the epidural space through sacral hiatus, which is preferable for postoperative pain management in children, especially those who have had procedures below the umbilicus [1,2]. Caudal block is being practiced as the first line for pain control above other options, including peripheral nerve blocks, because of its technical simplicity, high success rate (98%–100%), and ability to deliver reliable analgesia [1,3,4]. Pediatrics are at risk for a respiratory adverse event; the most significant benefit of a caudal block is reducing the post-operative opioid requirement that exacerbates postoperative respiratory depression [4].

In recent years, caudal block procedures have become increasingly popular, adding local anesthetics with adjuvants such as fentanyl, dexamethasone, neostigmine, ketamine, morphine, magnesium sulfate, clonidine, and dexmedetomidine being practiced [2,5]. The use of these adjuvants will prolong the duration of analgesia, resulting in a longer duration of first analgesic demand and a reduction in opioid administration [2,4–6].

Ketamine has demonstrated to exhibit analgesic effects through epidural, caudal, and spinal routes through a variety of mechanisms including N-methyl-D-aspartate (NMDA), cholinergic, adrenergic, and 5-hydroxytryptamine receptors or 5-HT receptors, as well as adrenergic and noradrenergic receptors. Because of the evidence of neurotoxicity associated with ketamine preservatives, preservative-free formulations of ketamine are suggested for neuraxial administration [6–8].

When used with a local anesthetic, ketamine can give long-lasting postoperative analgesia with minimal side effects; caudal ketamine has a demonstrable benefit, although there are still questions [6,8,9].

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For postoperative analgesia in children, this review aims to address the controversy surrounding ketamine-added caudal block by presenting the currently available shreds of evidence.

2. Methods

2.1. Protocol and registration

Under the unique identification number (UIN): reviewregistry1273, this study's protocol has been added to the registry of systematic reviews. In contrast to other studies, the systematic review study did not require ethical approval from the ethical review committee. This systematic review has been reported in line with the Preferred Reporting item for Systematic Review and Meta-analysis (PRISMA) [10] and Assessing the methodological quality of systematic reviews (AMSTAR 2) criteria [11].

2.2. Eligibility criteria

Randomized or non-randomized controlled trials published between January 2010 and November 2021 that recruited pediatric patients in the 2–16 age group with operations below the umbilicus were eligible for inclusion. The studies we looked at did not include nonhuman studies and case reports.

2.3. Data source and searching process

Following the guidelines in Fig. 1, a systematic review of the literature was undertaken using the PubMed, Cochrane Review, and Google Scholar databases, with no language or publication type limitations. Free-text keyword searches were conducted using keywords and the Boolean operators "AND" and "OR," as well as the search terms themselves. In this case, there were the following combinations: (caudal block) OR (caudal)) OR (caudal epidural)) OR (caudal epidural block)) AND (Ketamine) OR (ketamine added local anesthetic) OR (ketamine adjuvant).

After reviewing the retrieved citations, abstracts were read to recuperate the clinical investigations of a ketamine-added caudal block. Additionally, the investigator double-checked references to confirm that no publications were missing from the database. Because of this, reference lists of all articles were verified twice, once using the entire text then using the title with the abstract of the article.

2.4. Data collection procedure

When two reviewers (Amanuel S, Endeshaw and Abdi T, Tesema) looked at the data by extracting, two reviewers (Esubalew M, Aligaz and Befekadu A, Mekonnen) looked at the full-text article to make sure it was complete. Finally, differing viewpoints were discussed and, if required, settled by a senior researcher (Assistant professor Fantahun Tarekegn Kumie).

3. Discussion

3.1. Clinical use and adverse effects

Local anesthetics alone are frequently utilized throughout the world during caudal blocks to manage pediatric postoperative pain [1,4,12]. However, it is recently becoming popular and indicated to add adjuvants including ketamine to local anesthetics during caudal blocks,

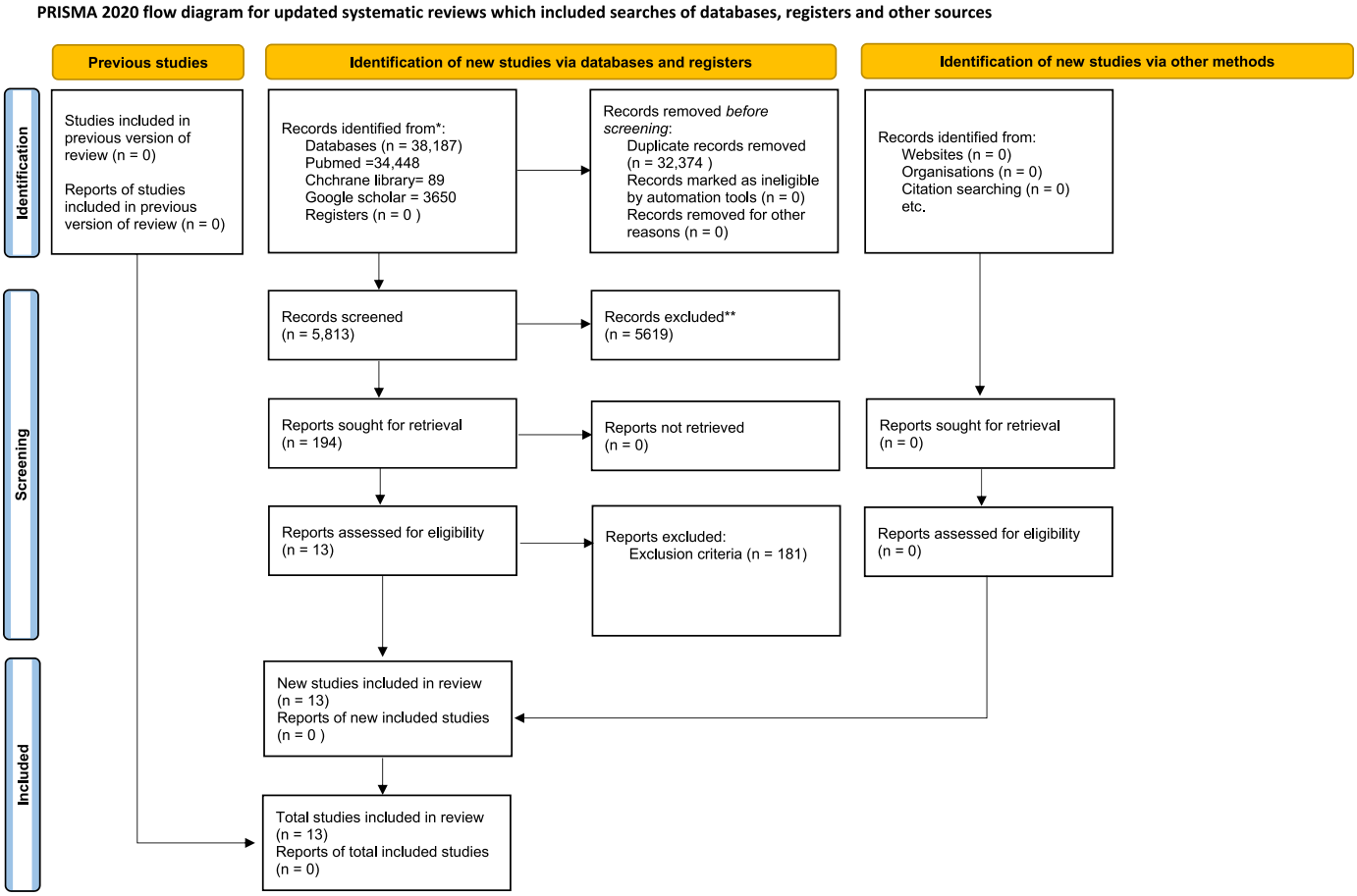

Fig. 1. The search strategy with the form of preferred reporting items for systematic review and meta-analysis (PRISMA) flow diagram.

significantly to prolong analgesia and reduce the need for systemic analgesics commonly for those children undergoing sub-umbilical procedures, most commonly urologic, hernia, lower abdominal and lower limb orthopedic surgeries [4,7,8].

After the administration of caudal block with ketamine added local anesthetics, fewer adverse effects occurred but were very infrequent. Although most studies did not detect a significant difference in unwanted effects between children who had a caudal block with and without ketamine, nausea, vomiting, and extended sedation are prevalent but likely to be clinically insignificant [4,8]. Other than allergy to ketamine, no specific contraindication was identified to use ketamine added local anesthetics in a caudal block for children.

3.2. Safety

The use of ketamine added local anesthetics in a caudal block has demonstrated a good safety profile despite neurotoxicity being the primary safety concern following this technique in children [8,9]. However, there has been no evidence of this unintended side effect in clinical studies using ketamine-containing local anesthetics in a caudal block.

3.3. Dosage

The dose of ketamine (preservative-free), which is routinely used and with no negative effects, for caudal block in adjuvant to local anesthetics is 0.5–1 mg/kg [6,13] given to 0.5 up to 1.25 ml/kg (based on the dermatome level intended to be blocked) [1,14], but it has not yet been proven whether different dosages or repeated doses would have an impact and need to be looked into more.

3.4. Effect of ketamine added local anesthetics in a caudal block for children

3.4.1. Ketamine added local anesthetics versus local anesthetics alone

According to almost all randomized clinical trials, the primary impact of mixing ketamine with bupivacaine/levobupivacaine for a caudal block is that the analgesia produced is prolonged compared to local anesthetics are administered alone. Studies have also demonstrated that ketamine-added local anesthetics caudal block effectively reduces postoperative analgesic intake, particularly opioid consumption [15–18]. Only one retrospective chart analysis study found no benefit to the extended analgesia caused by mixing ketamine with levobupivacaine for caudal block compared to the control group [13].

It has been shown that the use of ketamine in the caudal block resulted in prolonged analgesia and reduced postoperative analgesic demand, but that the minimum local anesthetic concentration (MLAC) of ropivacaine is necessary for intraoperative pain control does not change [19].

3.4.2. Ketamine added local anesthetics versus other adjuvants added local anesthetics

Compared to other adjuvants, such as dexamethasone, fentanyl, morphine, and adrenaline, adding ketamine to local anesthetics for a caudal block controlling childrens' postoperative pain is a recent developing trend. Adding neostigmine, midazolam, and ketamine to bupivacaine alone for caudal block in children results in decreased quantity of rescue analgesia. Increased time to initial rescue analgesic administration compared to pure bupivacaine at the same time, there were no significant differences in the number of complications that happened in the first 24 hours of the postoperative period between the four study groups [20]. Ketamine showed to be superior in prolonging the duration of analgesia and blunting neuroendocrine stress response without side effects than fentanyl when added to bupivacaine/ropivacaine for caudal block in children who underwent sub-umbilical surgery [21,22]. Extension of analgesia duration from ketamine added local anesthetics in a caudal block is also superior to magnesium sulfate added local anesthetics [23].

Dexmedetomidine provides a more extended duration of analgesia than ketamine with fewer side effects (nausea and vomiting) when added to levobupivacaine/bupivacaine during caudal block for postoperative pain management in children [24]. Compared to adjunct clonidine in a caudal block, evidence shows contradictory results in analgesia's duration provided by ketamine but no difference in complications [13,22,25,26].

3.5. Evidence

Pieces of evidence dictate that the conjunction use of ketamine with local anesthetics for caudal block in children is safe and has very few side effects. According to findings, preservative-free ketamine at a dosage of 0.5 mg/kg used in combination with local anesthetics used for caudal block in the treatment of postsurgical pain in pediatric patients has been found to be equally effective with the majority of adjuvants [20,26].

When compared to other adjuvants, such as dextrometomidine and clonidine, ketamine has the benefit of being readily available in low-resource situations, which makes it a good alternative as an adjuvant for caudal block.

3.6. Future directions

Ketamine is a good alternative to be an adjuvant to caudal block in pediatric postoperative pain treatment, but fentanyl, neostigmine, and dexamethasone are being clinically practiced in Ethiopia and other resource-poor areas [27–29]. In many nations, the rationale for the underuse of ketamine for a caudal block concerns neurotoxicity, dose, and uncertainty associated with the child's age, among other factors. Further studies should be done to overcome these issues despite the current evidence not demonstrating neurotoxicity as a side effect.

There are a few limitations to this study that should be highlighted. Firstly, our review did not evaluate publication bias. Also, due to the authors' differing study goals, numerous analytic parameters had a small sample size.

4. Conclusion

This review discussed the clinical use, dosage, and effect of ketamine when used as an adjuvant for a pediatric caudal block for pain control after infra umbilical surgeries. Despite unanswered questions exist, ketamine can be safely used as an adjuvant for caudal block in pediatrics for postoperative pain management to extend analgesic duration provided by local anesthetics alone with rare side effects. This adjuvant also decreases postoperative opioid consumption by prolonging the first analgesic requirement time.

Ethical approval

Because it is a systematic review, ethical approval is not applicable.

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We did not receive funding from any source.

Author contribution

All authors contributed equally on conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article or revising data content, and approval of the final the version.

Consent

Not applicable.

Registration of Research Studies

Name of the registry: Researchregistry.com.

Unique Identifying number or registration ID: reviewregistry1273.

Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-the-registry#registryofsystematicreviewsmeta-analyses/

Guarantor

Amanuel Sisay Endeshaw: Corresponding author.

Availability of data and materials

No additional data are required; all information was presented in the main manuscript.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103480.

References

[1] Kenneth D. Candido ART, Alon P. Winnie. Caudal Anesthesia [Available from: https://www.nysora.com/techniques/neuraxial-and-perineuraxial-techniques/caudal-anesthesia/.
[2] C.Y. Keyser, Caudal blockade for children undergoing infra-abdominal surgery, AORN J. 100 (3) (2014) 306–322.
[3] S.G. Beyaz, O. Tokgöz, A. Tüfek, Caudal epidural block in children and infants: retrospective analysis of 2088 cases, Ann. Saudi Med. 31 (5) (2011) 494–497.
[4] M. Wiegele, P. Marhofer, P.-A. Lönnqvist, Caudal epidural blocks in paediatric patients: a review and practical considerations, Br. J. Anaesth. 122 (4) (2019) 509–517.
[5] M. Jöhr, T.M. Berger, Caudal blocks, Paediatr. Anaesth. 22 (1) (2011) 44–50.
[6] M. Lundblad, P.-A. Lönnqvist, Adjunct analgesic drugs to local anaesthetics for neuroaxial blocks in children, Curr. Opin. Anesthesiol. 29 (5) (2016) 626–631.
[7] A. Swain, D.S. Nag, S. Sahu, D.P. Samaddar, Adjuvants to local anesthetics: current understanding and future trends, World J. Clin. Cases 5 (8) (2017) 307.
[8] A. Schnabel, D. Poepping, P. Kranke, P. Zahn, E. Pogatzki-Zahn, Efficacy and adverse effects of ketamine as an additive for paediatric caudal anaesthesia: a quantitative systematic review of randomized controlled trials, Br. J. Anaesth. 107 (4) (2011) 601–611.
[9] P.-A. Lönnqvist, S. Walker, Ketamine as an Adjunct to Caudal Block in Neonates and Infants: Is it Time to Re-evaluate? Oxford University Press, 2012.
[10] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, et al., The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, Int. J. Surg. 88 (2021) 105906.
[11] B.J. Shea, B.C. Reeves, G. Wells, M. Thuku, C. Hamel, J. Moran, et al., AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both, BMJ 358 (2017) j4008.
[12] E. Pincus, Regional anesthesia: an Overview, AORN J. 110 (3) (2019) 263–272.
[13] K. Davies, G. Wilson, T. Engelhardt, Caudal additives do not improve the analgesia afforded by levobupivacaine after hypospadias repair, Anesthesiol. Pain Med. 1 (3) (2012) 174.
[14] S. Suresh, C. Ecoffey, A. Bosenberg, P.-A. Lonnqvist, G.S. De Oliveira, O. de Leon Casasola, et al., The European Society of regional anaesthesia and pain Therapy/American Society of regional anesthesia and pain medicine recommendations on local anesthetics and adjuvants dosage in pediatric regional anesthesia, Reg. Anesth. Pain Med. 43 (2) (2018) 211–216.
[15] S.P. Aliena, C. Lini, J.J. Chirayath, Comparison of postoperative analgesic effect of caudal bupivacaine with and without ketamine in Pediatric subumbilical surgeries, J. Anaesthesiol. Clin. Pharmacol. 34 (3) (2018) 324.
[16] D. Kaur, S. Anand, Comparison between caudal bupivacaine and bupivacaine with ketamine for postoperative analgesia in children: a prospective randomized clinical study, Anesth. Essays Res. 10 (3) (2016) 488.
[17] M. Nasir, A. Fayyaz, M. Ahmad, Caudal bupivacaine alone versus bupivacaine with ketamine to compare postoperative analgesia, Med. Forum 29 (10) (2018) 105–109.
[18] R. Ödeş, Ö.L. Erhan, M. Demirci, H. Göksu, Effects of ketamine added to ropivacaine in pediatric caudal block, Agri 22 (2) (2010) 53–60.
[19] H.-Z. Wang, L.-Y. Wang, H.-H. Liang, Y.-T. Fan, X.-R. Song, Y.-J. She, Effect of caudal ketamine on minimum local anesthetic concentration of ropivacaine in children: a prospective randomized trial, BMC Anesthesiol. 20 (2020) 1–8.
[20] M. Shirmohammadie, A.E. Soltani, S. Arbabi, K. Nasseri, A randomized-controlled, double-blind study to evaluate the efficacy of caudal midazolam, ketamine and neostigmine as adjuvants to bupivacaine on postoperative analgesic in children undergoing lower abdominal surgery, Acta Biomed.: Atenei Parmensis 89 (4) (2019) 513–518.
[21] S. Ahuja, S. Yadav, N. Joshi, S. Chaudhary, S. Madhu, Efficacy of caudal fentanyl and ketamine on postoperative pain and neuroendocrine stress response in children undergoing infraumbilical and perineal surgery: a pilot study, J. Anaesthesiol. Clin. Pharmacol. 31 (1) (2015) 104.
[22] J. Singh, D. Hamal, A. Karmacharya, Comparision of caudal ropivacaine, ropivacaine plus ketamine and ropivacaine plus fentanyl administration for postoperative analgesia in children, J. Nepal Paediatr. Soc. 32 (3) (2012) 210–215.
[23] W.S. Farrag, A.S. Ibrahim, M.G. Mostafa, A. Kurkar, A.A. Elderwy, Ketamine versus magnesium sulfate with caudal bupivacaine block in pediatric inguinoscrotal surgery: a prospective randomized observer-blinded study, Urol. Ann. 7 (3) (2015) 325.
[24] G.K. Ram, P.K. Dubey, P. Akhileshwar, A. Ranjan, Dexmedetomidine and ketamine as an adjuvant to levobupivacaine for pediatric caudal analgesia: a randomized, controlled study, Anesth. Essays Res. 14 (2) (2020) 253.
[25] J. Singh, R. Shah, N. Vaidya, P. Mahato, S. Shrestha, B. Shrestha, Comparison of ketamine, fentanyl and clonidine as an adjuvant during bupivacaine caudal anaesthesia in paediatric patients, Kathmandu Univ. Med. J. 10 (3) (2012) 25–29.
[26] O.D. Ribeiro, LCd Abreu, V.E. Valenti, J.R. Cisternas, D. Saletti, C.J. Lima, et al., Comparison between S-ketamine and clonidine in caudal analgesia, Afr. J. Pharm. Pharmacol. (2011) 2598–2604.
[27] G. Ataro, M. Bernard, Effectiveness of caudal epidural block using bupivacaine with neostgmine for pediatric lower extremity orthopedic surgery in cure Ethiopia Children's Hospital, J. Anesth. Clin. Res. 5 (12) (2014) 479.
[28] A. Gashaw, G. Dendir, B. Balcha, Z. Aweke, Postoperative analgesic efficacy of caudal dexamethasone added to bupivacaine vs bupivacaine alone for pediatric elective infra-umbilical surgery at (Tikur Anbesa Specialized Hospital), Ethiopia: prospective cohort study, Int. J. Surg. Open 24 (2020) 170–176.
[29] O. Aghadavoudi, A. Shafa, Z. Nowrozi, Comparison of adding neostigmine and fentanyl to bupivacaine in caudal analgesia in pediatric inguinal herniorrhaphy, J. Cell. Mol. Anesth. 2 (4) (2017) 165–170.