DOI: 10.7860/JCDR/2022/56478.16687

Review Article

Anaesthesia Section

Ropivacaine: A Review on the Pharmacological Features, Therapeutic Efficacy and Side-effects When used for Caudal Epidural Analgesia

SHILPA SHANKAR[1], VIVEK CHAKOLE[2]

ABSTRACT

Inadequate postoperative pain treatment can lead to clinical and psychological changes, as well as increased morbidity, mortality, and financial burden, all of which can influence quality of life. A review of the pharmacological characteristics, therapeutic efficacy in delivering postoperative analgesia, and side-effects of ropivacaine is presented in this article. Motor blockade is an unwanted effect during the postoperative period. The fear of side-effects and haemodynamic instability caused by the most of the analgesic drugs are the challenges faced in providing effective postoperative analgesia in children. Ropivacaine has lesser cardiotoxic effects, lesser motor blockade and minimal side-effects as compared to bupivacaine. These properties make it a promising drug for paediatric caudal analgesia and forms a cost-effective method by decreasing the requirement of systemic analgesics, morbidity and improving the life quality postoperatively.

Keywords: Haemodynamic instability, Motor blockade, Postoperative pain

INTRODUCTION

The definition of pain is that it is an unpleasant sensory and emotional subjective sensation associated with definite or possible tissue damage or characterised in terms of such damage that can only be felt, not expressed. Epidural analgesia using local anesthetic drugs provides postoperative pain relief which is much superior in comparison with systemic drugs [1].

ROPIVACAINE

Pharmacological Features

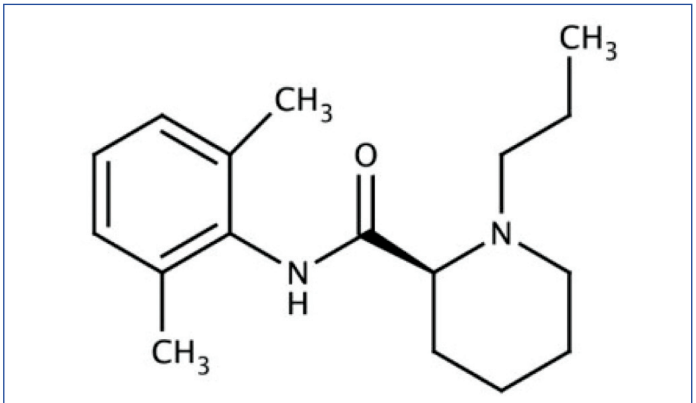
Mode of action: The drug blocks generation of action potential by blocking the sodium and potassium ion channels in the dorsal horn of spinal cord. Calcium ion channel inhibition in the spinal cord causes electrical input from nociceptive afferent neurons to be blocked, resulting in the powerful analgesic activity seen with centrally given local anesthetics. Also, the drug blocks the release of substance P and other neurotransmitters such as glutamate, substance P, Prostaglandins, Calcitonin Generated Peptide (CGRP), neurokinin-1 and -2 (NK1, NK2) at the presynaptic level. The production and transmission of pain signals are thereby inhibited [2-4].

Chemical properties: Ropivacaine is a pipecoloxylidide derivative and it belongs to amino amide type. It is a 99.5 percent chiral pure S enantiomer produced via alkylation of the S enantiomer of di-benzoyl-tartaric acid. There are 0.1 percent, 0.2 percent, 0.5 percent, and 0.75 percent preparations available [3,4]. S-1-propyl-2,6-pipecoloxylidide hydrochloride monohydrate is the chemical name. A propyl group replaces the butyl group on the aromatic ring of bupivacaine. Ropivacaine has a molecular weight of 274 kDa, a pka of 8.07, a pH of 7.4. The plasma half-life is 111 minutes, and the clearance rate is 10.3 litres per minute [5] [Table/Fig-1].

Ropivacaine inhibits sodium channels and hence serves as a sedative. It blocks the transmission of sodium ions as well as potassium ions through the channel. As a result, it inhibits the creation and transmission of nerve impulses [6].

Pharmacokinetics

Absorption: The plasma concentration of ropivacaine is affected by a number of factors such as route, dose and concentration of drug, vascularity of the site and haemodynamic condition of the patient.



[Table/Fig-1]: Chemical structure of ropivacaine [5].

It has biphasic elimination. The sluggish absorption of ropivacaine from the spinal area is the rate limiting factor. As a result of the epidural route, ropivacaine has a longer duration of effect [7].

Distribution: It binds mostly to alpha-1-acid glycoproteins. This glycoprotein is increased in conditions of stress, surgery causing increase in the bound form of drug [7].

Metabolism: Liver is the site of metabolism. Aromatic hydroxylation, which involves Cytochrome P4501A is used for aromatic hydroxylation of the drug and form the metabolites (hydroxy and dealkylated forms) which are excreted in urine. These are created in large quantities during continuous epidural infusion [7].

Elimination by urine: The kidneys eliminate approximately 86 percent of the whole medication. The 387 ml/min is the overall clearance rate. After an intravenous route, the half-life is roughly 1.8 hours, and after an epidural route, it's around 4.2 hours [7].

Pharmacodynamics

The characteristic of blockage generated by ropivacaine is determined on the drug's concentration. It inhibits both A and C fibers even at low concentrations. Because ropivacaine has a lower lipid solubility than bupivacaine, it penetrates the myelin layer less effectively. Hence, C fibers are blocked preferentially as compared to Aδ fibers. Toxicity is manifested by initial nervous system symptoms such as restlessness, tremor, seizure and later causes medullary depression and coma [8]. Its effects on various body systems which includes:

Cardiovascular System (CVS) and Central Nervous System (CNS) effects: Because of its less lipophilic nature and being a pure S enantiomer, ropivacaine has higher threshold for CVS and CNS toxicity. Only at high plasma concentrations CVS and CNS toxic manifestations will appear. They are primarily caused by sympathetic fiber blockade. As a result, there is a decrease in venous return and a decrease in heart rate, resulting in hypotension [8].

Respiratory system effects: Normal doses have no impact, but greater amounts cause toxicity, which causes respiratory depression as well as a medullary depressive effect [8].

Other effects: At 0.375% and 0.188% concentrations, it hinders platelet aggregation. It has antibacterial growth inhibitory property against *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Escherichia coli* [8].

Indications: Ropivacaine is utilised for subarachnoid, epidural, caudal, peripheral nerve blocks and for local infiltration in surgical procedures and in labor analgesia [9].

Contraindications: The drug is contraindicated in those with allergic to local anesthetic agents, sepsis, regional infections, unstable haemodynamics. Also, it should not be used for Bier's block and paracervical block [9].

Side-effects [9]

Excessive plasma levels caused by overdosing, unintentional intravascular injection, or sluggish metabolic breakdown are all causes of ropivacaine side-effects. The mean dosages of total and free plasma concentrations at which deleterious effects manifest are about 4.3 and 0.6 microgram/mL, respectively. The organ wise details of side-effects are discussed below:

Cardiovascular effects: bradycardia, hypotension, vasovagal response, syncope, and arrhythmias.

Neurological effects: involuntary motor activities, slow movements, neuropathy, vertigo, tremors and coma.

Digestive system: emesis, incontinence, and tenesmus

Hearing and vestibular: tinnitus, deafness

Liver: jaundice

Musculoskeletal system: muscle cramps

Psychiatric effects: confusion, anxiousness, amnesia, delusions, hallucination, decreased sleep and nightmares

Skin: urticaria

Genitourinary effects: incontinence of urine.

Blood vessels and haematological effects: Deep vein thrombosis, phlebitis, and pulmonary embolism.

The side-effects caused as a result of drug interactions are mentioned as follows:

- Used with caution in combination with other structurally similar amide type Local Anaesthetic (LA) drugs as it can cause additive toxic effects.
- Usage of fluvoxamine like cytochrome P4501A2 inhibitor drug in combination with ropivacaine, can lead to increased plasma concentration of ropivacaine.
- Interaction and competitive inhibition of drugs like theophylline and imipramine metabolized by CYP1A2 is also seen [10].

Therapeutic Efficacy: Administration, Route and Dosages

Ropivacaine is available in concentrations of 0.2 percent, 0.5 percent, 0.75 percent, and 1 percent in ampules of isobaric solution [Table/Fig-2] [11-14].

Indication	Concentration (%)	Volume	Dose
A. Adults			
Lumbar epidural [LSCS]	0.75	15-25 mL	113-188 mg
Lumbar epidural [other surgery]	1	15-20 mL	150-200 mg
Thoracic (single block for postoperative analgesia)	0.75	5-15 mL	38-113 mg
Intrathecal administration	0.5	3-4 mL	15-20 mg
Peripheral nerve block	0.75	10-40 mL	75-300 mg
Field block	0.75	1-30 mL	7.5-225 mg
Lumbar epidural continuous infusion	0.2	6-10 mL/hour	12-20 mg/hour
Thoracic epidural continuous infusion	0.2	6-14 mL/hour	12-28 mg/hour
Peripheral nerve block continuous infusion	0.2	5-10 mL/hour	10-20 mg/hour
Field block	0.2	1-100 mL	2-200 mg
Intra-articular injection	0.75	20 mL	150 mg
Lumbar epidural for labour analgesia			
Bolus	0.2	10-20 mL	20-40 mg
Intermittent top-ups	0.2	10-15 mL	20-30 mg
Continuous infusion	0.2	6-14 mL/hour	12-28 mg/hour
B. Children			
Caudal epidural (below T12)	0.2	1 mL/kg	2 mg/kg
Peripheral nerve block (ilio-inguinal block)	0.5	0.6 mL/kg	3 mg/kg

[Table/Fig-2]: Different route and doses of ropivacaine as data collected and inference drawn [11-14].

Literature Search and Review

This review article was prepared after a thorough study of the literature from 1990 to 2021 using data search engines such as 'Scopus', 'PubMed', 'Web of Science', and 'Google Scholar'. Focus was made on the articles using ropivacaine for caudal epidural in the paediatric age group. The articles using ropivacaine as the study drug but not for caudal epidural and study population other than paediatric group were not included in the review. Preference was given to the articles comparing ropivacaine with another local anesthetic drug or studies using different concentrations of ropivacaine [Table/Fig-3] [15-36].

DISCUSSION

Ropivacaine is Food and Drug Administration (FDA) approved drug for surgical anesthesia and acute pain management. It can be used in surgeries for epidural block, major nerve blocks and local infiltration, for caudal or epidural (continuous infusion or intermittent bolus) postoperative analgesia and for labour pain control, a concentration of 0.05 to 0.1% ropivacine provides only sensory block, 0.3% can be used for profound sensory and slight motor block and 1% for both profound sensory and motor block. Ropiovacaine has better safety profile than bupivacaine. Its lesser motor blockade and lesser potency as compared to bupivacaine limits its use in spinal anesthesia [37]. Li K et al., reported the use of ropivacaine as an adjuvant to patient controlled analgesia for wound infiltration in transforaminal lumbar interbody fusion. It was concluded that wound infiltration with ropivacaine effectively reduced opioid consumption and the side-effects of opioids [38]. Pere PJ et al., reported that pharmacokinetics of ropivacaine is not altered by impaired renal function/renal failure [39]. Van de Vossenberg G et al., reported a paediatric case in which long term high dose ropivacaine was used for continuous epidural administration without any severe side-effects or complications [40]. However, further studies need to be conducted in larger populations to evaluate its safety profile in immunocompromised and in paediatric continuous epidural administraion.

Ropivacaine selectively blocks A delta and C fibers involved in pain transmission to a great extent than A beta fibers involved in the motor function. Ropivacaine is also less lipophilic. Therefore, it is less

Author's name and year of study	Groups and drugs studied	Outcome	Other findings
Ivani G et al., [15]; 1991	Two groups- 0.2% ropivacaine group and 0.25% bupivacaine group	Almost equal efficacy	Nil
Da Conceicao MJ and Coelho L [16]; 1998	Two groups- 0.375% ropivacaine group and 0.375% bupivacaine group	Less motor blockade in ropivacaine group. Sensory blockade was similar in both the groups	Nil
Da Conceicao MJ et al., [17]; 1999	Two groups- 0.25% ropivacaine group and 0.25% bupivacaine group	Almost identical sensory and motor blockade in both the groups	Slightly longer duration of analgesia seen in ropivacaine group but statistically non significant
Koinig H et al., [18]; 1999	Three groups- 0.25% and 0.5% ropivacaine in 1st and 2nd groups and 0.25% bupivacaine in the 3rd group	Longer duration of analgesia seen in 0.5% ropivacaine group.	Children tolerate ropivacaine effectively
Ivani G et al., [19]; 2000	Two groups- 0.2% ropivacaine 1st group and 0.1% ropivacaine+clonidine 2 mcg/kg in 2nd group	Duration of analgesia longer in the clonidine adjuvant group.	Nil
De Negri P et al., [20]; 2001	Three groups- 0.2% ropivacaine, 0.2% ropivacaine with clonidine 2 mcg/kg and 2 mg/kg 0.2% ropivacaine with ketamine 0.5 mg/kg	Superior analgesic effect observed when ropivacaine is combined with ketamine	No side-effects/motor blockade/ sedation
Ray M et al., [21]; 2003	Two groups- 0.25% bupivacaine group and 0.25% ropivacaine group	Lesser motor blockade by ropivacaine group	No significant difference in quality and duration of postoperative analgesia
Turan A et al., [22]; 2003	Two groups- 0.2% ropivacaine alone group and 0.2% ropivacaine with 2mcg/kg neostigmine	Better postoperative analgesia in adjuvant group	nil
Gunes Y et al., [23]; 2003	Three groups- 0.4% ropivacaine (2 mg/kg) group and 0.2% ropivacaine (1 mg/kg) with 0.25 mg/kg ketamine group and 0.2% ropivacaine (1 mg/kg) with 1 mg/kg tramadol group	Acceptable analgesia in all the three groups. Prolonged duration of analgesia seen in the group which used tramadol as adjuvant.	Nausea and vomiting were more common in the adjuvant groups.
Akbas M et al., [24]; 2005	Three groups- 0.25% ropivacaine alone group, 0.25% ropivacaine with 2 mcg/kg clonidine group and 0.25% ropivacaine with ketamine 0.5 mg/kg group	Adjuvant groups showed prolonged duration of analgesia	Nil
Kawaraguchi Y et al., [25]; 2006	Two groups- 0.2% ropivacaine with fentanyl 1 mcg/kg group and 0.2% ropivacaine with 1 mL/kg saline	Similar analgesic efficacy in both the groups	Nil
Bajwa SJ et al., [26]; 2010	Two groups- 0.25% ropivacaine group and 0.25% ropivacaine with 2 mcg/kg clonidine group	Significant reduction in postoperative analgesic requirement in the adjuvant group	Nil
Neogi M et al., [27]; 2010	Three groups R, D and C- all groups getting 0.25% ropivacaine (1 mL/kg) ang group D and C getting dexmedetomidine 1 mcg/kg and clonidine 1 mcg/kg as adjuvant along with ropivacaine respectively	Using adjuvants with ropivacaine in caudal block provide high quality analgesic effect.	None of the three groups showed any signs of adverse events or haemodynamic instability.
Inanoglu K et al., [28]; 2010	Two groups- 0.2% ropivacaine alone group and 0.2% ropivacaine with 2 mg/kg tramadol as adjuvant group	Addition of adjuvant to ropivacaine improved the quality and duration of analgesia and reduced the need for rescue analgesic drug.	Nil
Shukla U et al., [29]; 2011	Two groups- 0.25% ropivacaine with clonidine 2 mcg/kg and 0.25% ropivacaine with fentanyl 1 mcg/kg	Similar duration and quality of analgesia in both the groups.	Lesser side-effects with clonidine group
Laha A et al., [30]; 2012	Two groups- 1 mL/kg 0.2% ropivacaine was used in both the groups. Clonidine 2 mcg/kg added as adjuvant to one of the group.	Better quality of analgesia noted with adjuvant group.	Nil
Doctor TP et al., [31]; 2013	Two groups- 0.25% ropivacaine with 1 mcg/kg fentanyl and 0.25% bupivacaine with 1 mcg/kg fentanyl	It was concluded that ropivacaine combined with fentanyl was a superior combination.	Nil
Krishnadas A et al., [32]; 2016	Three groups- 0.2% ropivacaine used in all the three groups with second group receiving tramadol 2 mg/kg as adjuvant and third group getting midazolam 50 mcg/kg as adjuvant	Longer duration of analgesia seen with tramadol group.	Nil
Gupta S and Sharma R [33]; 2017	Two groups- 0.25% ropivacaine used in both the groups with dexmedetomidine 2 mcg/kg as adjuvant in one group and 2 mg/kg tramadol as adjuvant in the other group.	Longer duration of analgesia seen with dexmedetomidine as adjuvant group.	Nil
Tao B et al., [34]; 2019	Two groups- 0.15% ropivacaine 1 mL/kg group and 0.15% ropivacaine 1.3 mL/kg group	The group which used 1.3 mL/kg ropivacaine had lower pain score, less usage of rescue analgesic and shorter hospital stay.	Study was on paediatric patients undergoing laparoscopic upper urinary tract surgery
Sharma TH et al., [35]; 2020	Two groups- 0.25% ropivacaine and 0.25% bupivacaine	Longer duration of analgesia and motor blockade with bupivacaine group.	No significant change in haemodynamics and side-effects
Armyda MRLA et al., [36]; 2021	Case series using ropivacaine 0.125%	The study concluded that 0.125% is safe and effective for paediatric caudal analgesia	Effective for day care surgery.

[Table/Fig-3]: Comparison of different studies on ropivacaine used for caudal analgesia.

likely to penetrate large myelinated motor fibers resulting in lesser amount of motor blockade and longer postoperative analgesia. Motor blockade in children during the postoperative period is one among the reason for undue anxiety in the parents. This greater degree of motor sensory differentiation makes utilising a preferred drug when motor blockade is undesired such as in providing postoperative analgesia. This can be used as a cost-effective method of postoperative analgesia by decreasing the requirement of systemic analgesics, associated side-effects of systemic drugs like opioids, duration of hospital stay, morbidity and improving the quality of life postoperatively [41].

CONCLUSION(S)

Ropivacaine is an excellent drug for providing intra and postoperative analgesia using caudal epidural technique. Epidural block via caudal route is used as a complement to general anesthesia in paediatric population. This technique utilising a good effective local anesthetic agent with the preferred characteristics of lesser motor blockade and prolonged analgesia with minimal side-effects, not only gives good postoperative analgesia but also helps in reducing the requirement of polypharmacy using inhalational and intravenous agents, decrease the stress response during surgery and helps in speedy recovery. This review article suggests that the duration of analgesia

is prolonged when ropivacaine is used along with adjuvant drugs. Also, the drug maintains haemodynamic stability with minimal side-effects and has the added advantage of lesser cardiotoxicity.

REFERENCES

[1] Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, et al. The revised International Association for the Study of Pain definition of pain: Concepts, challenges, and compromises. Pain. 2020;161(9):1976-82.
[2] Cousins MJ, Bridenbaugh PO, Carr DB, Horlocker TT. Cousins and Bridenbaugh's neural blockade in clinical anesthesia and pain medicine. 4th edition. Lippincott Williams & Wilkins; 2009.
[3] Höhener D, Blumenthal S, Borgeat A. Sedation and regional anaesthesiain the adult patient. Br J Anaesth. 2008;100(1):08-16.
[4] Nimmo SM. Benefit and outcome after epidural analgesia. Continuing Education in Anaesthesia, Critical Care & Pain. 2004;4(2):44-47.
[5] McClure JH. Ropivacaine. Br J Anaesth. 1996;76(2):300-07.
[6] Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55(2):104-10.
[7] Casati A, Putzu M. Bupivacaine, levobupivacaine and ropivacaine: Are they clinically different? Best Pract Res ClinAnaesthesiol. 2005;19(2):247-68.
[8] Simpson D, Curran MP, Oldfield V, Keating GM. Ropivacaine Drugs. 2005;65(18):2675-17.
[9] Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia on perioperative outcome: A randomized, controlled Veterans Affairs cooperative study. Annals of Surgery. 2001;234(4):560.
[10] Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55(2):104-10.
[11] McGlade DP, Kalpokas MV, Mooney PH, Buckland MR, Vallipuram SK, Hendrata MV, et al. Comparison of 0.5% ropivacaine and 0.5% bupivacaine in lumbar epidural anesthesia for lower limb orthopedic surgery. Anesthesia & Intensive Care. 1997;25(3):262-66.
[12] Gautier P, De Kock M, Huberty L, Demir T, Izydorczic M, Vanderick B. Comparison of the effects of intrathecal ropivacaine, levobupivacaine, and bupivacaine for Caesarean section. Br J Anaesth. 2003;91(5):684-89.
[13] Chung CJ, Yun SH, Hwang GB, Park JS, Chin YJ. Intrathecal fentanyl added to hyperbaric ropivacaine for cesarean delivery. Regional Anesthesia and Pain Medicine. 2002;27(6):600-03.
[14] Casati A, Borghi B, Fanelli G, Montone N, Rotini R, Fraschini G, et al. Interscalene brachial plexus anaesthesia and analgesia for open shoulder surgery: A randomised, double-blinded comparison between levobupivacaine and ropivacaine. Anaesthesia Analgesia. 2003;96(1):253-59.
[15] Ivani G, Lampugnani E, Torre M, Calevo Maria G, DeNegri P, Borrometi F, et al. Comparison of ropivacaine with bupivacaine for paediatric caudal block. British Journal of Anaesthesia. 1998;81(2):247-48.
[16] Da Conceicao MJ, Coelho L. Caudal anaesthesia with 0.375% ropivacaine or 0.375% bupivacaine in paediatric patients. BJA. 1998;80(4):507-08. Doi: 10.1093/bja/80.4.507. PMID: 9640159.
[17] Da Conceicao MJ, Coelho L, Khalil M. Ropivacaine 0.25% compared with bupivacaine 0.25% by the caudal route. Paediatric Anesthesia. 1999;9(3):229-33.
[18] Koinig H, Krenn CG, Glaser C, Marhofer P, Wildling E, Brunner M, et al. The dose-response of caudal ropivacaine in children. Anaesthesiology. 1999;90(5):1339-44.
[19] Ivani G, De Negri P, Conio A, Amati M, Roero S, Giannone S, et al. Ropivacaine-clonidine combination for caudal blockade in children. Acta Anaesthesiol Scand. 2000;44(4):446-49.
[20] De Negri P, Ivani G, Visconti C, De Vivo P. How to prolong postoperative analgesia after caudal anaesthesia with ropivacaine in children: S-ketamine versus clonidine. Paediatr Anaesth. 2001;11(6):679-83.
[21] Ray M, Mondal SK, Biswas A. Caudal analgesia in paediatric patients: Comparison between bupivacaine and Ropivacaine. IJA. 2003;47(4):275-78.
[22] Turan A, Memis D, Basaran UN, Karamanlioglu B, Sut N. Caudal ropivacaine and neostigmine in paediatric surgery. Anaesthesiology. 2003;98(3):719-22.
[23] Gunes Y, Secen M, Ozcengiz D, Gunduz M, Balcioglu O, Isik G. Comparison of caudal ropivacaine, ropivacaine plus ketamine and ropivacaine plus tramadol administration for postoperative analgesia in children. Paediatric Anaesthesia. 2004;14(7):557-63.
[24] Akbas M, Akbas H, Yegin A, Sahin N, Titiz TA. Comparison of the effects of clonidine and ketamine added to ropivacaine on stress hormone levels and the duration of caudal analgesia. Paediatr Anaesth. 2005;15(7):580-85.
[25] Kawaraguchi Y, Otomo T, Ota C, Uchida N, Taniguchi A, Inoue S. A prospective, double-blind, randomized trial of caudal block using ropivacaine 0.2% with or without fentanyl 1 microg kg-1 in children. Br J Anaesth. 2006;97(6):858-61.
[26] Bajwa SJ, Kaur J, Bajwa SK, Bakshi G, Singh K, Panda A. Caudal ropivacaine-clonidine: A better post-operative analgesic approach. Indian J Anaesth. 2010;54(3):226-30.
[27] Neogi M, Bhattacharjee DP, Chatterjee N, Dawn S. A comparative study between clonidine and dexmedetomidine used as adjuncts to ropivacaine for caudal analgesia in paediatric patients. Journal of Anaesthesiology Clinical Pharmacology. 2010;26(2):149-53.
[28] Inanoglu K, Ozcengiz D, Gunes Y, Unlugenc H, Isik G. Epidural ropivacaine versus ropivacaine plus tramadol in postoperative analgesia in children undergoing major abdominal surgery: A comparison. J Anesth. 2010;24(5):700-04.
[29] Shukla U, Prabakar T, Malhotra K. Postoperative analgesia in children when using clonidine or fentanyl with ropivacaine caudally. J Anaesthesiol Clin Pharmacol. 2011;27(2):205-10.
[30] Laha A, Ghosh S, Das H. Comparison of caudal analgesia between ropivacaine and ropivacaine with clonidine in children: A randomied controlled trial. Saudi J Anaesth. 2012;6(3):197-200.
[31] Doctor TP, Dalwadi DB, Abraham L, Shah N, Chadha IA, Shah BJ. Comparison of ropivacaine and bupivacaine with fentanyl for caudal epidural in pediatric surgery. Anesth Essays Res. 2013;7(2):212-15.
[32] Krishnadas A, Suvarna K, Hema VR, Tasnim M. A comparison of ropivacaine, ropivacaine with tramadol and ropivacaine with midazolam for postoperative caudal epidural analgesia. IJA. 2016;60(11):82732.
[33] Gupta S, Sharma R. Comparison of analgesic efficacy of caudal dexmedetomidine versus caudal tramadol with ropivacaine in paediatricinfraumbilical surgeries: A prospective, randomised, double-blinded clinical study. Indian J Anaesth. 2017;61(6):499-04.
[34] Tao B, Liu K, Wang D, Ding M, Yang N, Zhao P. Perioperative effects of caudal block on pediatric patients in laparoscopic upper urinary tract surgery: A randomised controlled trial. BMC Pediatr. 2019;19(1):427. Doi: 10.1186/s12887-019-1812-0.
[35] Sharma TH, Sharma K, Patel J, Chauhan D, Shah N. Comparison between ropivacaine 0.25% and bupivacaine 0.25% in paediatric caudal anesthesia in infraumbilical surgery. International Journal of Current Research and Review. 2020;12(24):111-14.
[36] Armyda MRLA, Sidemen GPS, Aryabiantara IW, Senapathi TGA. Continuous caudal anesthesia using ropivacaine 0.125% in pediatric patients undergoing infraumbilical surgery. Bali Journal of Anesthesiology. 2021;5(2):132-34.
[37] Agasti TK. Textbook of anesthesia for post graduates. 1st edition. Jaypee Brothers Medical Publisher; 2011.
[38] Li K, Ji C, Luo D, Feng H, Yang K, Xu H. Wound infiltration with ropivacaine as an adjuvant to patient controlled analgesia for transforaminal lumbar interbody fusion: A retrospective study. BMC Anesthesiol. 2020;20(1):288.
[39] Pere PJ, Ekstrand A, Salonen M, Honkanen E, Sjovall J, Henriksson J, et al. Phaemacokinetics of ropivacaine in patients with chronic renal failure. Br J Anaesth. 2011;106(4):512-21.
[40] Van de Vossenberg G, Van der Wal S, Müller A, Tan E, Vissers K. Ropivacaine plasma concentrations after 192-hour high dose epidural ropivacaine infusion in a pediatric patient without side effects. Case Rep Anesthesiol. 2018;2018:9150980. Published 2018. Doi: 10.1155/2018/9150980.
[41] Nimmo SM, Foo ITH, Paterson HM. Enhanced recovery after surgery: Pain management. J Surg Oncol. 2017;116(5):583-91.

PARTICULARS OF CONTRIBUTORS:
1. Junior Resident, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.
2. Professor and Head, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Shilpa Shankar,
Junior Resident, Department of Anaesthesiology, Jawaharlal Nehru Medical College, DMIMS, Sawangi Meghe, Wardha, Maharashtra, India.
E-mail: shilshank@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 31, 2022
- Manual Googling: May 12, 2022
- iThenticate Software: Jul 01, 2022 (13%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? NA
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 19, 2022**
Date of Peer Review: **Apr 26, 2022**
Date of Acceptance: **May 13, 2022**
Date of Publishing: **Aug 01, 2022**