DOI: 10.7860/JCDR/2023/56902.17189

Original Article

Anaesthesia Section

Low Dose Bupivacaine (0.25%) with Fentanyl vs Ropivacaine (0.25%) with Fentanyl for Caudal Analgesia in Paediatric Patients: A Randomised Clinical Study

BALWINDER KAUR REKHI[1], PARMOD KUMAR[2], KANICA MISHRA[3], MANJEET SINGH[4], GURJIT SINGH GANDHI[5]

ABSTRACT

Introduction: Caudal epidural block is one of the most common regional techniques in paediatric anaesthesia for infraumbilical surgeries. Though bupivacaine is widely used because of its long duration, ropivacaine is a newly emerging drug having differential neuraxial blockade with less motor block and reduced cardiovascular and Central Nervous System (CNS) toxicity. To further increase the duration and quality various adjuvants have been added.

Aim: To compare low dose bupivacaine-fentanyl with ropivacaine-fentanyl in terms of haemodynamic stability, duration of analgesia, postoperative pain, level of sedation, and side-effects profile among patients undergoing infraumbilical surgery.

Materials and Methods: A double-blind, randomised clinical study was conducted on 60 children undergoing elective infraumbilical surgery. Patients were randomly divided into two groups of 30 each into Bupivacaine-Fentanyl (BF) group and Ropivacaine-Fentanyl (RF) group, using a simple envelope method. After securing airway, caudal block was given. Group BF received 0.25% bupivacaine 0.5 mL/kg with fentanyl 0.5 mcg/kg and Group RF received 0.25% ropivacaine 0.5 mL/kg with fentanyl 0.5 mcg/kg. Postoperative pain was assessed using the Face, Legs, Activity, Cry, Consolability (FLACC) pain assessment scale, for 12 hours. The haemodynamics, duration of analgesia, rescue analgesia requirement and side-effects (bradycardia, hypotension, respiratory depression, retching, urinary retention, vomiting) were noted and analysed statistically.

Results: The mean duration of analgesia in the BF group was 270±46.60 minutes and in the RF group was 430±68.83 minutes (p-value <0.001). Patients requiring rescue analgesia were 12 in Group BF and 5 in Group RF. Mean FLACC reached ≥4 at 4.5 hours in group BF and at 7 hours in group RF. There was no significant difference in haemodynamics and side-effects profile (bradycardia, hypotension, respiratory depression, retching, urinary retention, vomiting) between the two groups.

Conclusion: Low dose caudal ropivacaine-fentanyl combination is superior to that of caudal bupivacaine-fentanyl with respect to duration and intensity of intraoperative and postoperative analgesia.

Keywords: Adjuvants, Haemodynamic stability, Infraumbilical surgeries, Postoperative analgesia, Sedation score

INTRODUCTION

Postoperative pain is an annoying subjective sensation for both children and their parents and relief from postoperative pain is challenging in children [1]. Caudal epidural, the most commonly used regional analgesia technique, is virtually free of measurable haemodynamic effects, thus adding a new dimension to the evolving necessity of paediatric postoperative pain management, but with the disadvantage of short duration of action after single injection [2,3].

Prolongation of caudal analgesia using a single-shot technique has been achieved by the addition of various adjuvants such as opioids, ketamine, clonidine and dexmedetomidine [3]. Bupivacaine was a popular drug in regional anaesthesia for years until toxic reactions were reported. Ropivacaine, the S-enantiomer of the amide local anaesthetic, produces differential neural blockade, with less motor blockade, cardiovascular and neurological toxicity, making it suitable for day-care surgery in children [4]. Fentanyl, a lipophilic opioid, acts on substansia gelatinosa on the dorsal horn of spinal cord by blocking fibres carrying nociceptive impulses both pre and postsynaptically. It comprises of certain undesirable side-effects like nausea, vomiting or respiratory depression [5,6].

The present study was conducted using low dosage of drugs to avoid any unwanted motor weakness, urinary retention and respiratory depression and, hence, to allow early ambulation and less hospital stay. Similar studies have encountered unnecessary motor blockade which might be because of usage of higher drug dosage [2,4].

Previous studies that used low dose drugs found remarkable analgesia intraopertively and postoperatively with minimal side-effects.

A study compared low dose ropivacaine 0.2% (0.5 mL/kg) alone (Group R) and in combination with fentanyl (0.5 mcg/kg) (Group RF) for caudal anaesthesia in paediatric patients found superior duration of analgesia in Group RF (14.86 hours) with no case of motor blockade, urinary retention and respiratory depression after the surgery [7] . Another study reported that caudally administered 0.5 mL/kg bupivacaine 0.25% plus ketamine 0.5 mg/kg or bupivacaine 0.25% plus tramadol 1 mg/kg provided significantly longer duration of analgesia in children undergoing inguinal hernia surgery [8].

Yet another study was conducted to compare the analgesic effect of clonidine 2 mcg/kg as an adjunct (administered i.v. or caudal) with bupivacaine 0.25%, 0.5 mL/kg for caudal block in hypospadias repair which revealed no difference in analgesic effect between the two groups and also an absence of motor blockade [9].

The aim of the present clinical trial was to compare the efficacy of low dose bupivacaine-fentanyl and low dose ropivacaine-fentanyl combinations in children aged 1-8 years undergoing infraumblical surgeries. The primary outcome measures were intensity of intraoperative and postoperative analgesia, duration of analgesia, and need for rescue analgesic. The secondary outcome measures were haemodynamic changes, level of sedation and side-effects.

MATERIALS AND METHODS

The present double-blind, randomised clinical study was conducted in 60 paediatric patients undergoing infraumbilical surgeries at Department of Anaesthesia, Rajindra Hospital, Government Medical College, Patiala, from April 2021 to January 2022. Ethical clearance was obtained from Institutional Ethics Committee (IEC No.BFUHS/2K21p-TH/5411).

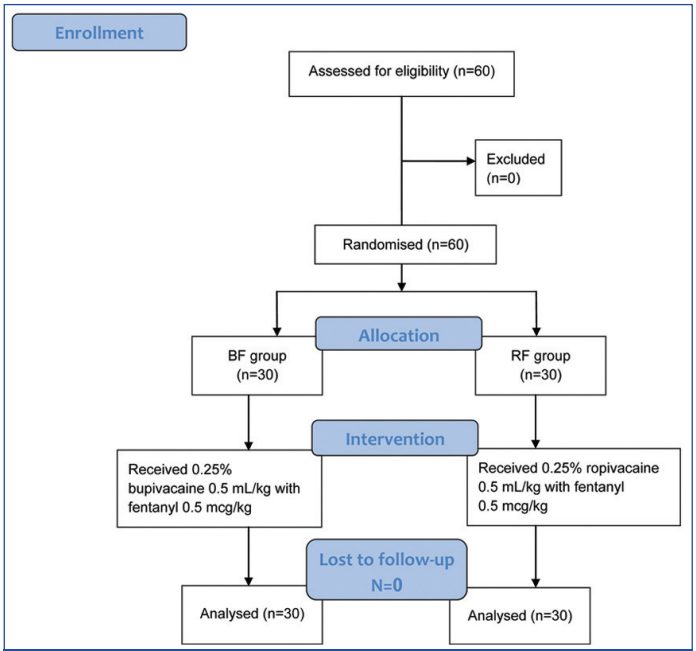
Inclusion criteria: Paediatric patients of either gender aged between 1-8 years {American Society of Anaesthesiologists (ASA) classification grade ASA I and ASA II}.

Exclusion criteria: Children whose parents refused to participate in the study, patients with history of developmental delay or delayed milestones, mental retardation, child with suspected coagulopathy or bleeding diathesis, hypersensitivity to local anaesthesia, sacral bone abnormality, spina bifida and local sepsis at puncture site.

Sample size calculation: Sample size was calculated with PS Power and Sample size Calculations Version 2.1.30 (William Dupont and Walton D Plummer). The sample size required was calculated considering an alpha error of 0.05, power 0.90 or 90%, assumed difference in dose of total amount of rescue analgesic as 5 with standard deviation of 5.5, which resulted in a predicted sample size of 28.6 [2]. Rounding up, 60 patients were included in the present study.

During enrollment 60 children of either sex were assessed for eligibility. They were randomised into two groups (30 children in each) using sealed envelopes.

- Group BF: received 0.25% bupivacaine 0.5 mL/kg with fentanyl 0.5 mcg/kg diluted in normal saline.
- Group RF: received 0.25% ropivacaine 0.5 mL/kg with fentanyl 0.5 mcg/kg diluted in normal saline [Table/Fig-1].



[Table/Fig-1]: CONSORT flow diagram.

Volume of drug was kept constant in all groups to avoid bias. The investigator, who did not participate in care of the patients, prepared all the study medications according to group assignment. Another investigator, who was blinded to group assignments, performed caudal blocks in all patients. Follow-up and analysis were done.

Technique

Fasting protocol was followed and premedication with intranasal midazolam 0.2 mg/kg was given to each child 30 minutes prior to surgery [10]. Multi parameter monitoring was done for Electrocardiograph (ECG), Partial pressure of Oxygen (SpO_2), Blood Pressure (BP), Heart Rate (HR), End-Tidal Carbon Dioxide ($EtCO_2$). Caudal block was given. Surgery was allowed to proceed after 15 minutes of caudal block. The caudal block was considered failure, if increase in heart rate or mean arterial pressure was more than 20% of baseline. In case of failure, patient was excluded from study.

The haemodynamic parameters SpO_2, HR, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) were monitored continuously during preoperative and intraoperative period and documented intraoperatively for every five minutes up to 30 minutes and then every 10 minutes up to completion of surgery.

Face, Legs, Activity, Cry, Consolability (FLACC) scale: [Table/Fig-2] for pain assessment was measured at 30 minutes, 1 hour, 2 hours, 3 hours, 6 hours and 12 hours after surgery was used [11]. The duration of analgesia was defined as the time from caudal placement of drug to the first recording of FLACC scale ≥4. Rescue analgesia had been provided with syrup paracetamol 10 mg/kg whenever the pain score was ≥4.

Sedation score: [Table/Fig-3] was assessed when the patient was shifted to recovery room upto 12 hours [12].

FLACC	0	1	2
Face	No expression	Frequent to occasional grimace	Constant quivering chin
Leg	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quiet	Squirming shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry	Moans or whimper	Crying steadily
Consolability	Content, relaxed	Reassurance, hugging	Difficult to console

[Table/Fig-2]: Face, Legs, Activity, Cry, Consolability (FLACC) score.

Score	Response
0	Arousable
1	Arousable to voice
2	Arousable to pain
3	Unarousable

[Table/Fig-3]: Sedation score [12].

STATISTICAL ANALYSIS

Data was analysed using IBMM Statistical Package for the Social Science (SPSS) software version 22.0. Numerical data was expressed as mean and standard deviation and statistical analysis was done using the Analysis of Variance (ANOVA) test to compare both the groups. For skewed data/scores Kruskal Wallis H-test was used. Distribution of gender was compared using Chi-square test. The p-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 paediatric patients of age group 1-8 years were enrolled in the study. Caudal block was successful in all the patients. The demographic data of the two groups did not differ [Table/Fig-4]. There was no significant difference in the preoperative haemodynamic parameters between the two groups [Table/Fig-5,6].

Data	Group BF	Group RF	p-value
Age (years) (Mean±SD)	4.78±1.76	4.66±1.81	0.815
Weight (kgs) (Mean±SD)	16.5667±5.17076	15.1000±3.74488	0.213
Male	26 (86.7)	25 (83.3)	0.500
Female	4 (13.3)	5 (16.7)	

[Table/Fig-4]: Demographic data.

Parameters	Groups	Mean±SD	p-value
Heart rate (Beats/minute)	Group BF	107.57±6.97623	0.090
	Group RF	110.77±7.41240	
Systemic blood pressure (mm/Hg)	Group BF	105.03±6.28892	0.493
	Group RF	105.97±3.91710	
Diastolic blood pressure (mm/Hg)	Group BF	60.8667±5.42493	0.237
	Group RF	59.3667±4.23030	
Mean arterial pressure	Group BF	74.6333±4.44494	0.286
	Group RF	73.5667±3.10376	
Respiratory rate (Breaths/minute)	Group BF	20.0000±1.25945	0.925
	Group RF	20.0333±1.47352	
SpO_2 (%)	Group BF	99.7333±0.44978	0.098
	Group RF	99.9000±0.30513	

[Table/Fig-5]: Preoperative vital parameters.

Heart rate (Minutes)	Groups	Mean±SD	p-value
0	Group BF	109.17±6.78275	0.336
	Group RF	110.77±5.96359	
5	Group BF	111.50±5.89418	0.325
	Group RF	110.00±5.80725	
10	Group BF	111.40±6.09466	0.361
	Group RF	109.97±5.96243	
15	Group BF	111.23±6.42561	0.299
	Group RF	109.57±5.87034	
20	Group BF	105.43±5.70954	0.981
	Group RF	105.40±5.22989	
25	Group BF	103.50±5.75805	0.633
	Group RF	104.17±4.95555	
30	Group BF	104.04±5.26682	0.937
	Group RF	104.14±4.84359	
40	Group BF	103.92±4.01918	0.742
	Group RF	103.50±5.01303	
50	Group BF	105.45±2.83725	0.863
	Group RF	105.21±5.41170	
60 min	Group-BF	108.40±2.19089	0.832
	Group-RF	107.82±5.74140	

[Table/Fig-6]: Mean heart rate (per minute) at different time intervals during intraoperative period.

Mean duration of analgesia was significantly earlier (4.5 hrs) in Group BF than in Group RF (7 hours) [Table/Fig-7]. Patients requiring rescue analgesia were significantly more in Group BF (n=12) than in Group RF (n=5) [Table/Fig-7]. Mean FLACC reached ≥4 earlier in group BF (4.5 hours) as compared to group RF (7 hours) [Table/Fig-8].

Parameters	Group BF	Group RF	p-value
Mean duration of analgesia (minutes)	270±46.60	430±68.83	<0.001*
No. of patients for rescue analgesic	12 (40%)	5 (16.7%)	0.045

[Table/Fig-7]: Mean duration of analgesia (minutes) and number of patients for rescue analgesic in postoperative period.
*p-value <0.05 was considered statistically significant

FLACC	Groups	Mean±SD	p-value
30 minutes	Group BF	0	0.154
	Group RF	0.0667±0.25371	
1 hour	Group BF	0.1000±0.30513	0.305
	Group RF	0.0333±0.18257	
2 hours	Group BF	0.5333±0.62881	<0.001*
	Group RF	0.0333±0.18257	
3 hours	Group BF	1.8333±0.98553	<0.001*
	Group RF	0.6000±0.67466	
6 hours	Group BF	4.1333±0.62881	<0.001*
	Group RF	1.3000±0.98786	
12 hours	Group BF	4.6667±0.66089	<0.001*
	Group RF	2.8333±1.91335	

[Table/Fig-8]: FLACC score during postoperative period in two groups.
*p-value <0.05 was considered statistically significant

Vomiting was noticed in five patients in Group BF and in three patients in group RF. No other side-effects (bradycardia, hypotension, respiratory depression, retching, urinary retention) were noticed in either group [Table/Fig-9].

Complications	Groups	Yes	No	p-value
Vomiting	Group-BF	5	25	0.706
	Group-RF	3	27	

[Table/Fig-9]: Side-effects.

DISCUSSION

In recent years paediatric regional anaesthesia has gone through significant development with advances in safety, pharmacology and block techniques [2]. Among various techniques of regional analgesia caudal epidural analgesia in combination with general anaesthesia or alone provides safe, reliable and efficient analgesia for both high-risk and general paediatric surgical patients undergoing various sub umbilical surgeries [4]. This long acting regional technique provides good postoperative analgesia and smooth recovery period facilitating early discharge [2].

In this study 0.5 mL/kg (low dose) of 0.25% ropivacaine or 0.25% bupivacaine was used for caudal analgesia to avoid motor blockade in postoperative period which could be explained by drug concentration being insufficient in blocking large motor fibres [13].

Duration of analgesia and postoperative pain: In the present study, ropivacaine-fentanyl group had prolonged duration of analgesia. The mean FLACC reached ≥4 earlier in group BF as compared to group RF, which is similar to other studies.

Doctor TP et al., compared ropivacaine (0.2 or 0.25%) or bupivacaine (0.25%) with fentanyl for caudal block. They concluded that time for first rescue analgesic for group the former was superior than the later, and the requirement of inhalational agent intraoperatively was less in the ropivacaine-fentanyl group [4].

Sengupta S et al., (2015) compared bupivacaine 0.25% 0.7 mL/kg with fentanyl 1 mcg/kg and ropivacaine 0.25% 0.7 mL/kg with fentanyl 1 mcg/kg for infraumbilical surgeries and found that the duration of analgesia was longer in the ropivacaine group [2]. Kumar M et al., found a higher postoperative pain score in Group B {Bupivacaine 0.2% (1 mL/kg)} as compared to Group A {Ropivacaine 0.2% (1 mL/kg)}, with group A having good analgesia clinically [13].

Rescue analgesia requirement: In the present study, more number of patients in group BF required rescue analgesia as compared to group RF signaling superiority of ropivacaine fentanyl group. Ahmad S et al., in a study found that the rescue analgesia requirement was significantly lower in group B {Ropivacaine 0.2% (1 mL/kg)} as compared to group A {Bupivacaine 0.25% (1 mL/kg)} [14]. Sengupta S et al., concluded that intensity of postoperative analgesia produced by ropivacaine was better than bupivacaine [2].

Sedation score: In the present study, the mean sedation score (SS) during postoperative period was comparable at all intervals in both groups [12]. A study conducted by Kumar M et al., revealed no statistical difference in sedation score between two groups {0.2% ropivacaine (1 mL/kg) or 0.2% bupivacaine (1 mL/kg)} which is in agreement with present study [13].

Side-effects: In the present study, some of the patients had episodes of vomiting which was similar in both the groups. None of the patients in both groups developed bradycardia, hypotension, respiratory depression, pruritis, fever and urinary retention.

Acharya R et al., (2013) compared caudal bupivacaine (0.25%, 2 mg/kg) alone and with two different doses of fentanyl (0.5 mcg/kg and 1 mcg/kg) and also reported that the incidence of vomiting was similar in both the groups. No patient suffered from respiratory depression, urinary retention and pruritus similar to the present findings [15]. Chipde SS et al., also found no adverse effects such as nausea, vomiting, pruritus during a comparative study between bupivacaine (0.25%, 1 mL/kg) and ropivacaine (0.25%, 1 mL/kg) for caudal block [16]. Sengupta S et al., while comparing ropivacaine-fentanyl and bupivacaine-fentanyl for caudal analgesia also found no significant adverse effects between the two groups [2].

In contrast to forementioned studies, there are two studies where authors observed urinary retention in patients. Metzelder ML et al., in a retrospective study compared the incidence of impaired postoperative micturition between penile block anaesthesia and caudal anaesthesia and found that the rate of impaired postoperative micturition was significantly higher in children undergoing caudal anaesthesia. The use of high volume (0.2%, 1 mL/kg) ropivacaine as compared to low dose, as used in the present study, could be the probable explanation [17].

Kumar M et al., in a study found that more number of patients had urinary retention in group B 0.2% bupivacaine (1mL/kg)} than group A {0.2% ropivacaine (1 mL/kg)} [13]. The probable reason could be the higher dose of bupivacaine and ropivacaine used as compared to the present study. None of the children in both groups were found to have respiratory difficulty and pruritis [13].

Limitation(s)

Since it is a landmark-based study (blind procedure) and due to non availability of ultrasound machine, the spread of local anaesthetic solution could not be visualised in the epidural space.

CONCLUSION(S)

Low dose and low concentration of drugs have an equipotent analgesic efficacy with lesser side-effects including motor block. Ropivacaine-fentanyl combination has a better intraoperative and postoperative analgesic property in comparison to bupivacaine-fentanyl combination. However, a similar haemodynamic and side-effect profile exist for the two. Hence, low dose ropivacaine-fentanyl combination can be used as an alternative to bupivacaine-fentanyl combination for paediatric postoperative pain care through the caudal route as a safe and effective agent.

REFERENCES

[1] Elfawal SM, Abdelaal WA, Hosny MR. A comparative study of dexmedetomidine and fentanyl as adjuvants to levobupivacaine for caudal analgesia in children undergoing lower limb orthopedic surgery. Saudi J Anaesth. 2016;10(4):423.
[2] Sengupta S, Mukherji S, Sheet J, Mandal A, Swaika S. Caudal-epidural bupivacaine versus ropivacaine with fentanyl for paediatric postoperative analgesia. Anaesthesia, essays and researches. 2015;9(2):208.
[3] Yousef GT, Ibrahim TH, Khder A, Ibrahim M. Enhancement of ropivacaine caudal analgesia using dexamethasone or magnesium in children undergoing inguinal hernia repair. Anesth Essays Res. 2014;8(1):13-19.
[4] Doctor TP, Dalwadi DB, Abraham L, Shah N, Chadha IA, Shah BJ, et al. Comparison of ropivacaine and bupivacaine with fentanyl for caudal epidural in pediatric surgery. Anesth Essays Res. 2013;7(2):212-15.
[5] Scott DA, Beilby DS, McClymont C. Postoperative analgesia using epidural infusions of fentanyl with bupivacaine: A prospective analysis of 1,014 patients. Anesthesiology. 1995;83(4):727-37.
[6] Saldman LJ, Cousins MJ, Mather LE. Intrathecal and epidural administration of opioids. Anesthesiology. 1984;61(3):276-10.
[7] Grewal DTK, Kaur DB, Kumar DP, Kaur DS. Comparison of ropivacaine 0.2% alone and in combination with fentanyl for caudal anaesthesia in paediatric patients. IJIRMS. 2019;4(02):103-07.
[8] Choudhuri AH, Dharmani P, Kumarl N, Prakash A. Comparison of caudal epidural bupivacaine with bupivacaine plus tramadol and bupivacaine plus ketamine for postoperative analgesia in children. Anaesth Intensive Care. 2008;36(2):174-79.
[9] Hansen TG, Henneberg SW, Walther-Larsen S, Lund J, Hansen M. Caudal bupivacaine supplemented with caudal or intravenous clonidine in children undergoing hypospadias repair: A double-blind study. Br J Anaesth. 2004;92(2):223-27.
[10] Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration: Application to Healthy Patients Undergoing Elective Procedures: An Updated Report by the American Society of Anesthesiologists Task Force on Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration. Anesthesiology. 2017;126:376-93.
[11] Manworren RC, Hynan LS. Clinical validation of FLACC: Preverbal patient pain scale. Pediatr Nurs. 2003;29(2):140-46.
[12] Ali G, Kala N, Rather MA, Taj A, Maqbool S, Bhat KA. Comparative evaluation of caudal ropivacaine and ropivacaine with clonidine for postoperative analgesia in children. J Evol Med Dent Sci. 2015;14:50-54.
[13] Kumar M, Gupta KK, Kataria AP. Comparison of caudal ropivacaine 0.2% with bupivacaine 0.2% in pediatric patients–a randomised controlled trial. Anesth Essays Res. 2015;19(2):141-46.
[14] Ahmad S, Mohammad K, Ahmad M, Nazir I, Ommid M, Nabi V. Caudal analgesia in pediatric patients: Comparison between bupivacaine and ropivacaine. Internet J Anesthesiol. 2012;30(3):01-07.
[15] Acharya R, Jena SK, Samal S, Mishra SN. Postoperative analgesia in pediatrics patients through caudal block with bupivacaine and two different doses of fentanyl-A comparative study. J Evol Med Dent Sci. 2013;2(2):7568-74.
[16] Chipde SS, Banjare M, Arora KK, Saraswat M. Prospective randomized controlled comparison of caudal bupivacaine and ropivacaine in pediatric patients. Ann Med Health Sci Res. 2014;4(8):115-18.
[17] Metzelder ML, Kuebler JF, Glueer S, Suempelmann R, Ure BM, Petersen C, et al. Penile block is associated with less urinary retention than caudal anaesthesia in distal hypospadia repair in children. World J Urol. 2010;28(1):87-91.

PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Anaesthesia, Government Medical College, Patiala, Punjab, India.
2. Professor and Head, Department of Anaesthesia, Government Medical College, Patiala, Punjab, India.
3. Junior Resident, Department of Anaesthesia, Government Medical College, Patiala, Punjab, India.
4. Senior Resident, Department of Anaesthesia, Government Medical College, Patiala, Punjab, India.
5. Assistant Professor, Department of Anaesthesia, Government Medical College, Patiala, Punjab, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Gurjit Singh Gandhi,
House No. 617, Near Jain Temple, Modern Valley, Fatehgarh Sahib,
Patiala-140406, Punjab, India.
E-mail: drgurjitsingh07@yahoo.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 21, 2022
- Manual Googling: Aug 24, 2022
- iThenticate Software: Sep 02, 2022 (19%)

ETYMOLOGY: Author Origin

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

Date of Submission: **Apr 17, 2022**
Date of Peer Review: **May 21, 2022**
Date of Acceptance: **Sep 08, 2022**
Date of Publishing: **Jan 01, 2023**