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Dr. Suresh Kumar Bhargava
Professor, Department of Anaesthesia, National Institute of medical science and research Jaipur Rajasthan, India

Dr. Neena Tiwari
Associate Professor, Department of Anaesthesia, National Institute of medical science and research Jaipur Rajasthan, India

Corresponding Author:
Dr. Suresh Kumar Bhargava
Professor, Department of Anaesthesia, National Institute of medical science and research Jaipur Rajasthan, India

Comparison of Levobupivacaine with dexmedetomidine in Infraumbilical surgeries

Dr. Suresh Kumar Bhargava and Dr. Neena Tiwari

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Abstract
Introduction: Due to decreased cardiovascular and central nervous system toxicity, levobupivacaine is a good alternative for spinal anesthesia. Dexmedetomidine when used intrathecally is associated with prolonged motor and sensory block, hemodynamic stability, and less requirement of rescue analgesia in 24 h.
Materials and Methods: We assumed that sevoflurane will provide clinically acceptable conditions for endotracheal intubation comparable to propofol-suxamethonium in children. All patients received diazepam 0.2 mg/kg orally, the night before surgery. The patients were preloaded with Lactated Ringer's solution 15 mL/kg. They were monitored with automated noninvasive blood pressure, pulse oximetry, and electrocardiogram.
Results: In Group LD, increase in VAS was observed at 210 min and the first dose of rescue analgesia was given at 5th h postoperatively. The second dose of recue analgesia was given at 12th h and the third dose was given at 21st h. Postoperative VAS scores at different time intervals were significantly lower in Group LD than Group L, thus indicating superior analgesia. The time of request of the first dose of rescue analgesia was delayed in Group LD as it was demanded at 309.93 ± 23.19 min and in Group L was at 168.30 ± 12.32 min. The difference in the two groups was highly significant (P< 0.001).
Conclusion: Sevoflurane provides clinically acceptable intubating conditions and can be a suitable alternative to propofol-suxamethonium for endotracheal intubation in children.

Keywords: Levobupivacaine, Levobupivacaine, Dexmedetomidine, Infraumbilical Surgeries, Spinal Anesthesia

Introduction
As we are moving ahead in time, there is renewed interest in the use of regional anesthesia techniques for a number of common surgeries replacing the general anesthesia [1]. Regional anesthesia has many benefits over general anesthesia as it eliminates the pain both intraoperatively and postoperatively, provides excellent muscle relaxation, and reduces intraoperative bleeding [2]. Regional anesthesia techniques are also superior to systemic opioid agents with regard to analgesia profile and adverse effects [3]. Spinal anesthesia is the most commonly used technique due to its unmatchable reliability, simplicity, and cost-effectiveness. It provides a fast and effective onset of sensory and motor block, excellent muscle relaxation, and prolonged postoperative analgesia [4]. Due to decreased cardiovascular and central nervous system toxicity, levobupivacaine is a good alternative [5]. This could also have led to reduction in the proportion of cases of inhalation agent-related cardiovascular depression resulting in cardiac arrest in the United States [6]. The introduction of sevoflurane into clinical anaesthetic practice started in Japan in May 1990, and by 1993, one million patients had received it [7]. Since then, its use has superseded the use of halothane for inhalational induction and intubation in paediatric anaesthesia. Several studies have compared intubation in children without the use of muscle relaxants. These studies employed sevoflurane with or without nitrous oxide in oxygen. Others employed use of sevoflurane with opioids and also in combination with propofol and benzodiazepines such as midazolam [8-11]. All these combinations showed comparable conditions with the traditional use of suxamethonium which is thought to provide the optimal condition for tracheal intubation [12-15].

Materials and Methods

Inclusion criteria included ASA I or II and elective procedures lasting <90 min. The exclusion criteria were ASA III or IV, anticipated difficult airway, known allergy to study drugs and those patients who could not be intubated after two attempts at laryngoscopy. Regarding sample size calculation, Blair *et al.* [5] reported that the excellent intubating conditions which occurred in 45% of patients were achieved with a combination of 8% sevoflurane and 60% nitrous oxide [5]. An acceptable intubation success rate of 80% was considered clinically significant in this study. We assumed that sevoflurane will provide clinically acceptable conditions for endotracheal intubation comparable to propofol-suxamethonium in children. All patients received diazepam 0.2 mg/kg orally, the night before surgery. The patients were preloaded with Lactated Ringer's solution 15 mL/kg. They were monitored with automated noninvasive blood pressure, pulse oximetry, and electrocardiogram. Oxygen was given at the rate of 5–6 L/min through a face mask. The anesthesiologist performing the technique recorded the intraoperative data and followed the patient postoperatively until discharged from post anesthesia care unit. Assessment of sensory block by the loss of sensation to pinprick of 22 gauge blunt hypodermic needle and motor block by modified Bromage score [10] was done every 2 min for first 10 min, then every 5 min up to 30 min, every 15 min up to 120 min, half-hourly up to 240 min, and hourly until 12 h of surgery. Continuous multi-parameter monitoring of respiratory rate, heart rate, noninvasive systolic and diastolic blood pressure, SpO2, and electrocardiogram was done for hemodynamic response. Readings were recorded preoperatively, then intraoperatively at 0, 3, and 5 min, then at an interval of every 5 min up to 30 min, every 15 min up to 120 min, half-hourly up to 180 min, hourly until 12 h, and thereafter 3 hourly till 24 h of surgery in both the groups. Bradycardia (defined as heart rate <60 bpm) was treated with injection atropine sulfate intravenously according to heart rate. Hypotension (defined as systolic blood pressure <20% less than base value) was treated with intravenous ephedrine intravenously as per required and additional Ringer's lactate solution. The operation was started when surgical anesthesia (up to the T10 sensory dermatome) has developed. In case of failed or partial neuraxial block, the patient was given general anesthesia and that patient was excluded from the study.

Results

The mean age, sex, weight, ASA grading, duration of surgery, baseline parameters, and quality of surgical analgesia were comparable in the two groups as shown in Table 1.

Table 1: The mean age, sex, weight, ASA grading, duration of surgery, baseline parameters, and quality of surgical analgesia were comparable

Parameters	Group L	Group LD	P	Significance
Age (years)	42.9±14.4	42.64±14.71	0.865	NS
Sex				
Male	23	25	0.43	
Female	17	15		
Weight distribution	67.29±9.31	68.68±9.42	0.546	NS
ASA grading (%)				
Grade I	75	65	0.418	
Grade II	35	45		
Duration of surgery	58.45±6.61	58.03±7.14	0.745	NS
Heart rate (/min)	83.11±6.20	83.61±8.92	0.778	NS
Systolic blood pressure (mmHg)	129.01±5.9	125.50±13.04	0.146	NS
Diastolic blood pressure (mmHg)	80.22±9.51	79.75±8.40	0.826	NS
Saturation of peripheral oxygen (%)	98.68±0.61	99.55±0.68	0.833	NS
Respiratory rate (/min) (mean±SD)	17.04±2.05	18.22±0.91	0.529	NS

In Group LD, increase in VAS was observed at 210 min and the first dose of rescue analgesia was given at 5th h postoperatively. The second dose of recue analgesia was given at 12th h and the third dose was given at 21st h. Postoperative VAS scores at different time intervals were significantly lower in Group LD than Group L, thus indicating superior analgesia. The time of request of the first dose of rescue analgesia was delayed in Group LD as it was demanded at 309.93 ± 23.19 min and in Group L was at 168.30 ± 12.32 min. The difference in the two groups was highly significant ($P < 0.001$). A dose-dependent reduction in rescue analgesia requirements was noted in our study.Anumber of rescue analgesia doses were 3.60 ± 0.49 in Group L, whereas 2.90 ± 0.31 in Group LD and the difference was highly significant ($P < 0.001$) [Table 2].

Table 2: Visual analog scale score and rescue analgesia in postoperative period

VAS score postoperative period (mean±SD)			Rescue analgesia (mean±SD)		
	Group L	Group LD	P Value	Group L	Group LD
90 min	0.000±0.0000	0.000±0.0000	0.000±0.0000	0.000±0.0000	90 min
105 min	0.101±0.3055	0.034±0.1829	0.308	0.000±0.0000	0.000±0.0000
120 min	0.803±0.8471	0.435±0.6792	0.070	0.000±0.0000	0.000±0.0000
150 min	2.835±2.5108	0.201±0.4069	<0.0001	0.236±0.4305	0.000±0.0000
180 min	3.968±2.6295	0.738±0.7399	0.000	0.669±0.4798	0.000±0.0000
210 min	3.436±1.2785	2.464±1.0086	0.002	0.135±0.3459	0.000±0.0000
4 h	2.269±0.9075	3.106±0.8851	0.001	0.000±0.0000	0.000±0.0000
5 h	0.000±0.0000	3.339±1.0615	0.000	0.000±0.0000	0.368±0.4903

6 h	0.000±0.0000	1.805±1.3236	0.000	0.000±0.0000	0.634±0.4905
7 h	0.035±0.1829	0.868±0.7764	0.000	0.000±0.0000	0.000±0.0000
8 h	0.435±0.7740	0.069±0.2539	0.018	0.000±0.0000	0.000±0.0000
9 h	3.403±2.1924	0.304±0.5966	0.000	0.234±0.4306	0.000±0.0000
10 h	2.636±1.6299	1.302±0.9525	0.000	0.469±0.5078	0.000±0.0000
11 h	1.105±2.7295	2.706±1.0559	0.000	0.202±0.4069	0.306±0.4668
12 h	0.468±2.2526	2.708±1.8419	0.000	0.104±0.3056	0.635±0.4908
15 h	2.336±1.7489	0.536±1.1369	0.045	0.269±0.4499	0.068±0.2534
18 h	2.606±1.8864	2.834±1.3669	0.589	0.634±0.4905	0.506±0.5089
21 h	2.203±1.4950	1.934±2.0501	0.121	0.168±0.3791	0.468±0.5072
24 h	4.001±1.4629	2.569±1.6755	0.001	0.501±0.5088	0.234±0.4305

None of the patients of Group L had urinary retention while it was observed in only 3% of patients of Group LD and the difference was statistically nonsignificant. Other side effects such as pruritus, nausea, vomiting, headache, backache, local anesthetic toxicity, and respiratory depression were not recorded in any of the patients of both the groups.

Discussion

In which induction time was longer revealed that total time to completion of intubation was 6.7 min (402 s) compared to this study which was 4.1 min (247.18 ± 64.66 s). This longer time might be due to non-use of opioid analgesic and the use of TEC3 vaporiser (maximum sevoflurane that can be delivered was 7%) compared to TEC 7 used in this study which can deliver a maximum of 8%.In Blair *et al*.'s study and Sabapathy *et al*.'s study, [8, 16] the success rate of acceptable clinical conditions for intubation using 8% sevoflurane in 60% nitrous oxide and oxygen was 87.5%. This study demonstrated a higher success rate where all the patients had acceptable clinical conditions for intubation. These studies used a fixed induction time for intubation (150 and 180 s, respectively); their high success rate despite short induction time could be attributed to overpressure technique in which the circuit was primed with sevoflurane. In this index study, conventional incremental dosing was used so that the children could tolerate the agent and prevent excitement associated with overpressure technique. The quality of tracheal intubation as determined by Helbo–Hansen score which is a score of 1–4 in each criterion and included laryngoscopy, vocal cords position, coughing and limb movements [See Appendix 1] [17]. Excellent intubating conditions is a score of 3–4, good intubating conditions is a score of 5–6, while 9–12 is considered poor and 13–16 is bad. Excellent and good scores are considered as clinically acceptable, fair and poor scores are considered as clinically unacceptable. Blair *et al*. [8] demonstrated that excellent intubating conditions- which was a score of 1 in each criterion-were achieved in 70% of the propofol suxamethonium group in 45% of the sevoflurane group. In this present study, excellent intubating condition score was seen in 84.8% of patients in propofol-suxamethonium group and 45.5% in sevoflurane group. The excellent intubating conditions were similar in sevoflurane groups of both studies, but lower value of 70% obtained in their propofol-suxamethonium group could be attributed to the lack of analgesics used in their study whereas our patients were given intravenous fentanyl 2 µg/kg before intubation in this study. Analgesics, especially opioids, have been shown to deepen anaesthesia and attenuate laryngopressor response. Excellent intubating conditions were seen in 100% of patients in a study by Kumar *et al*., [18] sevoflurane was used for induction and intubation following apnoea at 4.5 min, and then, intravenous propofol 1 mg/kg was administered. Thereafter, laryngoscopy and intubation were done at 5.5 min [18]. This high success rate could be attributed to the use of sevoflurane till the patients were apnoeic at 4.5 min and use of propofol which causes apnoea in all their patients. Propofol also causes suppression of pharyngeal and laryngeal reflexes. Local anesthetic agents act by blocking sodium channels. The prolongation of effect may result from synergism between local anesthetic and á2-adrenoceptor agonist, while the prolongation of the motor block of spinal anesthetics may result from the binding of á2-adrenoceptor agonists to motor neurons in the dorsal horn [19]. Intrathecal á2-receptor agonists have been found to have antinociceptive action for both somatic and visceral pain [20]. Fentanyl is a lipophilic µ-receptor agonist opioid. Intrathecally, fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of spinal cord and [21] may have a supraspinal spread and action. The use of intrathecal clonidine has been studied with local anesthetics [22]. Studies using a combination of intrathecal dexmedetomidine and local anesthetics are lacking. In our study, the intrathecal dose of dexmedetomidine selected was based on previous animal studies [23]. A number of animal studies conducted using intrathecal dexmedetomidine at a dose range of 2.5–100 µg did not report any neurologic deficits with its use [24-28]. There was no statistical difference in change in the respiratory rate at different time intervals between the two groups ($P > 0.05$). This lack of respiratory depression with dexmedetomidine has also been demonstrated in studies done by Esmaoğlu *et al*. [29] and Basuni and Ezz [30]. Similarly, the mean heart rate at various intervals intraoperatively was found to be comparable in both the groups. The mean dose of atropine given in Group LD was 1.7 mg and in Group L was 1 mg. It was in accordance with a study conducted by Esmaoğlu *et al*. [29] Basuni and Ezz [30] observed bradycardia in 3.3% of patients in levobupivacaine and dexmedetomidine group, whereas it was in 13% of patients in our study. This can be explained by the fact that dose of levobupivacaine used in the study by Basuni and Ezz was 4 mg, whereas the dose was 15 mg in the present study. However, there was no statistically significant difference in the mean heart rate of both the groups during the perioperative and postoperative period ($P > 0.05$) in both the studies. The addition of dexmedetomidine to levobupivacaine intrathecally does not cause significant hypotension as was observed in studies done by Esmaoğlu *et al*. [29] and Raval and Chaudhary [31]. The time to onset of sensory block was decreased with the addition of dexmedetomidine to levobupivacaine in the present study and the same was observed by Dizman *et al*. [32] and Sathitkarnmanee T *et al*. [33].

Conclusion

Sevoflurane provides clinically acceptable intubating conditions and can be a suitable alternative to propofol-suxamethonium for endotracheal intubation in children. Although sevoflurane is not as effective as propofol-suxamethonium for endotracheal intubation in children, it could be used as an alternative in elective procedures. We recommend the use of sevoflurane to facilitate intubation in elective procedures in children. It is concluded from our study that both the groups were effective in providing surgical anesthesia and hemodynamic stability, but Group LD was better than Group L as regards:

- Early onset of sensory and motor block
- Prolonged duration of sensory and motor block
- Longer duration of postoperative analgesia
- Lesser number of doses of rescue analgesia required.

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