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Emergence and Recovery Characteristics After Low Flow Anaesthesia With Desflurane and Sevoflurane in Cancer Patients Administered Combined Epidural and General Anaesthesia.

Mesha Srivastava[1], Itee Chowdhury[2], A.K. Bhargava[3]

[1]Senior resident, Department of Anaesthesiology, ESIPGIMSR, Manicktala, Kolkata.
[2]Senior consultant,Department of Anaesthesiology, Rajiv Gandhi cancer institute and research centre ,Delhi.
[3]Director and Head, Department Anaesthesiology, Rajiv Gandhi cancer institute And research centre,Delhi.

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ABSTRACT

Background: Desflurane and sevoflurane have low blood gas partition coefficients which lead to rapid emergence at the end of surgery. Epidural administration of local anaesthetics and opioids decreases minimum alveolar concentration (MAC) of inhalational anaesthetics. Aim: To compare emergence and recovery characteristics after low flow anaesthesia with desflurane and sevoflurane in cancer patients administered combined epidural and general anaesthesia. **Methods**: Randomised controlled trial was conducted with 30 patients each in desflurane or sevoflurane groups. Volatile anaesthetic concentration was titrated to 0.8MAC and epidural infusion of 0.25% bupivacaine and 2µg/ml fentanyl at 8 ml/hr was administered. Immediate and intermediate recovery parameters were compared. **Results:** Mean duration of anaesthesia was comparable and more than four hours. Immediate recovery parameters were significantly shorter for desflurane ($p<0.01$). Intermediate recovery parameters namely Modified Aldrete Recovery Score and digit symbol substitution test were higher in desflurane group but the difference was not statistically significant. Postoperative VAS scores were minimal and comparable. Adverse effects were limited to nausea and vomiting. The intraoperative haemodynamics were stable. **Conclusion**: Low flow anaesthesia with volatile anaesthetic concentration titrated to 0.8MAC and epidural infusion of 0.25% bupivacaine and 2µg/ml fentanyl provides optimum intraoperative anaesthesia for patients undergoing cancer surgeries. Immediate recovery and wake-up in long duration surgeries is faster with desflurane but does not have any clinical advantage. Intermediate recovery and time to discharge from postoperative care unit is comparable.

Keywords: Inhalational, postoperative recovery, desflurane, sevoflurane.

INTRODUCTION

Rapid emergence and faster recovery from anesthesia is an anesthesiologist's aim. Newer volatile anaesthetic agents like desflurane and sevoflurane have significantly lower blood/gas partition coefficient (0.45 and 0.65 respectively) which facilitates rapid emergence from anaesthesia.[1,2] The clinical advantages due to favourable pharmaco kinetic properties of desflurane has been proved beyond doubt after short duration desflurane anesthesia in day care surgeries as well as major surgeries lasting 90-120 minutes,[14-18] but increased duration of anesthesia may amplify pharmacokinetic profile difference between halogenated agents of different solubilities.

Name & Address of Corresponding Author
Dr. Mesha Srivastava
Senior Resident,
Dept. of Anaesthesiology.

Epidural bupivacaine and lignocaine reduce the amount of inhalational agent required for maintanence of anesthesia. This may be either due to deafferentation caused by the local anaesthetic or direct rostral spread within the cerebrospinal fluid.[5] Most of the previously published studies comparing emergence with sevoflurane and desflurane have not used epidural blocks to supplement anaesthesia and thus have targeted a minimum alveolar concentration (MAC value) of 1-1.2.

The aim of this prospective randomized study was to compare the emergence and recovery parameters of desflurane and sevoflurane in cancer patients administered combined epidural and general anaesthesia for abdominal surgeries.We hypothetised that use of epidural analgesia for long duration surgeries may minimize the difference in recovery profile of patients anaesthetized by desflurane and sevoflurane.

MATERIALS AND METHODS

After getting approval from Institutional Ethics Research Committee and written informed consent, a prospective randomized trial was conducted on 60 patients aged 35-55 years belonging to American Society of Anaesthesiology (ASA) physical status classification I-III. All were scheduled for elective abdominal cancer surgeries. Patients with preoperative haematocrit<25%, significant coronary artery disease, chronic pulmonary disease, renal failure/hepatic dysfunction, body mass index>30 or neuropsychiatric illness were excluded from the study.

Patients were randomly allocated into two equal groups:

Group D: Inhalational anaesthesia with desflurane (2-6%)/nitrous oxide (66%)

Group S: Inhalational anaesthesia with sevoflurane (0.6-1.75%)/nitrous oxide (66%)

All patients were premedicated with oral ranitidine hydrochloride (150 mg HS and 6 AM), alprazolam (0.5mg HS) and granisetron (2mg at 6 AM). Prior to induction an epidural catheter was placed in T8-T10 intervertebral space in lateral position by using 18 G Touhy needle with loss of resistance technique. After negative test dose (3 ml of 2% lignocaine and 5µg/ ml adrenaline) for blood and CSF an initial bolus of 10 ml of 0.25% bupivacaine and 2µg/ml fentanyl was given followed by a continuous infusion of 8 ml/hr.

Patients were induced with midazolam (0.02 mg/kg) intravenous (iv), fentanyl citrate (2 µg/kg) iv, and propofol (1-1.5 mg/kg) iv and trachea intubated after relaxation with atracurium besylate (0.5 mg/kg) iv. Oxygen saturation, end-tidal CO2 concentration, electrocardiogram (lead II and V5), non-invasive blood pressure (NIBP), temperature, urine output, central venous pressure and minimum alveolar concentration of inhalation agent (MAC) was monitored. The inspired concentration of volatile anaesthetic agents was adjusted to achieve an end tidal concentration of 0.8 MAC in a total gas flow of 2 litre/minute. Acute haemodynamic changes (±20% of baseline) were managed by a 25% change in end tidal concentration of volatile agent. Additional doses of fentanyl (0.5 micrograms/kg, maximum of 5ug/kg throughout the surgery) were administered if the increase of heart rate and blood pressure persisted even after raising the inspired concentration of inhalational agent. Atracurium besylate infusion was used to maintain a single twitch in train of four (TOF). Surface warming (Warmer-Bair Hugger –W arming Unit –Model 505) and fluid warmer (HL-9023O V Level 1Hotline Smiths fluid warmer) were used. At the end of surgery neuromuscular blockade was reversed with neostigmine bromide 0.05mg/kg and glycopyrrolate 0.08mg/kg IV.

Variables noted to compare "immediate recovery"were as follows:

T0-Discontinuation of inhalation anaesthetic agent

T1-Time to spontaneous movement (swallowing, spontaneous eye opening, limb movements)

T2-Time to establishment of regular spontaneous breathing pattern

T3-Time to respond to verbal commands (eye opening/ tongue protrusion)

T4-Time to extubation

T5-Time to state name on command

T6-Time to state date of birth on command

T7- time taken to squeeze examiners fingers on command

Variables used to compare "intermediate recovery"were:

1) Modified Aldrete Recovery Score (MARS): It was measured every 5minutes from the time of discontinuation of inhalational agent (T0) until optimal score (Score9) and then subsequently at 15 minute intervals for the first 45 minutes.
2) Digit Symbol Substitution Test (DSST) was also assessed at the same time intervals

VAS Score and any other side effect (nausea, vomiting,breath holding,laryngospasm or agitation) were also recorded.

Statistical analysis

Time taken to achieve a Modified Aldrete Recovery Score of 9 was used to calculate sample size. For a power of 0.8 and p value of 0.05, power analysis showed that 45 patients would be required to demonstrate a difference of 5 minutes. We took 60 patients instead. Pearson Chi-square test was used for demographic data and Student's t-test for duration of anaesthesia, immediate and intermediate recovery parameters. Mann Whitney test was used for comparisons of VAS score and side effects.

RESULTS

The two groups were comparable with respect to demographic data and duration of anaesthesia [Table 1].

Table 1: Demographic data and duration of anaesthesia.

Demographic variables	Group D (Desflurane) (n=30)	Group S (Sevoflurane) (n=30)	P Value
Sex ratio (Male: Female)	3:27	2:28	0.64
Age(years)	47.8±4.7	47.4±6.0	0.77
Weight(kg)	61.7±8.6	57.9±7.3	0.07
Height(cms)	156.3±6.9	155.0±6.1	0.45
BMI Wt/ht^2(m)	25.3±3.6	24.0±2.4	0.11
Duration of anaesthesia (min)	286.5±21.8	277.3±21.0	0.10

All are in Mean±S.D. except sex ratio

Immediate recovery parameters were significantly shorter (p<0.01)for desflurane than sevoflurane (Figure 1).Time taken for MARS to reach 9 was 32±0.2 minutes and 37±0.1 minutes in patients administered desflurane and sevoflurane. Values of MARS was comparable at all time intervals. Thus,

no statistically significant difference was noted in the intermediate recovery [Table 2]. VAS scores measured in desflurane and sevoflurane groups at 15 minutes and 30minutes from T0 were minimal and comparable between the two groups; 1.8±0.92 vs 1.68±0.89 and 0.97±0.71 vs 0.97±0.78 respectively

Table 2: Intermediate recovery parameters.

Recovery Parameter		Group D	Group S	'P 'value
MARS	B1(15 min from T0)	7.97± 1.06	7.47± 1.07	0.076
	B2(30 min from T0)	8.60± 1.03	8.20± 1.09	0.152
	B3(45 min from T0)	9.40± 0.62	9.17± 0.69	0.177
Time taken for DSST Score to reach baseline value		26.50± 6.45	28.50± 4.57	0.171

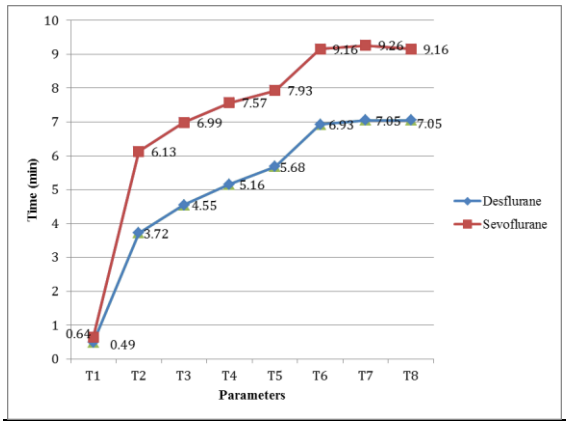

Figure 1: Comparison of immediate recovery parameters between the two groups.

Incidence of nausea was 13.3% with desflurane and 20% with sevoflurane; incidence of vomiting was 6% in both the groups. None of the patients in both the groups had any episode of post-operative laryngospasm, agitation or breathe holding. Intraoperative hemodynamics were stable.[Figure 2]

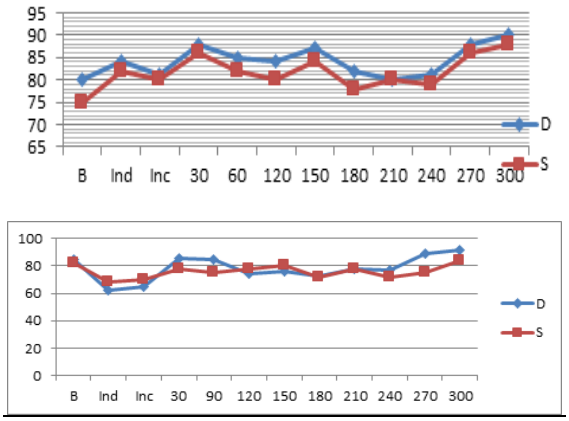

Figure 2: Heart rate and Mean arterial pressure (baseline (B), induction (Ind), Before incision (Inc), indicated times during maintenance of anaesthesia (mean (SD) P <O.O5).

DISCUSSION

We have performed a prospective comparision of emergence and recovery characteristics after general anaesthesia with sevoflurane and desflurane using low flow anaesthesia and titrated to 0.8MAC in patients undergoing long duration cancer surgeries .We obtained that immediate recovery and emergence was significantly faster with desflurane compared to sevoflurane. But no statistically significant difference exists in intermediate recovery and time to discharge from postoperative care unit.

Although numerous studies lasting for 90-120 minutes,[40,41,,48,51,55-57] and others lasting greater than 180 minutes have proved that recovery is faster with desflurane than sevoflurane,[42,43,47,49] we conducted our study with the aim to compare recovery between the two volatile agents after prolonged oncological surgery. Prolonged duration of anaesthesia is also known to delay emergence due to tissue uptake of the anaesthetic agent and so we compared recovery profiles in this subset of patients.

In our study,a baseline anesthetic regimen was used with both groups to avoid the potential differences between the two groups. Similar intraoperative medications (Fentanyl, bupivacaine infusion, atracurium) were used in the two groups. ._Fentanyl is a potent synthetic narcotic analgesic with a rapid onset and short duration of action, as compared to morphine which has more cumulative effect.

Desflurane and sevoflurane have low blood gas partition coefficients; 0.42 and 0.69 respectively. Average emergence time after desflurane has been reported to be half that of sevoflurane in patients undergoing pulmonary surgery.[6] We in our study used seven different parameters to assess immediate recovery and compared time intervals to achieve the same between the two groups. Recovery with sevoflurane was significantly delayed in all the seven parameters and was 1.3-1.6 times that with desflurane.

For the assessment of intermediate recovery, although the Modified Aldrete scores were higher for desflurane group at all time points,but the difference was not significant statistically. Similarily for DSST, though the baseline score was achieved 2 minutes earlier in the desflurane group ,but it was not statistically significant.

Our results are consistent with the results of Strum et al (2004) who studied the emergence and recovery characteristics in morbidly obese patients (lasting for about 4 hours)and with Heavner (2003)who did their study on elderly patients (lasting for 2 or more hours).[47,49] Emergence characteristics in the ambulatory settings with oxygen and air as the carrier gases are however different from the results of our study.[7] Both early and intermediate (psychomotor) recovery were significantly early with desflurane. Difference in results could be due to

the use of short acting drugs like propofol and alfentanil and minor operative interventions in the form of video arthroscopic knee surgeries in this study. In our study the mean surgical duration was more than 4 hours and major oncosurgical procedures were performed in all the patients.

Postoperative recovery and cognitive function has been compared in patients receiving sevoflurane or desflurane for excision of supratentorial expanding intracranial lesions by Magni et al.[8] Time taken for eye opening was similar but significant shorterextubation and recovery times were noted with desflurane. The Short Orientation Memory Concentration Test score differed between the two groups only at one point of time i.e.15 min after extubation. They targeted an anaesthetic depth of 1.2 minimum alveolar anesthetic concentration (MAC) values whereas we had used 0.8 MAC and this could partly account for the difference in the results. However differences in postoperative cognitive recovery with the two anaesthetic agents was more marked in overweight and obese patients undergoing craniotomy.[4] Thus, relative advantage of desflurane in terms of recovery profiles are more prominent in patients with obesity.

Lower end-tidal concentrations of sevoflurane were required when general anaesthesia was supplemented with caudal bupivacaine in paediatric patients.[9] Lidocaineadministered for epidural anesthesia has been reported to reduce the MAC of sevoflurane by approximately 50%.[5] Epidural morphine reduces the MAC of halothane by 28% and isoflurane by 14%.[10,11] Strum et al had supplemented general anaesthesia with epidural analgesia for open surgical procedures in morbidly obese patients.[6] But he administered age adjusted 1 MAC end-tidal concentrations of inhalational agents (desflurane/sevoflurane) and did not account for the MAC sparing effect of epidural local anaesthetics and opioids. None of the other studies comparing emergence with sevoflurane or desflurane have used epidural analgesia. Ours is the first to account for all the interactions and is thus a reflection of what is actually practiced in the operation theaters.

None of our patients developed any hemodynamic instability. No patient showed any sign of inadequate anaesthesia in the form of tachycardia or hypertension. Thus, no patient needed an increase in inhalational anaesthetic delivery or supplemetal dosage of fentanyl. Nausea was reported in 13.3% of the patients in desflurane group and 20% patients in the sevoflurane group; $p<0.05$whereas vomiting was experienced by 6.6% of patients in both the groups. None of the patients in either groups had any episode of post-operative laryngospasm, agitation or breath holding. This is in contrast to a study by Karlsenet al who reported a higher incidence of postoperative nausea/vomiting rate (24 hour in PACU and ward) with desflurane (67%) and sevoflurane (36%).[12] The combined approach of administering intraoperative opiates, local anesthesia, and NSAIDs is associated with significantly shorter discharge times, lower pain scores, and a lower incidence of nausea and vomiting, compared with traditional opiate-based anesthetic technique.

Limitations of this study are due to its inherent design which does not permit a double-blind comparison of the two volatile anaesthetics. However, all patients were undergoing identical anaesthetic management with 0.8MAC value as the target. A cost analysis with the use of the two agents was not a part of this study. The cost saving due to lesser use of inhalational anaesthetics with the combined approach and low flow anaesthesia with sevoflurane and desflurane could have further supported the use of one over the other. Sex distribution in our study was comparable between the two but not equally distributed between the two genders. More than 90% of the patients were females. Women generally report greater sensitivity to pain than do men but study by Wadhwa et al establish that MAC of desflurane does not differ in young, healthy men and women.[13] Similar studies conducted with sevoflurane do not suggest any influence of gender on hypnotic requirements.[14]

We conclude that use of epidural infusion of local anaesthetic and opioid permits a reduction in the amount of inhalational anaesthetic administered for optimum intraoperative anaesthesia. Immediate recovery and emergence is faster with desflurane when administrated using low flow anaesthesia and titrated to 0.8MAC in patients undergoing long duration cancer surgeries. But no statistically significant difference exists in intermediate recovery and time to discharge from postoperative care unit. Thus the clinical benefits of an early wake up are limited to neurosurgical cases where rapid awakening facilitates neurological assessment but has no clinical advantages for patients operated for malignancies.

CONCLUSION

Low flow anaesthesia with volatile anaesthetic concentration titrated to 0.8MAC and epidural infusion of 0.25% bupivacaine and 2µg/ml fentanyl provides optimum intraoperative anaesthesia for patients undergoing cancer surgeries. Immediate recovery and wake-up in long duration surgeries is faster with desflurane but does not have any clinical advantage. Intermediate recovery and time to discharge from postoperative care unit is comparable.

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