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A COMPARATIVE STUDY OF RECOVERY CHARACTERISTICS FOLLOWING DESFLURANE VERSUS SEVOFLURANE ANAESTHESIA FOR LONG DURATION OF SURGERY IN ELDERLY PATIENTS

Anaesthesiology

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ABSTRACT

Introduction: Delayed postoperative recovery is common in elderly patients due to physiological changes of aging with varied post-operative Haemodynamic complications. Post operative cognitive decline or dysfunction may occur following general anaesthesia, and patients may develop dementia following general anaesthesia. Some investigation reports similar post operative cognitive dysfunction incidence with sevoflurane and desflurane while others reported mild cognitive impairment with sevoflurane. Present study was undertaken to compare recovery characteristics following desflurane versus sevoflurane anaesthesia for long duration surgery in elderly patients.

Objectives: To assess and compare the recovery characteristics following Desflurane and Sevoflurane anaesthesia for long duration surgery in elderly patients, to compare Hemodynamic variables and side effects after their administration.

Methods: A Prospective study was carried out on 60 patients, divided randomly into 2 groups of 30 patients each,
Group D received Desflurane maintenance anaesthetic agent;
Group S received Sevoflurane maintenance anaesthetic agent

Result: After stopping anaesthetic agents, time to respond to painful stimulus was 4.3 min in Group D and 7.0 min in Group S, Time to respond to verbal command was 5.3 min in Group D and 8.2 min in Group S, Time to spontaneous eye opening was 5.7 min in Group D and 8.7 min in Group S, Time to respond by telling name was 7.4 min in Group D and 10.7 min in Group S, Time to limb lift was 8.7 min in Group D and 13.30 min in Group S. Modified Aldrete Score was 7.6 at arrival, 8.8 at 5 min, 9.5 at 10 min in Group D and 7.0 on arrival, 8.0 at 5min, 8.9 at 10 min in Group S.

Conclusion: Post operative recovery was earlier with Desflurane as compared with the use of sevoflurane anaesthetic agent in elderly patients undergoing long duration surgery.

KEYWORDS

Sevoflurane, Desflurane, Recovery, Elderly patient

INTRODUCTION:

A delayed postoperative recovery is common in elderly patients due to physiological changes of aging. Post-operative Haemodynamic complications are also more common. Increased sensitivity to drugs is common in elderly patients, and interindividual variability in drug responses results in differing sensitivity. These factors make predicting precise doses difficult. Post operative cognitive decline or dysfunction (POCD) may occur following general anaesthesia, and patients may develop dementia following general anaesthesia. Some investigation reports similar post operative cognitive dysfunction incidence with sevoflurane and desflurane while others reported mild cognitive impairment with sevoflurane. Therefore, cognitive dysfunction after desflurane and sevoflurane need to be studied. Moreover, a shorter emergence time following desflurane maintenance anesthesia than sevoflurane has been reported [5,7,8]. Anaesthetic concentration has been guided by use of age-adjusted estimations of minimum alveolar concentrations (MAC). MAC fraction is the ratio of anaesthetic concentration divided by MAC for the specific agent, and is used to facilitate assessment of clinical differences between inhaled anaesthetics. Many studies had been done previously to assess recovery and haemodynamic profiles of maintenance anaesthesia with desflurane and sevoflurane. We planned comparative study on recovery characteristics following desflurane versus sevoflurane anaesthesia for long duration surgery in elderly patients, to study effect of drug on haemodynamic variables and to observe side effect of drug.

AIMS AND OBJECTIVES:

1. To assess and compare the recovery characteristics following Desflurane and Sevoflurane anaesthesia for long duration surgery in elderly patients.
2. To study the effect of both the drugs on Haemodynamic variables (HR, BP).
3. To observe for any adverse events related to study drug.

METHODOLOGY:

STUDY DESIGN: - A randomized, prospective and controlled study was done. 60 patients were divided into two equal groups, of 30 each Group D, patients receiving Desflurane maintenance anaesthetic agent 6% for initial 6 min, then 3% to 4% till end of surgery Group S, patients receiving Sevoflurane maintenance anaesthetic agent 1% to 2% till end of surgery

INCLUSION CRITERIA: Patients of age >55years
Sex: both gender
Patient giving Written and informed consent
ASA GRADE 1 and GRADE 2 patients
Patient undergoing long duration surgery

EXCLUSION CRITERIA:
Those with clinically significant cardiovascular, respiratory, hepatic, renal, neurologic, psychiatric or metabolic disease.
ASA GRADE 5, GRADE 4 and GRADE 3 patients
Pregnant women
Morbid obesity
Coagulopathy
History of infection and malignant disease
History of allergic reaction

A pre-anaesthetic assessment was done in all patients which included a detailed History, General physical and Systemic Examination and Routine Investigations: Complete blood count, Chest x-ray, ECG, Renal function test, liver function test, Blood sugar, serum electrolytes day before surgery. Patients were kept nil by mouth (NBM) for 6 hours. On the day of surgery after taking written informed consent. After arrival in operating room, Routine and standard monitoring like ECG, pulse oximetry, NIBP applied and baseline values noted in operation theatre. Intravenous access established using 18G or 20G cannula.

Patients in both groups were Premedicated with inj. Glycopyrrolate IV 0.004mg/kg, Inj. Emset IV 0.15mg/kg and Inj. Fentanyl IV 2mcg/kg. Preoxygenation with 100% o2 done for 3-5 minutes. Induction was done with Inj. Propofol 2 mg/kg, Inj. Succinylcholine 2 mg/kg IV and airway was secured with cuffed endotracheal tube. Anaesthesia was maintained with Muscle relaxant – Inj. Vecuronium 0.1mg/kg loading dose and incremental dose 0.05mg/kg and O2 50%+N2O 50%+ DESFLURANE in Group D OR O2 50%+N2O 50% + SEVOFLURANE in Group S. After completion of surgery, residual neuromuscular blockage was reversed with Inj.

Neostigmine 0.05mg/kg and Inj.Glycopyrrolate 8µg/kg IV. Patient was extubated when a regular spontaneous breathing pattern was re-established. After thro ugh oral and endotracheal suction cuff deflated, tube removed, and extubation time was noted.

In all cases, Desflurane and Sevoflurane was discontinued when the last skin suture taken. Spontaneous breathing, Eye opening, and Extubation time were measured from time of termination of anaesthetic gas.

PARAMETERS TO BE OBSERVED

1) RECOVERY PROFILE OF PATIENT AFTER STOPPING MAINTENANCE ANESTHETIC AGENT

- Response to painful stimuli
- Response to Verbal commands,
- Spontaneous eye opening,
- Response by telling name
- Limb lift
- Modified Aldrete Score was recorded on arrival in recovery room, 5 min and 10min.

2)HEMODYNAMIC PARAMETERS after stopping of inhalational agents, immediate after extubation and at 1,2,5 min post extubation
3) Any intraoperative postoperative complications developed due to inhalational anaesthetic agents

ANALYSIS: Results are expressed as mean +/- SD. For qualitative data chi-square test was applied and for quantitative data students t-test was applied. The level of significance was taken as P<0.05.

RESULTS:

(1) RESPONSE TO PAINFUL STIMULUS

Table no 1

Responds to painful stimulus	Desflurane(mins)	Sevoflurane(mins)
Mean	4.300	7.033
Standard deviation	1.317	1.564
Standard error	0.2404	0.2856
Mean+/-SD	4.300+/-1.317	7.033+/-1.564
P value	<	0.0001

As shown in table no 1 response to painful stimuli was faster in patient receiving desflurane than sevoflurane and the results were statistically significant.

(2) RESPONSE TO VERBAL COMMAND

Table no 2

Follow verbal command	Desflurane	Sevoflurane
Mean	5.333	8.200
Standard deviation	1.422	1.690
Standard error	0.2596	0.3086
Mean+/-SD	5.333+/-1.422	8.200+/-1.690
P value	<0.0001	

As shown in table no 2 response to verbal command was faster in patient receiving desflurane than sevoflurane and the results were statistically significant.

3) SPONTANEOUS EYE OPENING

Table no 3

Spontaneous eye opening	Desflurane(mins)	Sevoflurane(mins)
Mean	5.700	8.733
Standard deviation	1.149	1.507
Standard error	0.2098	0.2752
Mean+/-SD	5.700+/-1.149	8.733+/-1.507
P value	<0.0001	

As shown in table no 3, time to spontaneous eye opening was faster in patients receiving desflurane than sevoflurane and the results were statistically significant in both groups.

4) RESPONSE BY TELLING NAME

Table no 4

Telling name	Desflurane(mins)	Sevoflurane(mins)
Mean	7.433	10.733
Standard deviation	1.357	1.660
Standard error	0.2478	0.3031
Mean+/-SD	7.433+/-1.357	10.733+/-1.660
P value	<0.0001	

As shown in table no 4, time to response by telling name was faster in patient receiving desflurane than sevoflurane and the results were statistically significant in both groups.

5) LIMB MOVEMENT AND LIFT

Table no 5

Telling name	Desflurane(mins)	Sevoflurane(mins)
Mean	8.667	13.300
Standard deviation	1.446	1.860
Standard error	0.2640	0.3396
Mean+/-SD	8.667+/-1.446	13.300+/-1.860
P value	<0.0001	

As shown in table no 5, time to spontaneous eye opening was faster in patient receiving desflurane than sevoflurane and the results were statistically significant in both groups.

6) HAEMODYNAMIC PARAMETERS:

Mean blood pressure

Table no 6

Mean blood pressure	Desflurane (mean+/-SD)	Sevoflurane (mean+/-SD)	P value
After stopping maintainace anaesthetic agent	88.1+/-7.783	89.2 +/ 9.102	0.616
After extubation	107.067+/-6.746	105.4+/-9.137	0.42
1min after extubation	100.533+/-6.377	99.6+/-7.356	0.602
3min after extubation	97.933+/-5.459	98.3+/-6.320	0.81
5min after extubation	97.667+/-5.320	97.967+/-6.620	0.85

Heart rate

Table no 7

Heart rate	Desflurane (mean+SD)	Sevoflurane (mean+SD)	P value
After stopping maintainace anaesthetic agent	88.167+/-7.144	84.5+/-7.793	0.0624
After extubation	111.2+/-8.497	103.8+/-9.636	0.0025
1min after extubation	101.333+/-9.760	95.167+/-7.996	0.0097
3min after extubation	96.1+/-7.622	90.0+/-6.571	0.0016
5min after extubation	92.7+/-6.758	87.33+/-8.083	0.0071

As shown in table no 6 and 7, Haemodynamic parameters heart rate and mean blood pressure measurement didn't vary significantly between patients receiving desflurane and sevoflurane anaesthesia. Postoperative haemodynamic parameters were comparable in both study groups. P value was not statistically significant.

7) Modified aldrete score

Table no 8

Modified aldrete score	Desflurane (Mean+/-SD)	Sevoflurane (mean+/SD)	P value
After arrival	7.667+/-0.711	7.033+/-0.66	0.0007
After 5 mins	8.866+/-0.73	8.066+/-0.639	<0.0001
After 10 mins	9.533+/-0.50	8.966+/-0.615	<0.0001

As shown in table no, it was concluded that achievement of higher aldrete score in comparable time was faster in patients receiving desflurane than sevoflurane. P value was statistically significant in both groups.

8) Post operative complications

Table no 9

Postoperative complications	Desflurane	Sevoflurane
Nausea and vomiting	3	2
Bradycardia	-	-
Respiratory depression	-	-
Convulsion	-	-

Dizziness	-	-

As shown in table no 9, nausea and vomiting in 3 patients following desflurane and in 2 patients following sevoflurane anaesthetic agent. Postoperative respiratory and haemodynamic complications did not occur in both groups.

DISCUSSION:

- **MECHANISM OF ACTION OF INHALATIONAL ANESTHETIC AGENTS:**

can be subclassified as macroscopic (brain and spinal cord), microscopic (synapses and axons), and molecular (pre- and post-synaptic membranes). Immobilizing effect of inhalational anaesthetic involves site of action at spinal cord. Sedation, hypnosis, amnesia involves supraspinal (amygdale, hippocampus, cortex) mechanisms. Inhaled anaesthetic agent may disrupt normal synaptic transmission by interfering with the release of neurotransmitters from pre-synaptic nerve terminal (enhance or depress excitatory or inhibitory transmission), by altering the re-uptake of neurotransmitters, by changing the binding of neurotransmitters to the post-synaptic receptor sites or by influencing the ionic conductance change that follows activation of the post-synaptic receptor by neurotransmitters. These agents have been shown to bind to and alter membrane proteins, to alter cellular calcium ion processes, and potentiation at GABA receptors and inhibition at N-methyl-D-aspartate (NMDA) receptors. The Meyer-Overton theory describes the correlation between lipid solubility of inhaled anaesthetics and MAC and suggests that anaesthesia occurs when a sufficient number of inhalational anaesthetic molecules dissolve in the lipid cell membrane. The Meyer-Overton theory postulates that it is the number of molecules dissolved in the lipid cell membrane, and not the type of inhalational agent, that causes anaesthesia.

- **DESFLURANE:** is a tetrafluoroethyl difluoromethyl ether, colourless, non-flammable, volatile liquid (below 22.8°C) administered via special vaporizer as an inhalational anaesthetic agent.

PHARMACOKINETICS: Desflurane has lowest blood gas solubility of all inhalational anaesthetic agents and thus results in fastest induction and recovery. It is almost exclusively eliminated through lungs.

PHARMACODYNAMICS:

Cardiovascular system effects: Desflurane causes dose dependent tachycardia associated with depression in myocardial contractibility and decrease in systemic vascular resistance from peripheral vasodilatation. Increase in concentration to greater than 1MAC causes increase in heart rate and blood pressure. Cardiovascular stimulation is greater with desflurane so during induction it may causes myocardial ischemia. It can be attenuated by small dose of opioid, clonidine or esmolol.

Central nervous system: Desflurane causes dose dependent cerebral vasodilatation thus increases CBF, cerebral blood volume and intracranial pressure at normotension and normocapnia. Cerebral oxygen consumption is decreased during desflurane anaesthesia. During periods of hypotension CBF is adequate to maintain aerobic metabolism despite low cerebral perfusion pressure. Desflurane produces a dose-dependent decrease in EEG activity. It does not produce convulsive activity in the EEG (as has been observed with enflurane).

Respiratory system: Desflurane is potent respiratory depressant. Desflurane causes decrease in tidal volume and increase in respiratory rate with overall reduction in minute alveolar ventilation. Unsuitable for induction because of its airway irritating property and may cause breath holding, coughing, increases secretion, laryngospasm during induction.

DOSE AND ADMINISTRATION: Desflurane can be administered by trained person. Only vaporizer specifically designed to deliver desflurane should be used for its administration. Facilities for maintenance of patent airway, mechanical ventilation, oxygen source should be available. MAC value of desflurane decreases with increasing age.

Induction In adults, a common starting concentration was 3% desflurane via inhalation, increased in 0.5-1.0% increments every 2 to 3 breaths. End-tidal concentrations of 4-11%, desflurane with and without N2O, produced anaesthesia within 2 to 4 minutes. When desflurane was used as the primary anaesthetic induction agent, the incidence of upper airway irritation (apnoea, breath holding, laryngospasm, coughing and secretions) was high. Inspired concentrations of desflurane greater than 12% have been safely administered to patients, particularly during induction of anaesthesia. Such concentrations dilute the concentration of oxygen; therefore, maintenance of an adequate concentration of oxygen may require a reduction of nitrous oxide or air if these gases are used.

Maintenance: Surgical levels of anaesthesia in adults can be maintained with concentrations of 2.5-8.5% desflurane with or without the concomitant use of nitrous oxide. Concentrations of desflurane exceeding 1 MAC may increase heart rate. Thus, with this drug, an increased heart rate may not serve reliably as a sign of inadequate anaesthesia. Desflurane is indicated for maintenance of anaesthesia in infants and children after induction of anaesthesia with agents other than desflurane, and tracheal intubation, In old age MAC of desflurane decreases.

- **SEVOFLURANE:**
- Is a Fluoromethyl 2,2,2, -trifluoro-1-(trifluoromethyl) ethyl ether, volatile liquid for inhalation, a non-flammable and nonexplosive liquid administered by vaporization, is a halogenated general inhalation anaesthetic drug. Sevoflurane acts as a positive allosteric modulator of the GABAA receptor in electrophysiology studies of neurons and recombinant receptors. However, it also acts as an NMDA receptor antagonist, potentiates glycine receptor currents, and inhibits Nicotinic ACh and 5- HT3 receptor currents.

- **PHARMACOKINETICS:** Sevoflurane has slightly higher blood gas solubility than desflurane and thus results in slightly delayed recovery than desflurane. Elimination of sevoflurane is also faster. Metabolism- sevoflurane undergoes metabolism via liver microsomal enzyme P450 2E1 isoform at rate 10-25 times higher than desflurane. Approximately 5% of absorbed sevoflurane is metabolized to hexafluoroisopropanol (HFIP), with release of inorganic fluoride and CO2 (or a one carbon fragment). Once formed, HFIP is rapidly conjugated with glucuronic acid and eliminated. Nephrotoxicity can occur because of rise in inorganic fluoride. However, there is no association between peak fluoride concentration and renal abnormality. Alkali such as barium hydroxide and soda lime can degrade sevoflurane and produce compound A (fluoromethyl -2,2-difluoro-1-[trifluoromethyl]vinyl ether) which is proven nephrotoxic.

- **PHARMACODYNAMICS:**
- Cardiovascular system: Sevoflurane causes mild depression of myocardial contractibility. Systemic vascular resistance falls slightly less than with isoflurane. sevoflurane may prolong QT interval.
- Respiratory system: Sevoflurane depresses respiration and reverse bronchospasm. Deepening of anaesthesia by increasing concentration causes loss of respiration in spontaneously ventilating patients.
- Central nervous system Sevoflurane may cause slight increases in CBF and intracranial pressure at normocarbia. cerebral metabolic oxygen requirement decreases and seizure activity not reported.
- Neuromuscular effect: potentiate effect of non-depolarizing muscle relaxant.
- Renal system: decreases renal blood flow. It's degradation products inorganic fluoride and compound A associated with decreased renal tubule function.
- Hepatic system: decreases portal vein flow and increases hepatic artery blood flow thereby maintaining total blood flow and oxygen delivery.

- **DOSES AND ADMINISTRATION:** Sevoflurane can be administered by trained person. Only vaporizer specifically designed to deliver sevoflurane should be used for its administration. Facilities for maintenance of patent airway, mechanical ventilation, oxygen source should be available. Hypotension and respiratory depression increase as anaesthesia with desflurane deepens.MAC value of sevoflurane decreases with increasing age.

- **Induction:** Sevoflurane has a non-pungent odour and does not cause respiratory irritability; it is suitable for mask induction.

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Induction with sevoflurane may be achieved in oxygen or in combination with oxygen-nitrous oxide mixtures. In adults inspired concentrations of up to 5% sevoflurane usually produce surgical anaesthesia in less than 2 minutes.

- **Maintenance:** Surgical levels of anaesthesia can usually be achieved with concentrations of 0.5 - 3% sevoflurane with or without the concomitant use of nitrous oxide. Sevoflurane can be administered with any type of anaesthesia circuit.

For long duration surgery, the use of anaesthetic drugs that maintain haemodynamic stability and allow fast changes in intensity while maintaining anaesthesia, early recovery and have no or minimal postoperative side effects are suggested[2,4] . Considering these characteristics, fast induction and early recovery based on low blood/gas partition coefficients is expected from newer inhalational agents' sevoflurane and desflurane compared with traditional agents like isoflurane, halothane and propofol. Early postoperative recovery is desired to prevent immobilization, complications associated with it like deep vein thrombosis and to reduce hospital stay.

Recovery characteristics following desflurane and sevoflurane anaesthesia in terms of time to respond to painful stimulus, eye opening, respond to verbal command; and respond by telling name and limb lift were significantly different in both groups.

Recovery following desflurane was significantly faster than sevoflurane group[3] . Desflurane is a highly fluorinated methyl ethyl ether used for maintenance anaesthesia. Recovery following desflurane is faster compared to sevoflurane because of low solubility in blood. Partition coefficients at 37°C blood/gas 0.424, brain/gas 0.54. Postoperative complications nausea and vomiting was observed in 3 patients of group D and patients of group S[1] . Other complications like bradycardia, convulsion, dizziness and respiratory depression were not observed in both groups[6].

CONCLUSION: From overall analysis of our study, it can be concluded that post operative recovery is earlier in patients receiving desflurane than sevoflurane in older patients undergoing long duration surgery. Lesser time is required to achieve response to painful stimulus, response to verbal command, spontaneous eye opening, response by telling name, limb movement and lift, and higher Modified Aldrete score is achieved rapidly in desflurane receiving patients. Therefore, Desflurane is preferred in older patients undergoing long duration surgery over sevoflurane.

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