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Original Research Article

Comparison of recovery profile between sevoflurane and isoflurane as volatile agents in neurosurgery in Indian population

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ABSTRACT

Background: In most instances rapid emergence from general anesthesia after intracranial neurosurgery is desirable. The most compelling reason for this is the need for the patient to cooperate with a postoperative neurological examination intended to screen for such potential intracranial disaster as hematoma formation, herniation, and cerebrovascular accidents. Anesthetic techniques were adopted to achieve rapid emergence. In this respect, inhaled anesthetic agents have an important role in influencing the recovery time after anesthesia and surgery. The aim of this study is to compare isoflurane and sevoflurane as regard to speed of recovery from anesthesia and recovery of post-operative cognitive function in Indian population

Methods: The study was carried out as randomized control, blinded study of patients undergoing neurosurgery in tertiary care hospital. Sample sizes of 60 patients were studied. They were divided into two groups.

Results: Sevoflurane shows faster emergence, extubation, motor control (in form of hand squeeze) and orientation time as compared to isoflurane. Though clinically the time difference for the various variables studied was 0.8 to 2.7 min only, statistically the results were significant and supported the basis for this difference as the difference in blood gas solubility coefficient between sevoflurane and isoflurane

Conclusions: Sevoflurane is recommended for use for faster extubation, emergence and post-operative neurological examination. The observation shows good brain relaxation with the use of both volatile anesthetic agents

Keywords: Halogenated anesthetics, Emergence, Blood gas solubility coefficient

INTRODUCTION

In most instances rapid emergence from general anesthesia after intracranial neurosurgery is desirable. The most compelling reason for this is the need for the patient to co-operate with a postoperative neurological examination intended to screen for such potential intracranial disaster as hematoma formation, herniation, and cerebrovascular accidents. Under these circumstances, residual anesthesia may give either false impression of a neurosurgical deficit or prevent the early diagnosis of a developing intracranial pathology. In complication like above a rapid diagnosis and treatment of same can reduce the post-operative morbidity and mortality in these cases. Anesthetic techniques were adopted to achieve rapid emergence. Since rapid emergence will help in these situations for a rapid diagnosis of any unwanted complication. In this respect, inhaled anesthetic agents have an important role in influencing the recovery time after anesthesia and surgery.[1] The aim of this study is to compare the clinical properties of halogenated anesthetic compound isoflurane

and sevoflurane as regard to speed of recovery from anesthesia and recovery of post-operative cognitive function in Indian population. Isoflurane has been used for long period in neurosurgery as volatile agent and its safety and other profile is well established. Sevoflurane is also halogenated compound supposed to have faster induction and recovery profile though quite expensive as compared to isoflurane.[1] This study specifically tries to study advantage of sevoflurane as compared to isoflurane in cranial neurosurgery as well as cost effectiveness. Faster emergence and rapid assessment of mental function is of utmost importance and as the blood gas solubility coefficient of sevoflurane is less than that of isoflurane and theoretically there has to be rapid emergence as compared to the use of isoflurane. The advantage of this rapid recovery for the assessment of mental status and cost effectiveness by using sevoflurane will be compared than use of isoflurane in same setting.[2]

METHODS

After obtaining permission from the hospital ethics committee at command hospital Lucknow the study was carried out at command hospital Lucknow between January-2020 to Jun 2021. It's a randomized control, double blinded study of patients undergoing neurosurgery in tertiary care hospital. Sample sizes of 60 patients were studied. They were divided into two groups. Randomization was carried out to ensure equal distribution of various types of surgery to each group taking help of random number table generated by computer, allocating patient to either Isoflurane or Sevoflurane group. Data was collected by residents in table provided working under different anesthesiologist and they kept blind about variables and scope of study.

Inclusion and exclusion criteria

Patients undergoing intracranial neurosurgery with age between 15-70 years of either sex and in ASA grades I, II, III were included in the study. Patients with severe intracranial tension more than 5 mm of midline shift on the CT scan or with GCS less than 12 were excluded. Also, patients with severe cardiac disease, severe hypertension, renal failure, uncontrolled diabetes, and pregnant women were excluded from the study.

In the operation theatre routine monitoring in form of ECG, SpO_2, NIBP and $ETCO_2$ was attached. In all cases invasive arterial blood pressure monitoring was applied. Patients in both the groups were induced with titrated dose of injection thiopentone 3-5 mg/kg body weight, and injection fentanyl 2 mcg/kg body weight IV. Intubation was carried out by vecuronium 0.1 mg/kg body weight, and patients were mechanically ventilated to maintain end tidal CO_2 level between 30-35 mmHg. Both the volatile agent's isoflurane and sevoflurane were used in 0.8-1.2 minimum alveolar concentration (MAC) concentration to maintain depth of anesthesia. Both the groups were given fresh gas flow of 3 litre/min consisting of oxygen 1 litre/min and nitrous oxide 2 litre/min. Injection mannitol 0.6-1 gm/kg body weight was administered to both the groups before craniotomy. We used Penlon anesthesia workstation (PRIMA 450) having isoflurane and sevoflurane vaporizers. Patients with an increase of MAP or heart rate of more than 20% from base line value were administered 1 mg boluses of metoprolol to reduce blood pressure and heart rate. Episode of hypotension was initially managed by titration of concentration of volatile anesthetics and after that intermittent use of injection mephentermine in 3 mg incremental doses to bring the blood pressure within normal limit and keeping MAP more than 70 mmHg. Injection PCM 1 gm I/V was given intra operatively for additional analgesia before anticipated time of completion of surgery. Injection fentanyl 1 mcg/kg was given in addition to the starting dose of fentanyl on hourly basis for analgesia to both the groups. Patients were reversed with injection neostigmine 0.05 mg/kg and injection glycopyrrolate 0.01 mg/kg at the end of surgery (with the completion of skin sutures) and at the same time volatile and nitrous oxide was also cut off. Last dose of neuromuscular blocker was given around 25-30 min before the anticipated time of completion of surgery. Fresh gas flow was increased to 6 liter/min of 100% oxygen at the end of surgery.

Primary outcome measures were recorded as emergence time from anesthesia. Secondary outcome measures as time of extubation after discontinuation of anesthesia, response to command, orientation was recorded. Brain relaxation as assessed by neurosurgeon was also noted down. Recovery end points were defined as follows:

Emergence: Time from discontinuation and reversal till opening of the eyes.

Extubation: It was performed when the patient's respiratory movements became regular and adequate and eye lash reflexes returned/obeyed verbal commands.

Basic neurological examination: It was estimated from time of discontinuation of anesthesia to obeying specific commands like "squeeze hand"/"move feet" every min.

Orientation time: By asking name and current location on verbal command every minute after extubation.

Statistical analysis

The data was analyzed using the statistical software SPSS (version 20). The data collected for individual variables of study was analyzed using unpaired 't' test, means have been compared and presented as mean ± standard deviation (SD). Standard deviation was calculated to establish any statistical significance of results. $P<0.05$ was considered as statistically significant.

RESULTS

Patient's characteristic was similar in both groups (Table 1). Gender, age and weight characteristic were similar in

both the groups (Figure 1). Out of total 30 patients 26 patients of brain tumour and 4 patients of arterial aneurysmal clipping were included in isoflurane (group I). In sevoflurane (group II), 25 patients were taken for craniotomy for tumour and rest for other diseases. Mean operative time period was around 240 min for isoflurane group and 238 min for sevoflurane group (Figure 2) and mean MAC hour of volatile anesthetic of 3.4 for isoflurane and 3.5 for sevoflurane group.

Mean time of emergence in case of isoflurane group was found to be 7.18 min with standard deviation (SD) of 0.8, while in case of sevoflurane it was 5.68 (SD 0.7) (Table 2). The difference of emergence of 1.5 min was found between two agents was faster with the use of sevoflurane as volatile agent.[3] P value was statistically significant with actual value $p<0.05$ and $t=7.32$ at 58 degree of freedom.

Similarly, extubation was found to be faster in case of sevoflurane group in comparison to isoflurane. Mean extubation time was 4.98 (SD 0.67) in case of sevoflurane while it was 5.83 (SD 0.98) in case of isoflurane with a statistically significant $p<0.05$, $t=3.89$ at 58 degree of freedom.[4]

Table 1: Demographics and intra-operative data, (n=30).

Variables	Isoflurane	Sevoflurane
Sex M:F	24:6	25:5
Age (year)	53.48	53.66
Craniotomy for tumour	26	25
Craniotomy for aneurysm and other	4	5
Length of exposure (min)	240 (SD10.9)	238 (SD 11.36)
Av MAC 20 min period before the end of surgery	1.0	0.99
Av MAC hour	3.95	3.98
Brain relaxation	Well relaxed	Well relaxed

Table 2: Recovery variables (min), (n=30).

Variable	Isoflurane, mean (±SD)	Sevoflurane, mean (±SD)	P value
Emergence	7.18 (0.8)	5.68 (0.7)	0.015*
Extubation	5.83 (0.98)	4.98 (0.7)	0.024*
Squeeze hand/move feet on command	14.35 (0.9)	11.7 (1.26)	0.002*
Orientation give name	17.9 (1.83)	16.3 (1.35)	0.025*

*p<0.05 considered significant

In both the groups extubation was before emergence as they were extubated as soon as the breathing became regular and eye lash reflexes returned. Suctioning of throat was not done till the end so that the patient does not cough or buck on the tube as this can lead to rise in intracranial pressures and may lead to bleeds.

Hand squeeze and feet move time was found earlier in case of sevoflurane group. The difference in time for this variable between sevoflurane and isoflurane group was 2.65 min. Mean time for hand squeeze or feet move was 11.70 min (SD 1.26) in case of sevoflurane group, while in the isoflurane group it was 14.35 min (SD 0.90). This difference was also statistically significant with $p<0.05$ and $t=9.35$ at 58 degree of freedom.

Orientation was found faster in case of sevoflurane group though time difference was 1.6 minutes. Mean orientation time in case of sevoflurane was 16.3 min (SD 1.35), while it was 17.9 min (SD 1.83) in case of isoflurane group. The difference was significant with $p<0.05$ and $t=3.89$ at 58 degree of freedom.

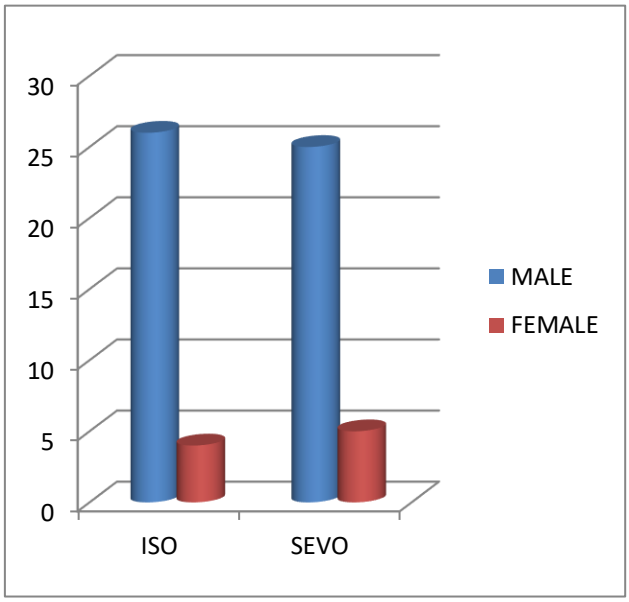

Figure 1: Gender distribution in isoflurane/sevoflurane group.

Brain relaxation was good in both the groups and no significant difference was found between two groups. Two patients in isoflurane group and three patients in sevoflurane group required additional dose of 20 mg of frusemide for good brain relaxation.

Out of sixty, six patients were diabetic on oral medication with good glycemic control (two cases of isoflurane group and 4 patient of sevoflurane group). They were put on regular insulin before surgery. The 7 patients in isoflurane group and 8 patients in sevoflurane group excluded from study as patients were not extubated and put on ventilator.

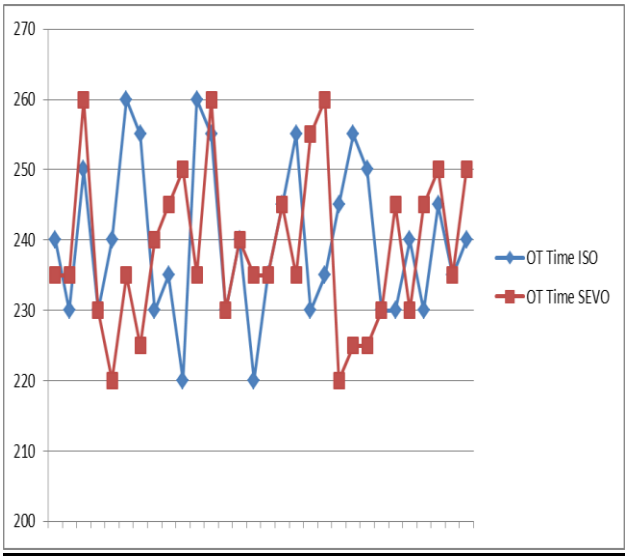

Figure 2: Operative time isoflurane group/sevoflurane group (min).

The degree of brain relaxation as mild, moderate and well relaxed assessed by neurosurgeon.[5] Neurosurgeon was kept blind about the type of volatile agent throughout the study.

DISCUSSION

The solubility of the inhaled anesthetic like isoflurane, sevoflurane and other inhalational agents in blood and tissues is denoted by the partition coefficient. A partition coefficient is a distribution ratio describing how the inhaled anesthetics distributes itself between two phases at equilibrium, means partial pressure equal in both phases. In this respect a blood: gas partition coefficient of 0.5 means that the concentration of inhaled anesthetic in blood is half that present in the alveolar gases when the partial pressure of anesthetic in these two phases is identical. Thus, partition coefficient may be thought as reflecting the relative capacity of each phase to accept anesthetic. The rate of increase of the PA (alveolar partial pressure) toward the inspiratory partial pressure PI (maintained constant by mechanical ventilation of lungs) is inversely related to the solubility of the anesthetic in the blood. When the blood: gas partition coefficient is high, a large amount of anesthetic must be dissolved in the blood before the Pa (arterial partial pressure) equilibrates with the PA. Thus, the high blood solubility of isoflurane than sevoflurane slows the rate at which the PA and Pa increase relative to the PI, and induction is slow. Similarly, the recovery from the effect of anesthetic effects of isoflurane takes longer time than sevoflurane at the time of recovery.[6]

Agent like sevoflurane with low blood: gas solubility low, minimal amounts of inhaled sevoflurane need to be dissolved before equilibrium is achieved, thus induction as well as recovery at the termination of anesthetic is faster in case of sevoflurane as compared to isoflurane.

The volatile anesthetic sevoflurane has low blood gas partition coefficient than isoflurane, this may result in a favorable recovery profile. This could be magnified in neurosurgical cases of long duration and this is proved by the result in our study. Sevoflurane has blood: gas partition coefficient at 37 degree is 0.63-0.69 and MAC is 2.0%.[7]

Isoflurane is also a halogenated methyl ethyl ether that exists as a clear non inflammable liquid at room temperature. The intermediate solubility in blood combined with a high potency permits rapid onset and recovery from anesthesia using isoflurane alone or in combination with nitrous oxide or injected drugs such as opioids. Blood: gas partition coefficient at 37 degree is 1.46 and MAC is 1.17%.

They can have improved recovery profile compared to the older volatile anesthetics because of their lower blood: gas partition coefficient. However, at equivalent fresh gas flow rates, sevoflurane costs 2-3 times more than equipotent concentration of isoflurane. Therefore, to justify increased expense of the sevoflurane use, a clear cost; benefit ratio needs to be shown.[8] Few researchers found sevoflurane anesthetic costlier as compared to isoflurane in short surgeries but in neurosurgery early neurological assessment becomes very important.[9] Hence this study is focused on defining the benefit of sevoflurane over isoflurane anesthesia in achieving clinically important recovery endpoints and we found results in support of sevoflurane.[10]

Similar study was carried out by other people in long duration neurosurgical cases. They used a mixture of air and oxygen with volatile agent isoflurane and sevoflurane. In different studies emergence was found faster in cases with use of sevoflurane as compared to isoflurane. We performed a similar study in Indian population and were using a mixture of oxygen and nitrous oxide along with the volatile agent sevoflurane and isoflurane in long duration neurosurgical cases. Meta-analysis of similar study in different kind of surgeries and of different duration has been carried out and it was found that emergence is faster in those cases of patients receiving sevoflurane than isoflurane. We found the same result in our study too. No significant results for quality of recovery were found in neurosurgical experimental animal cases by researcher. The two volatile agents presented a similar emergence quality profile, though using sevoflurane as an anesthetic was associated with a faster recovery, offering the possibility of conducting earlier post-operative neurological assessment.[11]

Brain relaxation was also studied by different researcher and, all of them found both the agents equally efficient. We found same result too for the effect of volatile agents over brain relaxation in Indian population. Brain swelling were higher with inhaled agents, more with isoflurane compared to sevoflurane found by few researchers.[12]

Limitations

The study has following limitations-It was a single center study and also subjects taken were few. Large multicentric studies involving larger number of subjects are required to further confirm our findings

CONCLUSION

Sevoflurane shows faster emergence, extubation, motor control (in form of hand squeeze) and orientation time as compared to isoflurane. Though clinically the time difference for the various variables studied was 0.8 to 2.7 min only, statistically the results were significant and supported the basis for this difference as the difference in blood gas solubility coefficient between sevoflurane and isoflurane. Sevoflurane is recommended for use for faster extubation, emergence and post-operative neurological examination. The observation shows good brain relaxation with the use of both volatile anesthetic agents.

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