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Comparison of Single Vital Capacity Breath with Breath Holding Versus Three Vital Capacity Breath Induction with Sevoflurane in Adults by BIS Monitoring: A Prospective Randomized Study

Dr. **Vyshnavi .R,** DNB[1], Dr. **Ananya nanda** MD[2*] ,Dr.**Pakhare Vandana,** DNB[2], Dr. **Ramachandran Gopinath,** MD[3], Dr. **Kalyani Surya Dhanalakshmi**, MD,[3] Dr. **Malipeddi Vamshidhar** DNB,[1]

[1]Senior resident, [2]Assistant Professor, [3]Professor
Department of Anaesthesia, ESIC Medical College and Hospital, Sanathnagar, Hyderabad
*nanda.ananya@gmail.com

Abstract:

Background and Aims: Single vital capacity breath with breath holding (SVCBH) was compared to three vital capacity breath (TVCB) technique for inhalational sevoflurane induction of adults using clinical end points and Bispectral index (BIS) as an objective monitor.

Methods: 80 patients were divided into two groups of 40 each after randomization and induced with a primed circuit containing 8% sevoflurane with either single vital capacity breath with breath holding technique or three vital capacity breath technique. Time taken to achieve clinical end points of induction and BIS were noted.

Result: 32 participants were induced in SVCBH group while 38 were induced TVCB group. Clinical end points such as loss of eyelash reflex were achieved faster in SVCBH (30.4±14.5s) compared to 39.6±11.4s in TVCB. Similarly return of conjugate gaze in SVCBH group was 31.8±15.0s compared to 41.1±11.6s in TVCB. BIS value was observed to be significantly higher in SVCBH 77.3±9.3 than TVCB 70.6±9.7. However faster induction (BIS value less than 60) was seen in SVCBH 45.0±18.9s compared to 48.4±11.9s (p value=0.357)**.** A lag time of 15s was observed between achievement of clinical end points and time taken to achieve BIS values less than 60.

Conclusion: Single vital capacity breath with breath holding has faster induction compared to three vital capacity breath technique.

MeSH Keywords: Sevoflurane, vital capacity, breath holding, adults

INTRODUCTION:

Awareness regarding various anaesthetic methods has increased expectation for painless anaesthesia, in needle phobic patients, making inhalationals an attractive method of inducing unconsciousness. Inhalational induction has cardio protective effects and haemodynamic stability and preferred in day care surgery. [1] It avoids undesirable effects such as apnoea, anaphylaxis, hypotension, hang-over effect and venipuncture in anxious conscious patients. Single vital capacity breath inhalation with breath holding and three vital capacity breath techniques have been described.

Bispectral index (BIS), objectively correlates with brain metabolism. Earlier studies using varying concentrations of sevoflurane were done on Caucasian population with above techniques but none comparing them with BIS or any objective parameters. Moreover their results cannot be postulated for our population due to pharmacogenomics variabilities. In this study we have compared primary outcomes using clinical end points– time taken (in seconds) for loss of eyelash reflex (LOER) and return of conjugate gaze in relation to BIS values and secondary outcomes were time taken (in seconds) for achieving BIS <60 and adverse events.

MATERIALS AND METHODS:

The prospective randomized comparative study was carried out in a tertiary hospital, over a period of one year from August 2019-2020, after Institutional Ethics Committee approval (ESICMC/SNR/IEC-DNB/S003/08/2019 dated 29/08/2019) and registered at Clinical Trials Registry- India (CTRI/2020/05/025303 dated 22/05/2020). The study was as per standards on human experimentation and the Helsinki declaration of 1975, after obtaining written informed consent from all participants.

Randomization was done by computerized random number generator into two groups – Group SVCBH (Single vital capacity breath with breath holding technique) and Group TVCB (Three vital capacity breath technique) and concealed using sealed envelope technique, where sealed opaque envelopes containing randomly generated treatment allocations were given. (Figure-1 CONSORT DIAGRAM)

Subjects of either gender in the age group of 18-55 years belonging to ASA PS I-II (American Society of Anaesthesiologist physical status) undergoing elective surgery under general anaesthesia who were willing to comply with the instructions for vital capacity breathing and breath holding were included in the study. Smokers, pregnant individuals and patients who were allergic or sensitive to volatile anaesthetics were excluded.

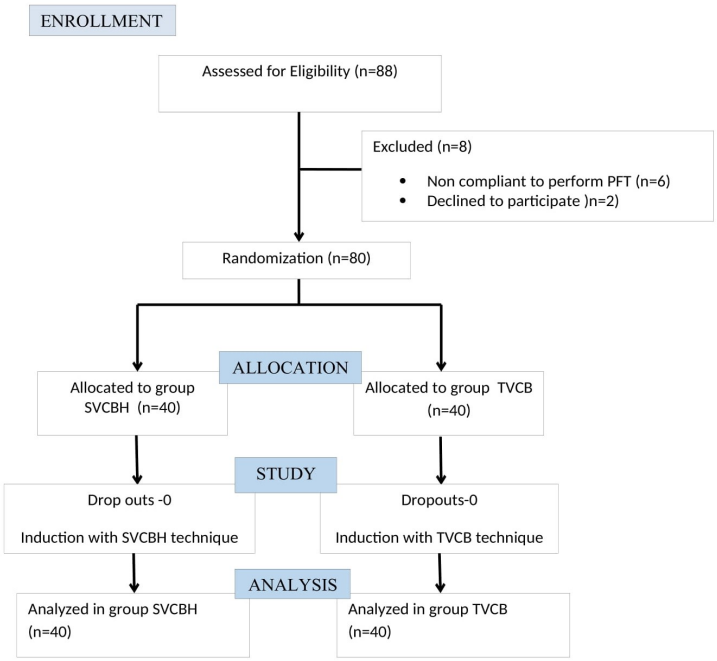

Fig1.: CONSORT flow diagram

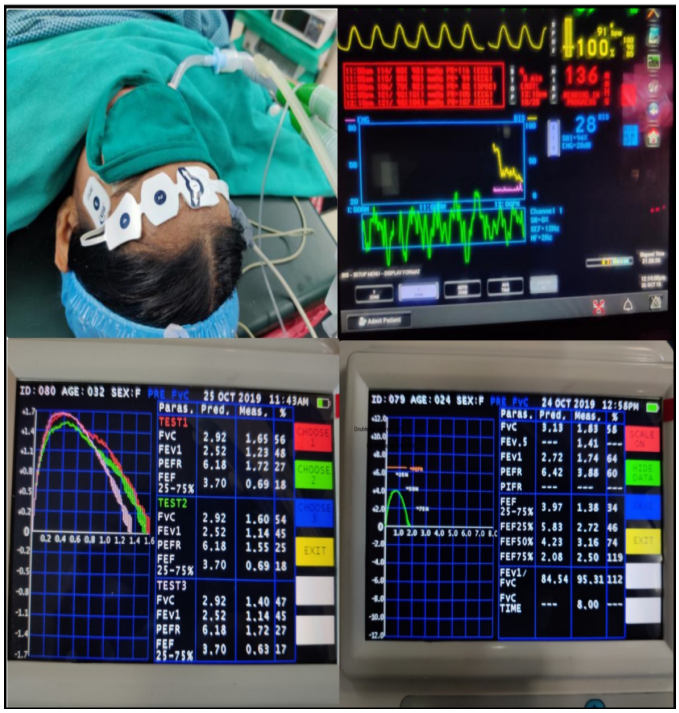

Fig2. (upper Left) BIS sensor applied on the forehead of a patient, (upper right) BIS monitor with values, (lower) Preoperative spirometry to assess the pulmonary function

After detailed preanaesthetic evaluation (PAE) the vital capacity of patients was ascertained using a spirometer (Figure-2, Contec MSA 100 spirometer) and correlated with age and body weight for its adequacy. SVCBH technique and TVCB technique were taught during the PAE and later in preoperative holding area on the morning of surgery. The participants were made to practice till they were confident in performing the technique. Patients were kept nil by mouth as per guidelines. Sedative premedication was withheld as it might influence BIS reading. Preoperative parameters-baseline pulse rate (PR), non invasive blood pressure (NIBP), peripheral oxygen saturation (SpO2) were recorded. Patients were brought into operation theatre, 18G intravenous cannula secured and standard monitors like electrocardiogram (ECG), NIBP, pulse oximeter, end tidal CO_2 ($EtCO_2$) were connected using a multiparameter monitor attached to the same anaesthesia workstation

(Space labs Blease Sirius - 700/900 series ventilator) as per guidelines. BIS Quatro 4 electrode sensor with BIS LoC four channel module (Medtronic, Minneapolis, USA) was attached to the forehead of the patients and connected as per manufacturer's instructions and BIS values were noted from the inbuilt BIS monitor in the Space labs machine (Figure-2).

Before induction, the circle breathing circuit was primed with required gas mixture by completely emptying the reservoir bag, and filling the circuit with 6 l/min fresh gas flow and 8% sevoflurane, with patients Y piece occluded after which the facemask was placed on patient's face at the end of exhalation. The volatile agent concentration was monitored by Spacelabs inbuilt infrared multi-gas analyzer with side stream sampling at 50ml/min. A constant sevoflurane concentration of >7% with gas flows of 6 l/min was ensured before proceeding as indicated by end tidal sevoflurane concentration. Anaesthetic gas scavenging system (MES medical limited) was used to scavenge the free anesthetic gases.

For induction participants were instructed to take a vital capacity breath (after priming the circuit with sevoflurane to a Minimum alveolar concentration of 8%) by inhaling maximally and holding their breath for atleast 20s as practiced before. Time taken to achieve the end points and BIS value were noted. The same technique was used for TVCB group and time taken for the endpoints to be achieved and BIS readings were recorded. All the timings from induction till end points were noted using a stop watch. Outcomes were observed by a single independent observer, familiar with the identification of all the endpoints. LOER was assessed by gently stroking the eyelashes every 5s with fingers till induction. Assessment for return of conjugate gaze was done by lifting the eyelids to observe for centralization of pupils every 5s. The timings were noted from application of facemask (connected to the primed circuit) to the participant's face. When the study was concluded, the anesthetic technique was converted to any technique of the attending anesthesiologist's choice. No attempt was made to analyze later factors such as time of awakening. Adverse events such as cough, laryngospasm, bronchospasm, breath holding, involuntary movements and excessive salivation if any were noted. Mean blood pressure < 65mmHg, was managed with intravenous fluids. Heart rate below 50/min was given bolus IV atropine 0.6 mg.

S.Y.Lee et al observed a mean time to LOER 53.6s with a pooled standard deviation (σ) of 16.1, giving a mean difference (d) of 9.9s. [2] At 5% level of significance ($\mathbb{Z}_{\alpha/2}$: 1.96) with power of 80% ($\mathbb{Z}_{1-\beta}$: 0.84), r = n1/n2 is taken as one since equal sample size was to be taken in both the groups and 40 patients were enrolled in each group with a total of 80 patients.

The sample size was calculated using the following formula:

$$N = \frac{(r+1)(\mathbb{Z}\alpha/_2+\mathbb{Z}_{1-\beta})^2\sigma^2}{rd^2}$$

Categorical data was tabulated in terms of frequency and percentage. Continuous data was presented as mean and standard deviation and analyzed by student's t-test, categorical data by Chi-square test and fisher's exact test. "p" value of less than 0.05 was considered significant and < 0.01 was considered highly significant. Data analysis was carried out using SPSS (Statistical Package for Social Sciences) package (version V22.0).

RESULTS:

A total of 80 patients underwent the study with 40 patients in each group. Demographic data like age, gender, and weight and ASA grade were comparable between the groups (Table1).

Haemodynamic parameters like PR, SBP, DBP and RR before induction, Mean preoperative breath holding time (BHT) and BIS were comparable between both groups and p value was statistically not significant (Table 1).

Comparing the number of patients induced by either method, 32 participants were induced in Group SVCBH while 38 were induced in Group TVCB as represented by Table 2. This was statistically significant (p value=0.043) as analyzed by unpaired t test. Clinical end points were achieved faster in group SVCBH, denoted by LOER in group SVCBH is 30.48±14.54s compared to 39.63±11.47s in group TVCB which was statistically significant (p value=0.004). Mean time taken for return of conjugate gaze in group SVCBH is 31.82±15.00s compared to 41.10±11.61s in group TVCB which was statistically significant (p value=0.004) as represented by Figure 3.

Table 1: Comparison of Age, weight, gender, ASA status, preoperative haemodynamic parameters, baseline breath holding time and preoperative BIS value between groups SVCBH and TVCB, df= degree of freedom

VARIABLE	SVCBH	TVCB	P value	Confidence interval	Fisher's Exact Test
					Exact sig. (1 sided) /(2 sided)
AGE (Yrs)	34.325 ± 9.4500	34.800 ± 10.0363	.828	32.43 – 36.69	-
WEIGHT (Kg)	60.275 ±11.3182	62.150 ± 14.6244	.523	58.37-64.05	-
GENDER (Female/ male)	34/6	37/3	.288	-	.241/.481 df=1
ASA I/ II	26/14	27/13	.813	-	.500/1.000 df=1
PULSE (beats/min)	82.900 ± 8.7583	86.550 ± 9.1510	.072	82.76-86.68	-
SBP (mmHg)	122.625 ± 13.6037	120.850 ± 13.1491	.555	118.8-124.7	-
DBP (mmHg)	79.100 ± 7.3128	78.875 ± 7.3001	.891	77.39-80.59	-
RR (beats/min)	13.500 ± 1.0127	13.475 ± 1.1091	.916	13.25-13.72	-
BHT (in s)	33.775 ± 10.8474	34.625 ± 5.6327	.661	32.39-36.01	-
PREOPBIS	96.700 ± .7579	96.975 ± .2762	.034	96.72-96.95	-

Table 2: Comparison of number of patients induced in SVCBH and TVCB groups

INDUCED/NOT INDUCED		GROUP		TOTAL
		SVCBH	TVCB	
INDUCED	N (%)	32 (80)	38 (95)	70 (87.5)
NOT INDUCED	N (%)	8 (20)	2 (5)	10(12.5)
TOTAL	N (%)	40 (100)	40 (100)	80 (100)
Fisher's Exact Test	Exact Sig. (2-sided): 0.087		Exact Sig. (1-sided): .044	
Df = 1				

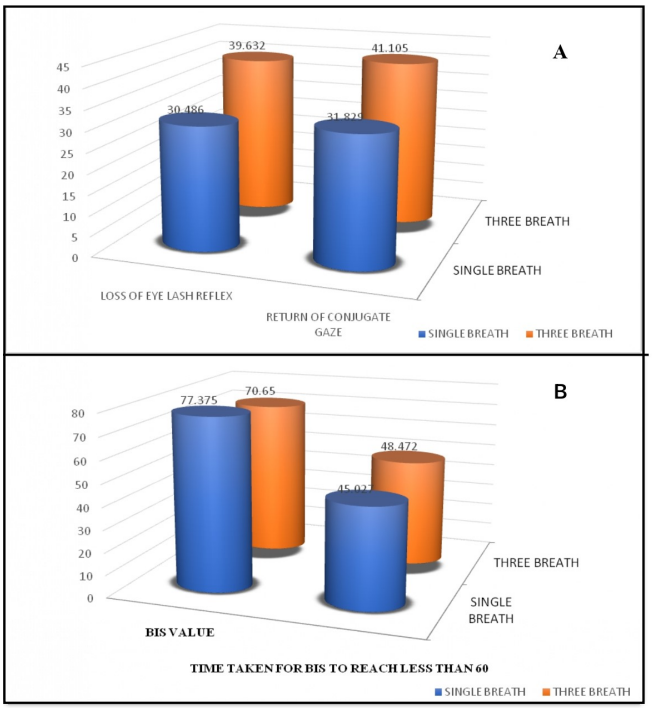

Fig3. Graphical representation of: A. (upper) time taken to achieve loss of eyelash reflex and loss of conjugate gaze in SVCBH and TVCB group (in seconds), B. (lower) BIS value at the time of loss of eyelash reflex and time taken to achieve a BIS less than 60 in both the groups (in seconds)

BIS value was observed to be significantly higher in group SVCBH 77.375±9.32 than group TVCB 70.65±9.78, (p value=0.002). However significantly faster induction, as measured by the time taken to achieve a BIS value less than 60 was seen in group SVCBH 45.02±18.90s compared to 48.47±11.94s (p value=0.357, Figure 3). A lag time of 15s was observed between achievement of clinical end points and time taken to achieve a BIS lesser than 60.

Comparing adverse events one patient in Group SVCBH had cough during induction which was self limiting and two patients had prolonged apnoea (28s and 26s respectively), however no such episodes were observed in TVCB group. No episodes of laryngospasm were noted in any of the patients of either group.

DISCUSSION

Successful induction for adults by inhalationals mandates use of potent yet poorly soluble and minimally irritant agent. [3] Sevoflurane combines all these properties and can be a reasonable option in adult patients as well. In our study, induction with sevoflurane was performed with single vital capacity breath with breath holding and compared to three vital capacity breath without breath holding technique. We aimed to study the effect of both of these methods on BIS and time taken to achieve objective clinical end points. We observed faster induction in SVCBH group compared to TVCB group; however a higher BIS value was noted in SVCBH than TVCB group. Significantly higher number of individuals were induced in TVCB group but the time taken to achieve a BIS value less than 60 was faster in SVCBH group.

In a study by J.E Hall, [4]the time to induction with 8% sevoflurane was found to be 69s ranging between 56-86s with priming technique which was more than that observed in our study wherein LOER was achieved in 30.4s and 39.6s in SVCBH and TVCB groups respectively. This could be due to breath holding of atleast 20s and vital capacity breath maneuvers that we used. Another study by Haque MM et al divided 50 adult patients into propofol and sevoflurane group. The mean time for loss of consciousness in the sevoflurane group was 27s which was similar to our study (30.4±14.5s and 39.6±11.4s in SVCBH and TVCB group). [5] In our study we observed a range of induction times between 12-48s and 12-56s in SVCBH and TVCB groups respectively.

Olofsen & Dahan et al noted a lag between half life of brain-alveolar equilibration for sevoflurane and speed of onset BIS, which was attributed to neuronal or receptor-related dynamics and time taken for sampling, processing and transmission of the parameters. [6] Similarly the time taken for BIS to come to below 60 was 45 and 48s respectively in both the groups, though we achieved our end-points of induction much earlier like LOER at 30 and 39s respectively in group SVCBH and TVCB at BIS of 77 and 70s and loss of conjugate gaze at 31.8 and 41.1s respectively. This lag time between achieving BIS values appropriate for airway placement and end points of induction has also been noted by others. [7]

In a study conducted by Hall JE et al, [8] on adults aged 20-30yrs, time taken for LOER was 71±37s with SVBC technique without breath holding. However time taken for LOER in our study was 30.4±14.5s which was significantly lower than the former study. This can be attributed to the two factors: first being breath holding included in our study and the other is lower mean weight in the earlier study (73±12Kg and 60.2±11.3kg), though the age of the participants is almost similar in both the study. The faster induction could be attributed to faster alveolar: arterial equilibration during breath holding and lower weight of the patient.

BIS has been used previously as an end-point to measure the time for loss of consciousness produced by induction of general anesthesia. Induction as measured by LOER was achieved at BIS values of more than 60 and hence this level of hypnosis may not be enough to safely proceed with the endotracheal intubation since the stimulus of tracheal intubation during light anesthesia could increase the chances of recall and airway complications. Our study was confined to induction with sevoflurane as established by LOER and loss of conjugate gaze rather than securing a definitive airway hence a BIS value of 60 was chosen, because BIS of 25 was shown to have superior intubating conditions than BIS 40. Time required to achieve BIS 25 was 6.6 min as compared to 5.1 min in BIS 40 group, when BIS was used as an isolated objective measure to assess the intubating conditions rather than clinical end points. [9]

Study by Goodwin N et al,[10] with 8% sevoflurane concentration using three breath technique with 10s breath holding has BIS (at LOER) of 81±18 while in our study it was 70.6±9.7 in three vital capacity breath group, and 77.3±9.3s in the SVCBH with a BHT of more than 20s in the SVCBH group. In our study 32 patients were induced in single breath with breath holding technique whereas 38 out of 40 could be induced in the three vital capacity breath technique. The patients who were not induced were sedated but did not reach the clinical end points after SVCBH and TVCB maneuvers. This could be due to pharmacogenomic profile of the patients. [11]

In our study faster induction was achieved in SVCBH than TVCB groups, similar to that observed by Viswanath R et al, [12]where rapid induction was observed in vital capacity rapid inhalation induction (43.8s) compared to tidal ventilation (65.8s) which was measured at the time of LOER. SVCBH technique gives a superior induction using the same inhalational agent when compared to the conventional TVCB inhalational technique, this can be attributable to breath holding which has shown to increase the efficiency of drug concentration in targeted site such as alveolar regions due to uniform distribution, thereby facilitating steady uptake into the blood across an concentration gradient ensuring steady increase in concentration of inhalational agent. [13]Adults have a smaller alveolar ventilation rate per kilogram when compared with children, hence priming the circuit with high concentration of sevoflurane together with breath holding hastens the induction and has 50 % lower rate of complications such as coughing, movement, laryngospasm as per various authors. [14]

BIS of less than 60 was achieved in SVCBH and TVCB group indicating that sevoflurane can be used as a sole agent for induction and maintenance of anaesthesia in subjects with coronary artery disease since it lowers pulmonary artery pressure and provides favourable haemodynamics such as stable heart rate which preserves the myocardial oxygen consumption and myocardial perfusion. [15]

Strength of the study is breath holding being a simple maneuver, can be performed on a day-to-day basis to improve oxygenation and faster induction. It also helps to reduce anxiety in needle-phobic patients. Induction with brief high concentration sevoflurane further reduced the haemodynamic fluctuation observed with bolus doses of intravenous drugs. Limitation of our study was that it was a single center study, hence wider scale multicentric study with larger population is required to generalize the results for all adults. Moreover, double blinding was not done.

CONCLUSION:

Sevoflurane induction with single vital capacity breath with breath holding provides a faster, more reliable and safer induction in adults when compared to three vital capacity breath technique, hence it can be used efficiently in day to day practice as an alternative to conventional intravenous induction for elective and emergency surgeries.

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Conflicting Interest: No conflict of interest

Ethical Approval: ESICMC/SNR/IEC-DNB/S003/08/2019.

Clinical Trials Registry: CTRI/2020/05/025303

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