Original Article

Effect of high fresh gas flow and pattern of breathing on rapid preoxygenation

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ABSTRACT

Background and Aims: Preoxygenation is supplementation of 100% oxygen prior to induction of general anaesthesia to increase the body's oxygen stores. Efficacy of preoxygenation can be increased by optimising fresh gas flow (FGF) rate and pattern of breathing. **Methods:** Based on pattern of breathing—Tidal Volume Breathing (TVB) or Deep Breathing (DB) and FGF-10 L/min or 15 L/min—100 subjects of the American Society of Anesthesiologists physical status I/II posted for elective surgery were recruited and randomised into four groups: T10 - TVB with 10 L/min; D10 - DB with 10 L/min; T15 - TVB with 15 L/min; and D15 - DB with 15 L/min. A tight-fitting anaesthesia mask along with continuous positive airway pressure of 5 cm of H_2O with 20° head-up was used for preoxygenation. The total time taken and the total number of breaths required to achieve end tidal oxygen concentration (EtO_2) of 90% were noted. Exhaled tidal volume (Vte), end tidal carbon dioxide, fraction of inspired oxygen, and EtO_2 were recorded at each breath. Analysis of variance (ANOVA) was used for inferential statistics and Tukey's honestly significant difference (HSD) test was used to calculate mean difference in total time and number of breaths amongst the groups. **Results:** Total time taken was significantly low ($P < 0.001$) in DB compared to TVB (D10: 70.2 ± 19.91, D15: 68.4 ± 20.27 vs T10: 112.28 ± 47.96, T15: 113.6 ± 48.57 seconds). Number of breaths was significantly high ($P < 0.001$) in TVB with 22.84 ± 8.73, 23.76 ± 11.64, 10.56 ± 3.69, and 8.32 ± 1.8 in T10, T15, D10 and D15, respectively. Vte was significantly low in TVB ($P < 0.001$). **Conclusion:** Rapid preoxygenation can be achieved by DB at high FGF of a minimum of 10 L/min.

Key words: Apnoea, hypoxia, oxygen, tidal volume, vital capacity

INTRODUCTION

Preoxygenation is the supplementation of 100% oxygen via face mask prior to induction of general anaesthesia (GA). It increases oxygen reserves, hence preventing hypoxia during a planned or unexpected period of apnoea during induction and intubation.[1] Preoxygenation also washes nitrogen out of the lungs, saturates haemoglobin (Hb) and allows some oxygen to dissolve in the plasma. Total oxygen stores build up and delay the onset of arterial desaturation and hypoxia during apnoeic period. Desaturation can lead to dysrhythmias, haemodynamic decompensation, hypoxic brain injury, and ultimately death; therefore, the maintenance of arterial oxyhaemoglobin saturation level is critical in an apnoeic patient until airway control has been achieved.[2]

End points of maximal preoxygenation are an end tidal oxygen concentration (EtO_2) of ≥90% or an end tidal nitrogen concentration (EtN_2) of 5%.[3] Maximal preoxygenation prior to induction of GA is a routine procedure and more essential in anticipated difficult mask ventilation, difficult intubation, or in emergency cases with rapid sequence induction.[4] The traditional method of preoxygenation with tidal volume breathing

(TVB) for 3 minutes at a fresh gas flow (FGF) of 5 L/min has been the honoured technique. Studies done previously used fixed regimens and these seem suboptimal in the presence of EtO_2 monitoring.[1,3–5] Rapid preoxygenation may be more practical and useful in certain clinical situations such as lifesaving emergencies, for rapid sequence induction, and in an uncooperative patient not willing for tight fit mask for 3 minutes. It is possible to observe the rise in EtO_2 on a breath-by-breath basis. Our primary objective was to estimate the time taken to achieve EtO_2 of 0.9 at the given FGF rates of 10 L/min and 15 L/min, and the given pattern of breathing with TVB and deep breathing (DB). The secondary objective was to estimate the average number of breaths required to achieve EtO_2 of 0.9 in each group.

METHODS

A randomised parallel group study was done between April 2018 and October 2019 at our tertiary care hospital. We included American Society of Anesthesiologists physical status I and II patients, aged between 18 years and 59 years undergoing elective surgical procedures requiring GA with endotracheal intubation. Patients who had a body mass index (BMI) of >30 kg/m^2, anticipated difficult airway, cardiac and respiratory diseases, were chronic smokers, pregnant, or those who did not consent were excluded from the study. The sample size of 100 was taken based on a pilot study done on patients. To find the mean difference of 30 seconds (100 seconds vs 70 seconds) between the groups and pooled standard deviation of 35 seconds between the groups, with 5% level of significance and 80% power, the total number required was 21 in each arm (84 subjects in total). We recruited 25 per group to account for any dropouts during the study**.** Ethics committee approval was obtained and trial was registered at Clinical Trial Registry of India (CTRI/2018/03/012747). Informed consent was taken and 100 subjects were randomised via computer generated tables and allocated, using sealed envelopes, into four different groups: T10 – TVB with 10 L/min FGF; D10 – DB with 10 L/min FGF; T15 – TVB with 15 L/min FGF; and D15 – DB with 15 L/min FGF.

The appropriate method of preoxygenation was explained to the subjects during the preoperative visit prior to start of induction of anaesthesia. Standard monitoring of electrocardiography (ECG), non-invasive blood pressure (NIBP), pulse oximetry (SpO_2) and capnography (end tidal carbon dioxide, $EtCO_2$) were connected. The General Electronics Avance CS2 anaesthesia machine was used. Circle anaesthesia system with 2 L capacity reservoir bag was primed with 100% oxygen. After noting baseline vital parameters, all subjects were placed at 20° head-up position and preoxygenated with a properly sized, tight-fitting anaesthesia mask. The FGF rate (10 L/min or 15 L/min) and the pattern of breathing (TVB vs DB) was started along with continuous positive airway pressure (CPAP) of 5 cm H_2O.

During the period of preoxygenation, the total time and number of breaths taken to achieve the EtO_2 of 90% were noted. Exhaled tidal volume (Vte), $EtCO_2$, fraction of inspired oxygen (F_IO_2) and EtO_2 were recorded at the end of each breath. The mean Vte, EtO_2 and $EtCO_2$ were measured retrospectively at four different intervals: 25%, 50%, 75%, and 100% of the total time taken to achieve $EtO_2 > 90\%$. The heart rate (HR), SpO_2, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at the beginning and at end of the procedure. The patient was premedicated and induced thereafter with standard GA technique required for surgery. The data collected were tabulated in an Excel sheet and statistically analysed.

Descriptive statistics were reported using mean and standard deviation for continuous variables, and numbers and percentages for categorical variables. Software R, version 4.1.0 (R core team 2021, Vienna, Austria) and two-factor analysis of variance (ANOVA) was used for inferential statistics. Post hoc analysis (Tukey's HSD test) was used to calculate mean difference in total time and total number of breaths amongst the intergroups. Probability value of less than 5% was considered statistically significant.

RESULTS

A total of 100 subjects were enroled and randomly allocated into one of the four groups. 25 subjects were allocated in each group [Figure 1]. The demographics were comparable between the groups [Table 1]. The mean respiratory parameters, that is, Vte, $EtCO_2$, EtO_2 at 25%, 50%, 75%, and 100% of total duration of time taken to achieve $EtO_2 > 90\%$ showed significant change in Vte ($P < 0.001$), with comparable $EtCO_2$ and EtO_2 [Table 2]. The haemodynamic variables were comparable in all groups with DBP showing significance of $P < 0.001$ [Table 3]. Total time taken
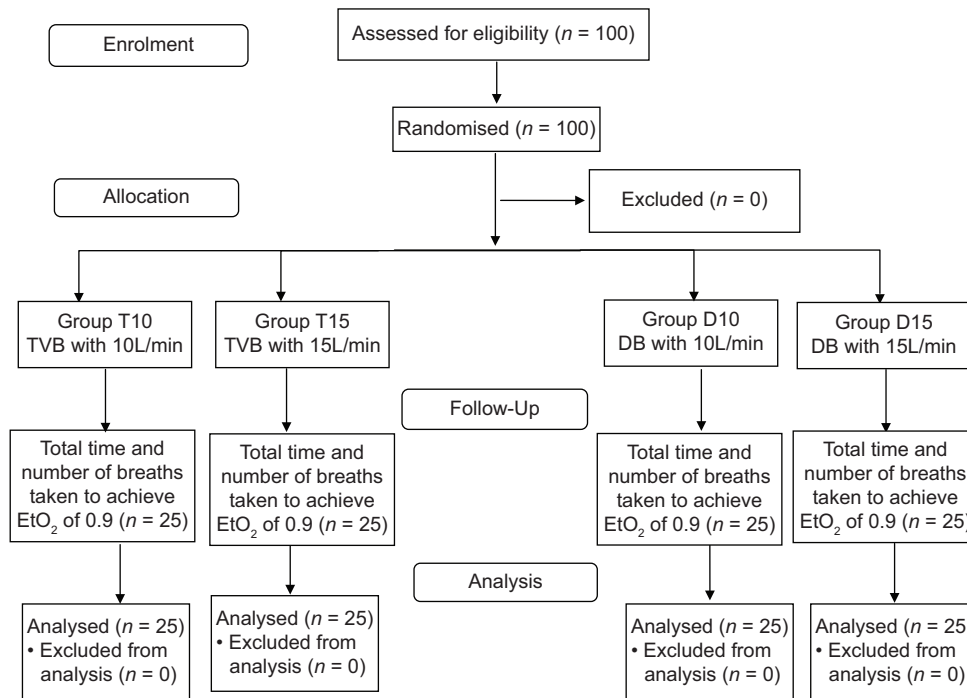
Figure 1: CONSORT diagram. EtO$_2$: End tidal oxygen concentration; *n*: Number

Table 1: Demographic variables					
Variables	**Group T10 (*n*=25)**	**Group T15 (*n*=25)**	**Group D10 (*n*=25)**	**Group D15 (*n*=25)**	***P***
Age (years) Mean±SD	37.76±9.68	32.92±10.59	35.2±11.45	38.32±10.75	0.256
Gender					
n (percentage)					
Male	12 (48%)	8 (32%)	11 (44%)	13 (52%)	0.526
Female	13 (52%)	17 (68%)	14 (56%)	12 (48%)	
Height (cm)	161.88±14.7	162.72±5.34	165.52±6.69	166.32±6.32	0.24
Weight (kg)	63.56±8.32	61.52±7.77	59.84±12.03	66.6±6.32	0.05
ASA PS					
I	14 (56%)	15 (60%)	17 (68%)	14 (56%)	0.801
II	11 (44%)	10 (40%)	8 (32%)	11 (44%)	

SD: Standard deviation, *n*: Number, ASA PS: American Society of Anesthesiologists physical status

was significantly low ($P < 0.001$) in DB compared to TVB (D10: 70.2 ± 19.91, D15: 68.4 ± 20.27 vs T10: 112.28 ± 47.96, T15: 113.6 ± 48.57 seconds). Total number of breaths was significantly different ($P < 0.001$) with 22.84 ± 8.73, 23.76 ± 11.64, 10.56 ± 3.69, and 8.32 ± 1.8 in T10, T15, D10, and D15, respectively [Figure 2]. Pairwise difference with 95% conference interval (CI) adjusted by Tukey's HSD test showed significant difference in total time duration and number of breaths taken to achieve EtO$_2$>90% amongst the groups [Figure 3].

DISCUSSION

The effectiveness of preoxygenation is assessed by its efficacy and efficiency.[3] Factors affecting efficacy include F$_I$O$_2$, duration of breathing, and the ratio of alveolar ventilation to functional residual capacity (FRC). Indices of efficacy include increase in the fraction of alveolar oxygen, increase in arterial oxygen tension, and decrease in fraction of alveolar nitrogen. Factors affecting efficiency are capacity of oxygen loading, oxygen consumption (preoperative diagnosis, surgical condition, surgical stress, etc.), alveolar oxygen concentration, FRC, arterial oxygen content, and cardiac output. Patients with reduced FRC or those with increased oxygen consumption will desaturate much faster during apnoea.[5] Maximal preoxygenation is achieved when the alveolar, arterial, venous, and tissue compartments are all saturated with oxygen.[6]

We found that rapid preoxygenation can be achieved by DB technique with minimum FGF of 10 L/min as

Table 2: Respiratory variables at four different intervals of 25%, 50%, 75%, and 100% of the time in total duration of breathing									
Variables	Group T10		Group T15		Group D10		Group D15		P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Vte 1	338.56	243.3	322.2	240.08	678.16	419.91	699.16	291.18	<0.001
Vte 2	447.76	291.5	310	112.53	960.56	408.27	931	345.28	<0.001
Vte 3	463.48	342.0	395.72	116.97	861.96	338.43	1032.2	287.99	<0.001
Vte 4	490.28	330.3	426.24	185.83	927.64	344.91	983.88	347.73	<0.001
$EtCO_2$ 1	30.64	5.31	29.0	6.03	28.96	4.22	30.08	0.68	0.545
$EtCO_2$ 2	34.2	9.62	31.2	3.29	29.68	2.75	30.08	2.27	0.027
$EtCO_2$ 3	33.0	4.59	31.64	2.34	29.76	3.81	29.76	2.83	0.003
$EtCO_2$ 4	29.92	5.74	30.44	3.15	29.08	3.37	29.28	2.91	0.607
EtO_2 1	55.52	12.54	50.2	10.88	51.76	10.49	51.48	12.46	0.41
EtO_2 2	75.54	5.45	74.76	4.92	75.08	5.95	72.04	7.82	0.19
EtO_2 3	83.82	2.96	84.44	2.5	85.44	2.14	84.6	2.58	0.16
EtO_2 4	90.4	0.71	90.4	0.82	90.4	0.58	90.56	0.71	0.81

*Vte: Exhaled tidal volume (ml); *$EtCO_2$: End tidal carbon dioxide (mmHg); *EtO_2: End tidal oxygen concentration; SD: Standard deviation

Table 3: Haemodynamic variables at the beginning and end of preoxygenation									
Variables	Group T10 (*n*=25)		Group T15 (*n*=25)		Group D10 (*n*=25)		Group D15 (*n*=25)		P
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
HR1	82.76	17.05	82.68	7.78	80.52	12.36	83.12	7.26	0.86
HR2	81.2	16.07	81.8	7.13	77.96	10.55	83.92	9.81	0.32
SBP1	137.08	22.98	127.92	11.75	126.12	13.74	132.36	12.12	0.07
SBP2	135.08	19.43	127.12	11.82	126.32	13.19	132.84	11.98	0.09
DBP I	82.6	8.86	74.28	9.05	70.92	8.52	73.4	8.39	<0.001
DBP 2	81.36	8.05	73.76	7.64	71.16	9.6	72.16	7.1	<0.001
MAP 1	101	18.02	91.68	13.87	93.16	10.71	92.92	9.59	0.064
MAP 2	97.6	14.79	89.96	13.91	92.56	9.23	93.08	8.16	0.155

HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; *n*: Number
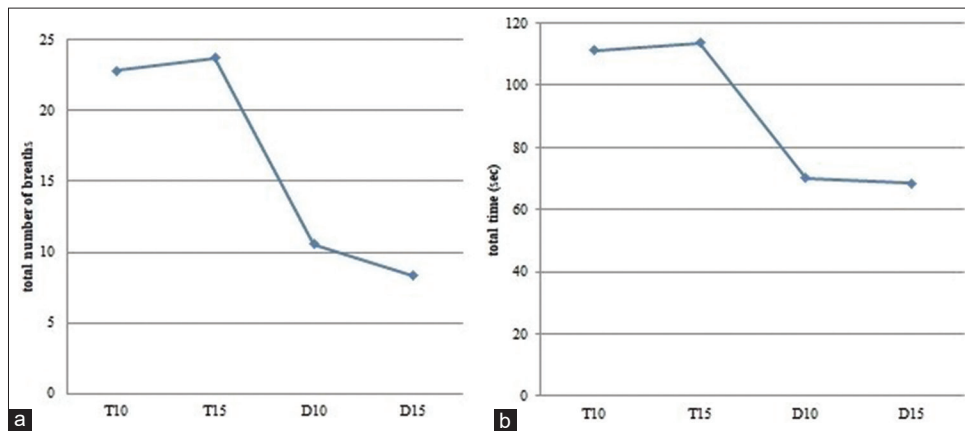

Figure 2: Pattern of breathing and fresh gas flow rates on (a) total number of breaths (b) total time taken to achieve end tidal oxygen levels (EtO_2) of 90%

it takes a shorter time and less number of breaths to achieve $EtO_2 > 90\%$. Common reasons for failure to achieve F_IO_2 close to 1.0 include inadequate time for preoxygenation, leak under face mask, use of system incapable of delivering high F_IO_2, and rebreathing of exhaled gases.[7] A leak as small as 4 mm in diameter can hinder preoxygenation significantly and is not compensated by increasing the preoxygenation time or high FGF.[8] Clinical end points of a good sealed system

is movement of reservoir bag during inhalation and exhalation, presence of normal capnogram, fractional concentration of inspired carbon dioxide (F_ICO_2) and $EtCO_2$. In the present study, we used appropriately sized tight-fitting mask to avoid air leaks, 20° head-up position, 100% oxygen of at least 10 L/min, application of continuous positive airway pressure (CPAP) of 5 cm H_2O, using primed closed circuit and achieving a target $EtO_2 > 90\%$.[9]

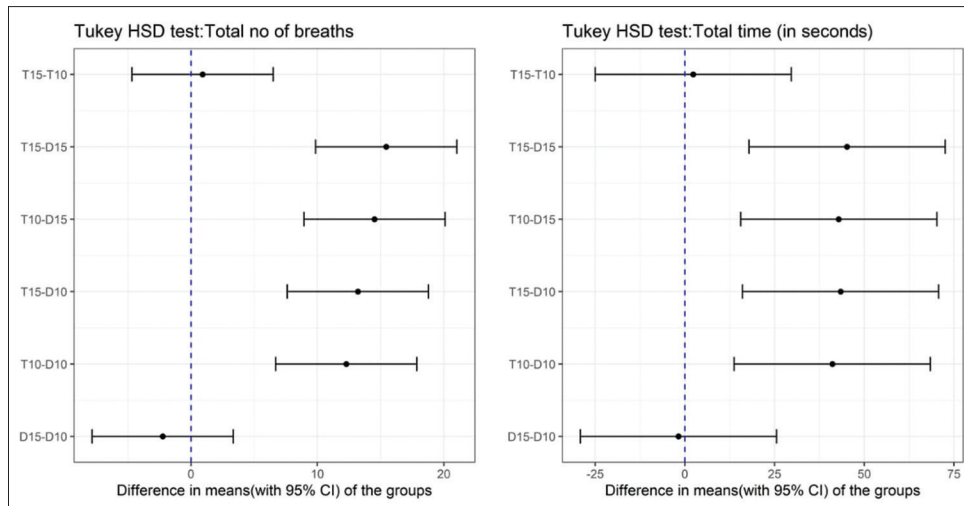**Figure 3:** Post hoc analysis of total number of breaths and total time taken to achieve end tidal oxygen EtO_2>90% between the groups. Error bar depicts the mean difference with 95% confidence interval. HSD: Honestly significant difference; CI: Confidence interval

Various anaesthetic circuits (Mapleson A, Mapleson D, Bain's circuit, circle absorber system non-rebreathing systems) and FGF ranging from 5 L/min to 35 L/min have been used successfully.[4,10–13] In spontaneous ventilation, the degree of rebreathing is less with Mapleson A and circle system requiring 5 L/min of FGF compared to Mapleson D that requires 10 L/min to achieve adequate preoxygenation with TVB within 3 minutes. We standardised the GE Avance CS2 anaesthesia workstation with circle absorber as a common circuit for the study because it is most frequently used in the operating room and is as effective as other systems specifically designed for preoxygenation.[11] To eliminate rebreathing, all groups received a minimum of 10 L/min of FGF and the circuit was denitrogenated with 100% oxygen before placement on the patient's face.

Supine position hinders a patient's ability to take deep breath, leading to dependent atelectasis and decreased FRC.[14,15] The head-up position improves the efficacy of preoxygenation and increases apnoea time than the supine position in normal and obese patients.[16–18] Positive end expiratory pressure and non-invasive positive pressure ventilation can increase FRC and mean airway pressure, thereby recruiting the alveoli.[19] Hence it is used in vulnerable population such as obese, pregnant, and critically ill patients.[8] Patients with decreased capacity for oxygen loading (decreased FRC, arterial partial pressure of oxygen (PaO_2) or cardiac output) or with increased oxygen consumption or both, desaturate much faster during apnoea than healthy adults.[7]

Nimmagadda *et al.*[4] investigated the impact of FGF on two methods of preoxygenation (TVB and DB) in healthy volunteers and concluded that increase in FGF from 5 L/min to 10 L/min did not enhance oxygenation in the lungs with either TVB or DB in 30 seconds. With 10 L/min, mean EtO_2>90% was achieved in 3–4 minutes of TVB and 1–1.5 min in DB. There was no difference in EtO_2, EtN_2, $EtCO_2$ or respiratory rate (RR) between 5, 7, and 10 L/min FGF in TVB. However, with DB and 10 L/min, it took 12 DB in 1.5 min and 16 DB in 2 min to achieve EtO_2>90%. They concluded that extending duration of DB to 1.5–2 minutes with high FGF of 10 L/min yields EtO_2 equivalent to TVB of 3 minutes. Baraka *et al.*[20] also observed that in both 4 DB/30 sec and in 8 DB/60s, 10 L/min, increasing oxygen flow from 5 L/min to 10 L/min to 20 L/min resulted in exponential increase of mean PaO_2 from baseline value of room air. Similarly, Singh *et al.*[1] also found that with 10 L/min of FGF, DB/60 sec showed higher mean PaO_2 than traditional TVB/3 min with FGF of 5 L/min, and resulted in slower Hb desaturation following subsequent apnoea. Though we did not study the PaO_2 or duration of Hb desaturation, our results showed that with 10 L/min of FGF, the DB patients took lesser time and less number of breaths compared to TVB [Figure 2], hence implying that rapid preoxygenation with DB can be provided with high FGF of 10 L/min. While comparing high flow rates with different patterns of breathing, we noted a significant reduction in the total time duration as well as number of breaths to achieve EtO_2 >90% in DB which were statistically significant [Figure 2]. Also, the post hoc analysis between the groups showed a statistical difference with respect to time duration and number

of breaths taken to achieve $EtO_2 > 90\%$ [Figure 3]. At both FGFs of 10 L/min and 15 L/min, the DB group achieved optimal preoxygenation faster with less number of breaths as compared to the TVB group.

The EtO_2 showed a steady rise irrespective of FGF rate or pattern of breathing in our study ($P > 0.5$). There was significant ($P < 0.001$) difference in the Vte amongst the groups, confirming that all patients did not hypoventilate during the preoxygenation period. Transient hypocapnia may have undesirable effects, including increased oxygen consumption, cerebral vasoconstriction, dizziness, nausea, etc. Nimmagadda *et al.*[4] observed $EtCO_2$ decrease to 34.5 ± 5.2 mmHg from room value of 40.2 ± 3.9 mmHg in DB/1.5 min, and to 33.8 ± 4.9 mm Hg in 16 DB/2 min. Benumof showed that there was a significant decrease in $PaCO_2$ and pH with 8 DB/60 sec, resulting in significant change in blood compartment oxygen transport variables such as position of oxy-Hb dissociation curve, oxygen consumption, cardiac output, blood and plasma volume, which could alter the rate of Hb desaturation.[7] This indicates that the blood compartment rather than alveolar compartment may be responsible for slower Hb desaturation. When PaO_2 is increased by inhalation of 100% O_2, the CO_2 dissociation curve for blood is altered (the Christiansen-Douglas-Haldane effect), such that there is a reduction in the affinity of blood for CO_2. This causes an increase in cerebral tissue PCO_2 and hydrogen ion concentration, which stimulates respiration with a result that $PaCO_2$ decreases, causing cerebral vasoconstriction.[21]

The cardiovascular responses during preoxygenation have received limited attention and have not been well characterized.[3] Breathing 100% oxygen causes modest decrease in HR, parallel decrease in cardiac output, increase in systemic vascular resistance and arterial blood pressure. These changes are attributable to a reflex loop, either chemoreceptor or baroreceptor in origin. Direct effect of oxygen on vascular smooth muscle or reflex-mediated via an arterial chemoreceptor or autonomic nerve may cause vasoconstriction and a decrease in blood flow in peripheral vascular beds, including the kidney, gastrointestinal tract and hind limb.[22] Similar to a study by Singh *et al.*,[1] ours did not show any statistical significance in haemodynamics (SBP, MAP and HR); however, we did get a significant difference of value ($P < 0.001$) in DBP amongst the four groups, but it did not show any clinical impact.

Recent advances have shown that preoxygenation followed by apnoeic diffusion oxygenation is an effective manoeuvre to enhance the safe duration of apnoea. Transnasal humidified rapid-insufflation ventilatory exchange (THRIVE) is gaining a lot of popularity; it is administered through a nasal, high-flow oxygen delivery system and insufflates oxygen up to 70 L/min. It prolongs the safe apnoea time while avoiding increase in CO_2 and can be used for critically ill patients and in patients with difficult airways.[23-25]

The limitation of our study is that a non-invasive method was adopted and we aimed for number of breaths and total time duration to achieve EtO_2 as the target. We did not measure duration of apnoea without desaturation (DAWD) for efficiency or have an objective measurement of arterial blood gas analysis to see parameters such as PaO_2. Though the patients were taught the breathing technique, some amount of anxiety and unpleasant feel of suffocation was seen with high gas flow in a tight-fitting mask. Further studies involving objective parameters such as DAWD, PaO_2 with the use of preoxygenation in newer workstation, and THRIVE can add more evidence for rapid preoxygenation.

CONCLUSION

DB technique at FGF of 10 L/min and 15 L/min is an effective method of rapid preoxygenation when compared to TVB. DB technique takes shorter time and a fewer number of breaths to achieve $EtO_2 > 90\%$.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of interest

There are no conflicts of interest.

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