A comparison of apnoeic oxygen techniques in term pregnant subjects: a computational modelling study

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Abstract

Background. Hypoxaemia during general anaesthesia can cause harm. Apnoeic oxygenation extends safe apnoea time, reducing risk during airway management. We hypothesised that low-flow nasal oxygenation (LFNO) would extend safe apnoea time similarly to high-flow (HFNO), while allowing facemask pre-oxygenation and rescue.

Method. A high-fidelity, computational, physiological model was used to examine the progression of hypoxaemia during apnoea in virtual models of pregnant women in and out of labour, with body mass indices (BMI) of 24 to 50 kg m^{-2}. Subjects were pre-oxygenated with 100% oxygen to reach $F_{E'}O_2$ of 60, 70, 80 or 90%. When apnoea started HFNO or LFNO was commenced. To simulate varying degrees of effectiveness of LFNO, 21, 60 or 100% periglottic oxygen (FgO_2) was configured. HFNO provided $FgO_2$100% and oscillating positive pharyngeal pressure.

Results. Application of LFNO ($FgO_2$100%) following optimal pre-oxygenation ($F_{E'}O_2$90%) resulted in similar or longer safe apnoea times than HFNO $F_{E'}O_2$ 80% in all subjects in labour. In BMI24 the time to reach SaO_2 90% with LFNO was 25.4 mins ($F_{E'}O_2$90%/$FgO_2$100%) vs 25.4 mins with HFNO ($F_{E'}O_2$80%). In BMI50 the time was 9.9 mins with LFNO ($F_{E'}O_2$90%/$FgO_2$100%) vs 4.3 mins with HFNO ($F_{E'}O_2$80%). A similar finding was seen in subjects with BMI ≥40 kg m^{-2} not in labour.

Conclusions. There is likely to be clinical benefit to using LFNO, given that LFNO and HFNO extend safe apnoea time similarly, particularly when BMI ≥40 kg m^{-2}. Additional benefits to LFNO include the facilitation of rescue facemask ventilation and ability to monitor $F_{E'}O_2$ during preoxygenation.

Keywords. Apnoea, computer simulation, high-flow nasal oxygenation, low-flow nasal oxygenation, obstetrics, obesity in pregnancy.

Suggested editor's key points:

1. In obstetric patients undergoing Caesarean delivery, low-flow nasal oxygen (LFNO) during apnoea following good pre-oxygenation appears to provide a similar extension to safe apnoea time as that provided by high-flow nasal oxygen.

2. The relative ease of facemask ventilation during LFNO is likely to provide clinically significant benefit. These benefits are particularly marked in patients with BMI ≥40 kg m^{-2}.

Introduction

Hypoxaemia during induction of general anaesthesia in the obstetric population has the potential to cause significant maternal and foetal harm. Current recommendations are to use a standard facemask technique to pre-oxygenate to an end-tidal oxygen fraction ($F_{E'}O_2$) of 90%; however, this can be difficult to achieve in clinical practice.[1] Maternal respiratory physiological adaptations seen during the third trimester, and the effects of labour, increase the risk of rapid deoxygenation and reduce safe apnoea time.[2]

Apnoeic oxygenation allows extension of the safe apnoea time. A tight-fitting facemask with continuous oxygen delivery to an open airway can provide apnoeic oxygenation but cannot be utilised during airway instrumentation. Other published apnoeic oxygenation techniques include the use of high-flow humidified nasal oxygen (HFNO) and low-flow nasal oxygen (LFNO) via standard nasal cannulae.[3] Standard nasal cannulae can also be used in conjunction with facemask preoxygenation to continue oxygen delivery during tracheal intubation.

Studies conducted in healthy pregnant volunteers show that HFNO achieves a lower $F_{E'}O_2$ after pre-oxygenation than a facemask technique.[4–7]After 3 minutes of tidal breathing, HFNO achieved a mean $F_{E'}O_2$ of 87% (95% confidence interval: 86–89%) while standard facemask preoxygenation achieved a mean $F_{E'}O_2$ of 91% (95% confidence interval 89-93%).[4] Other studies demonstrated that when HFNO is used with up to 20 vital capacity breaths, the median maximum $F_{E'}O_2$ achieved is 82% with the mouth closed and 73% with the mouth open.[7] Studies have also shown that in healthy pregnant volunteers, even with 8 minutes of pre-oxygenation, $F_{E'}O_2$ 90% is not achieved when using HFNO.[5] However, computational modelling has shown that HFNO extends the safe apnoea time even when an $F_{E'}O_2$ of only 60% is achieved, when compared to face mask preoxygenation without apnoeic oxygenation.[8]

The use of HFNO presents challenges in the obstetric environment, particularly out-of-hours or in the emergency setting. Due to the nature of obstetric care, this is often when general anaesthesia is required. Use of HFNO requires specialist equipment, which may be unfamiliar and time-consuming to set up. In contrast, LFNO is cheap, familiar and quick to set up in an emergency. It allows tightfitting facemask pre-oxygenation, measurement of pre-apnoea $F_{E'}O_2$, and apnoeic oxygenation even during airway instrumentation.

We hypothesised that, in pregnant women, LFNO after facemask pre-oxygenation ($F_{E'}O_2$ 90%) would provide a safe apnoeic period similar to that provided by HFNO following imperfect preoxygenation ($F_{E'}O_2$ <90%). In this computational investigation, we aimed to compare the effects on safe apnoea times of LFNO and HFNO apnoeic oxygenation techniques following pre-oxygenation to published ranges that HFNO generates [4,6,7] ($F_{E'}O_2$ 60%, 70%, 80% and 90%).

Methods

We used the Interdisciplinary Collaboration in Systems Medicine (ICSM) simulation suite, a high-fidelity, highly integrated model of the human respiratory and cardiovascular systems, based on the Nottingham Physiology Simulator, which has been described in detail previously.[9] The ICSM simulation suite has been widely validated and has been used in investigations into pre-oxygenation and apnoea in adults and pregnancy.[8–13] To model the apnoeic status and the gas exchange accurately during HFNO at a flow rate of 70 L min^{-1}, additional modules have been incorporated, including cardiogenic gaseous oscillations within the tracheobronchial tree and alveoli, gas-mixing within the respiratory dead space and pharyngeal pressure oscillations.[10] Further details are provided in the supplementary material of our recent paper. [8]

Ten virtual subjects were configured to be identical to those used in our previous investigations [8] using established data.[9,13–17] Where physiological values could not be obtained for term pregnant subjects, values were extrapolated from a combination of data from non-pregnant subjects and from established physiological theory. Subjects were configured in active labour and not in labour, with values of body mass index (BMI) of 24 (BMI24), 35 (BMI35), 40 (BMI40), 45 (BMI45), and 50 kg m^{-2} (BMI50).

Each subject underwent pulmonary denitrogenation (i.e. pre-oxygenation) via tidal breathing with inspired fraction of oxygen (FO_2) 100% to reach $F_{E'}O_2$ 60%, 70%, 80%, and 90%. At time zero, apnoea commenced, representing the induction of general anaesthesia. At this time, the functional residual capacity (FRC) was decreased by 20% in the BMI24 subject and by 30% in all other subjects, as per published data.[14,18] Also at this time, metabolic oxygen consumption (VO_2) decreased by 65 ml min^{-1} for all subjects at the onset of apnoea, representing the reduced metabolic oxygen consumption caused by general anaesthesia and muscle paralysis.[19]

During apnoea, four interventions were modelled:

- Complete upper airway obstruction, representing failure of maintenance of a patent airway.
- No apnoeic oxygenation (i.e. 21% oxygen at the open glottis), representing airway instrumentation without any provision of supplemental oxygen to the airway.
- Oxygen provision via nasal cannulae (i.e. low flow nasal oxygen, LFNO); providing periglottic oxygen (F_gO_2) 60% or 100% at the open glottis (reflecting perfect insufflation and the effect of dilution with air).
- High-flow nasal oxygen (i.e. 100% humidified oxygen at 70 L min^{-1} HFNO) with an open glottis.

Apnoea continued until the subject's haemoglobin oxygen saturation (SaO_2) reached 50%. The time taken to reach SaO_2 90% (termed the 'safe apnoea time') and to reach 50% were recorded. Data were recorded every 5 milliseconds from the start of the pre-oxygenation until the protocol was terminated. The model simulations ran on a 64-bit Intel Core i7 3.7 GHz Windows 10 personal computer, running MATLAB version R2018a.v9 (MathWorks Inc, Natick, MA, USA).

Results

Times to desaturation (SaO_2 90% and 50%) for the various pre-apnoea $F_{E'}O_2$ values are shown in Tables 1 and 2.

Preoxygenation to $F_{E'}O_2$ 90%, compared to lower values, extended the time taken to reach SaO_2 90% and 50% in all subjects, with exception of those with a BMI of 24 kg m^{-2} who were not in labour and were receiving HFNO during apnoea (where the safe apnoeic period was very long). In non-labour and in-labour subjects, as BMI increased, there was a reduction in the safe apnoea time. This trend was seen with all apnoeic oxygenation techniques.

Figure 1 shows the time course of SaO_2 for two subjects (BMI24 and BMI50) in labour. Both HFNO and LFNO apnoeic techniques increased the time to SaO_2 90% and 50% in comparison with absent oxygen supplementation, and in comparison with upper airway obstruction. This finding was observed in all subjects, in active labour and not in labour. Similar to our previous findings,[8] HFNO alters the speed of haemoglobin desaturation, with slower desaturation with respect to LFNO and all other interventions examined with the same $F_{E'}O_2$ during the initial fall from SaO_2 100% to 90% and the steeper fall from 90% to 50%. Our findings suggest that LFNO offers a slightly smaller, but clinically comparable, reduction in the speed of desaturation to HFNO. In the subject with BMI 50 kg m^{-2} who was in labour and pre-oxygenated to $F_{E'}O_2$ 90%, LFNO with FgO_2 100% during apnoea had a safe apnoeic period of 9.9 min in comparison to 12 min with HFNO, 7.6 min with LFNO FgO_2 60% and 3.1 minutes with no apnoeic oxygenation.

For the subjects in labour, LFNO with pre-apnoea $F_{E'}O_2$ 90% and $FgO_2$100% provided a similar or longer apnoeic period to SaO_2 90% and 50% than HFNO with pre-apnoea $F_{E'}O_2$ 80%. Moreover, except in BMI24, LFNO with pre-apnoea $F_{E'}O_2$ 90% and FgO_2 60%, provided a longer safe apnoea time to SaO_2 90% compared to HFNO with $F_{E'}O_2$ 80% or less (Table 2). A similar trend was seen in the subjects not in labour, but only in the subjects with BMI $\geq$ 40 kg m^{-2} (Table 1).

Figure 2 shows the gain in safe apnoea time between HFNO with pre-apnoea $F_{E'}O_2$ 80% and LFNO ($FgO_2$100%) with pre-apnoea $F_{E'}O_2$ 80% and 90%. With pre-apnoea $F_{E'}O_2$ 80%, HFNO provided a longer safe apnoea than LFNO, in all subjects, although this was less marked with larger BMI. Specifically, with pre-apnoea $F_{E'}O_2$ 80%, HFNO allows a gain in safe apnoea time ranging from 50.2 minutes to 1.2 minutes in the subjects not in labour and from 13.5 minutes to 0.7 minutes in the subjects in labour.

Discussion

The results of this computational modelling investigation demonstrate that, with good pre-oxygenation ($F_{E'}O_2$ 90%), HFNO provides the most effective apnoeic oxygenation, delivering the longest safe apnoea time in all subjects. These findings concur with other studies.[8,11,12,20-21] In 2015, Patel and colleagues found apnoea times of up to 65 min and no desaturation below 90% using nasal oxygenation at rate of 70 l min^{-1} in an adults patients with difficult airways were undergoing general anaesthesia for hypopharyngeal or laryngotracheal surgery.[20] In 2017, Gustafsson and colleagues oxygenating adult patients, undergoing shorter laryngeal surgery under general anaesthesia, with 100% of oxygen 40–70 l min^{-1}, found a mean apnoea time of 22.5 (4.5) min.[21] The extension of the safe apnoeic period is reduced when a patient is in labour.[8] However, studies of preoxygenation with HFNO have shown an $F_{E'}O_2$ of 90% is unlikey to be achieved.[4–7] There are also barriers to the routine use of HFNO. The equipment is time-consuming to set up, requires training and is likely to impede facemask ventilation. In contrast, standard nasal cannulae can deliver LFNO and the equipment required is cheap, accessible, familiar, easy to set up, and does not impede facemask ventilation. LFNO also can be provided during facemask pre-oxygenation, facilitating measurement of $F_{E'}O_2$.

We found that LFNO following pre-oxygenation to $F_{E'}O_2$ 90% produced equivalent or better safe apnoeic times compared to HFNO with pre-oxygenation to $F_{E'}O_2$ of 80% in all subjects. Due to the challenges of achieving $F_{E'}O_2$ 90% with HFNO, LFNO may provide a suitable alternative for apnoeic oxygenation, with lower cost and ease of use.

Use of LFNO to achieve comparable apnoeic oxygenation is dependent on achieving a pre-oxygenation $F_{E'}O_2$ of 90% with a facemask technique. Under clinical study conditions, only 70% of term pregnant women were able to achieve $F_{E'}O_2$ 90% with a facemask technique and up to 20 vital capacity breaths and an average of 3.6 minutes of tidal breathing was needed to achieve $F_{E'}O_2$ 90% in 90% of term parturients.[5,7] Therefore, in real world clinical situations, $F_{E'}O_2$ 90% may be difficult to achieve, particularly in emergency scenarios, where the parturient is in pain or distress and maintaining a tight facemask seal becomes difficult. A more clinically relevant comparison of apnoeic oxygenation between LFNO and HFNO may be from a baseline of $F_{E'}O_2$ 80% for both techniques, instead of 90% (Figure 2)**.** In this situation our data suggest that the extension in safe apnoea time seen with LFNO will be less than HFNO. At a smaller BMI, HFNO may provide twice the time to SaO_2 90% compared to LFNO at the same starting $F_{E'}O_2$. There are, however, diminishing gains in safe apnoeic time using HFNO as BMI increases. The increase in metabolic oxygen consumption that occurs with increasing BMI and active labour may explain this reduction in safe apnoea time.

In the subject with the largest BMI (50 kg m^{-2}), both HFNO and LFNO provided a comparatively small increase in safe apnoea time (Figure 1) even with pre-oxygenation to $F_{E'}O_2$ 80%. This group is also at risk of failure of apnoeic oxygenation, due to the increased risk of airway obstruction and increased shunt fraction caused by alveolar collapse. This scenario was modelled within the study (as airway obstruction) and when this occurs, a very short safe apnoeic period follows. There is also an increased risk of failed intubation and difficult facemask ventilation in this group, amplifying the risks. The modest increase in safe apnoea time gained with HFNO or LFNO, while buying critical thinking time, may not prevent the need for attempted rescue ventilation if intubation requires multiple attempts or fails in this group. LFNO provides easier access to bag and mask rescue ventilation, and unlike HFNO which needs to be removed to allow safe bag mask ventilation, LFNO can be left in place to restart apnoeic oxygenation during further attempts at intubation. As such, despite the modest increase in safe apnoeic times, LNFO may be a better strategy for providing apnoeic oxygenation in subjects with large BMI.

Consequently, we recommend that HFNO should be used with caution in those who have high BMI; there may be more benefit in LFNO techniques that allow the measurement of $F_{E'}O_2$ during pre-oxygenation and the use of rescue bag mask ventilation.

One assumption within this simulation model is that 100% oxygen may be provided at the glottis when LFNO at 15 L min^{-1} is administered. To the authors' knowledge, there are no data to refute or confirm this. Previous studies in non-pregnant patient groups have shown that 15 L min^{-1} oxygen via standard nasal cannulae achieves FgO_2 60% at the glottis during 'quiet breathing' as inspired oxygen is diluted by inspiration of surrounding air.[22] We accounted for the effect of this dilution in LFNO by creating an alternate model with FgO_2 60% at the glottis during apnoea. With pre-apnoea $F_{E'}O_2$ 90%, there is still benefit in using 'imperfect' LFNO (i.e. FgO_2 60%), with only small reductions in the safe apnoeic period compared to 'perfect' LFNO (i.e. FgO_2 100%). The extension in safe apnoea remains greater than that seen with HFNO with pre-apnoea $F_{E'}O_2$ <90%. During apnoea, air is unlikely to be entrained to dilute inspired oxygen, and so we would expect the glottic FgO_2 to be higher than 60%. Further work is required to establish the FgO_2 achieved at the glottis during apnoea when using LFNO.

This study utilised computational modelling to investigate an issue that is clinically difficult to address. The assumptions built into this model are a potential weakness of this approach; however, the simulation suite has been validated within obstetric and non-obstetric populations.[9–13] Studying intentionally inadequate pre-oxygenation and the limits of apnoeic hypoxaemia in the obstetric population would be ethically unacceptable; this modelling technique provides a safe and reproducible approach to this challenging issue.

In summary, our modelling investigation shows that while HFNO with good preoxygenation ($F_{E'}O_2$ 90%) provides the most effective extension in safe apnoea time, using LFNO following good pre-oxygenation ($F_{E'}O_2$ 90%) provides a comparable benefit to that provided by HFNO with pre-oxygenation to $F_{E'}O_2$ less than 90% (the expected result in clinical situations). The ease of performing facemask ventilation during LFNO apnoeic oxygenation and the ability to monitor $F_{E'}O_2$ during pre-oxygenation are likely to provide clinically significant benefits, especially in subjects with BMI ≥40 kg m^{-2}.

Author's contributions

Design of study: DS, AP, JGH

Design of computational models: JGH

Simulation runs: ML

Configuration of subjects & interpretation of data: RE, ML, AP, JGH

Writing and final approval of manuscript: RE, ML, RLV, AP, JGH

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None

Declaration of interest

JGH is associate Editor-in-Chief of the British Journal of Anaesthesia. JGH accepts fees for the provision of advice to the police, crown prosecution service, coroners and solicitors. The other authors have no relevant conflicts to declare.

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Tables

Table 1. Time (minutes) taken to reach arterial oxygen saturation (SaO_2) of 90% and 50% during apnoea for different pre-apnoea end-tidal oxygen fractions in subjects that were term pregnant but not in labour.

t90: time from onset of apnoea to SaO_2 90% in minutes; t50: time from onset of apnoea to SaO_2 50% in minutes; BMI24/35/40/45/50: body mass index 24/35/40/45/50 kg/m^2. FgO_2: periglottic oxygen; LFNO: low flow nasal oxygen; HFNO: high flow nasal oxygen; n.a.: not achieved.

		Closed glottis		Glottic FgO_2 21%		LFNO, glottic FgO_2 60%		LFNO, glottic FgO_2 100%		HFNO	
	End-tidal oxygen fraction (%)	t90	t50	t90	t50	t90	t50	t90	t50	t90	t50
BMI24	60	2.1	4.4	2.4	5.0	6.2	14.5	7.0	16.7	66.9	n.a.
	70	3.1	5.4	3.4	6.0	8.5	16.6	9.7	19.4	63.9	n.a.
	80	4.2	6.5	4.5	7.3	11.6	19.8	13.3	22.7	63.8	n.a.
	90	6.5	9.0	7.6	10.6	23.6	31.3	27.7	36.2	65.2	n.a.
BMI35	60	2.0	4.1	2.2	4.5	4.4	11.2	4.9	13.1	19.8	39.6
	70	2.8	4.8	3.0	5.3	5.9	12.9	6.7	15.0	21.4	40.0
	80	3.6	5.7	3.8	6.2	8.1	15.2	9.5	17.6	22.3	41.6
	90	5.3	7.5	6.1	8.8	18.5	25.4	21.9	29.7	34.2	49.0
BMI40	60	1.9	4.2	2.1	4.6	3.8	10.3	4.1	12.5	12.8	28.2
	70	2.6	4.8	2.8	5.2	4.9	11.9	5.5	14.0	13.9	29.1
	80	3.3	5.5	3.4	6.0	6.6	13.6	7.5	15.7	14.9	29.9
	90	4.8	7.1	5.5	8.3	16.8	23.8	20.7	28.8	25.9	37.9
BMI45	60	1.8	3.9	1.9	4.2	3.1	9.2	3.4	10.4	7.9	22.2
	70	2.4	4.4	2.5	4.8	3.9	10.2	4.2	11.7	8.9	23.2
	80	3.0	5.0	3.0	5.4	5.0	11.6	5.7	13.8	9.8	23.5
	90	4.0	6.3	4.4	7.2	12.6	19.5	15.9	24.0	19.5	30.9
BMI50	60	1.6	3.6	1.7	3.90	2.5	7.7	2.6	8.7	3.9	17.7
	70	2.1	4.0	2.2	4.32	3.0	8.5	3.1	9.7	4.3	18.3
	80	2.6	4.5	2.6	4.81	3.6	9.7	3.8	11.4	4.9	19.3

90	3.3	5.5	3.5	6.07	8.1	16.0	10.2	19.6	12.1	24.8

Table 2. Time in minutes taken to reach arterial oxygen saturation (SaO_2) of 90% and 50% during apnoea for different pre-apnoea end-tidal oxygen fractions in subjects in active labour.

t90: time from onset of apnoea to SaO_2 90% in minutes; t50: time from onset of apnoea to SaO_2 50% in minutes; BMI24/35/40/45/50: body mass index 24/35/40/45/50 kg m^{-2}. FgO_2: periglottic oxygen; LFNO: low flow nasal oxygen; HFNO: high flow nasal oxygen.

		Closed glottis		**Glottic FgO_2 21%**		**LFNO, glottic FgO_2 60%**		**LFNO, glottic FgO_2 100%**		**HFNO**	
	End-tidal oxygen fraction (%)	**t90**	**t50**	**t90**	**t50**	**t90**	**t50**	**t90**	**t50**	**t90**	**t50**
BMI24	60	2.2	4.4	2.5	4.9	5.6	12.5	6.5	14.8	22.7	39.8
	70	3.1	5.3	3.3	5.8	7.7	14.7	8.9	17.1	23.7	40.5
	80	3.9	6.1	4.1	6.8	10.2	17.1	11.9	19.9	25.4	41.6
	90	5.7	8.1	6.8	9.6	21.1	27.7	25.4	32.7	33.9	47.4
BMI35	60	2.4	4.1	2.6	4.4	5.2	10.2	5.9	12.0	11.4	20.5
	70	2.8	4.5	3.0	4.9	6.3	11.2	7.3	13.2	12.6	21.7
	80	3.1	4.7	3.2	5.2	7.0	11.9	8.1	14.1	14.3	22.9
	90	4.4	6.2	5.2	7.4	15.6	20.7	19.3	24.9	23.6	31.6
BMI40	60	2.2	3.7	2.3	4.0	3.94	8.56	4.3	9.9	8.6	17.5
	70	2.5	4.1	2.6	4.4	4.6	9.5	5.3	11.0	9.4	17.9
	80	2.8	4.3	2.8	4.6	5.1	10.1	6.0	11.7	9.9	18.2
	90	3.8	5.5	4.4	6.4	12.5	17.5	15.6	21.4	18.7	25.7
BMI45	60	2.1	3.6	2.1	3.9	3.0	7.7	3.2	8.9	4.9	15.7
	70	2.4	3.9	2.4	4.2	3.4	8.4	3.7	9.9	5.5	16.2
	80	2.6	4.1	2.6	4.4	3.7	8.9	4.0	10.5	6.3	17.0
	90	3.3	5.1	3.6	5.7	9.3	15.3	11.7	19.0	13.4	22.9
BMI50	60	1.5	3.5	1.6	3.7	2.4	6.8	2.5	7.8	3.7	14.1
	70	2.0	3.8	2.1	4.1	2.8	7.6	3.0	8.9	4.0	14.3
	80	2.4	4.2	2.4	4.5	3.3	8.6	3.5	10.1	4.3	14.7
	90	2.9	4.9	3.1	5.5	7.6	14.3	9.9	17.9	12.0	21.8

Figure legends

Figure 1. Oxygen saturation (SaO_2) during apnoea in the virtual subjects with BMI24 and BMI 50 kg m^{-2} in labour, during closed glottis, open airway with FgO_2 21%, LFNO and HFNO with end-tidal oxygen fraction ($F_{E'}O_2$) of 80 and 90%. Closed glottis simulates failure of LFNO and HFNO whereas FgO_2 21% $F_{E'}O_2$ of 90% simulates facemask technique during airway instrumentation with no oxygenation supplementation.

Figure 2. Gain in safe apnoea times, calculated as difference in minutes to reach SaO_2 90% between HFNO with $F_{E'}O_2$ 80% and LFNO at $F_{E'}O_2$ 80% and 90% with FgO_2 100% at the open glottis, in the subjects not in labour (upper panel) and in labour (lower panel).