OPEN ACCESS

Effect of interface dead space on the time taken to achieve changes in set FiO_2 during T-piece ventilation: is face mask the optimal interface for neonatal stabilisation?

Kolbrun Gunnarsdottir ,[1,2] Ben J Stenson,[3] Elizabeth E Foglia,[4] Vishal Kapadia,[5] Thomas Drevhammar ,[1,6] Snorri Donaldsson[1,7]

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/archdischild-2024-327236).

[1]Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Stockholm, Sweden
[2]Department of Neonatology, Astrid Lindgren Children's Hospital, Stockholm, Sweden
[3]Neonatal Unit, Royal Infirmary of Edinburgh, Edinburgh, UK
[4]The Children's Hospital of Philadelphia Division of Neonatology, Philadelphia, Pennsylvania, USA
[5]Department of Pediatrics, The University of Texas Southwestern Medical Center Division of Neonatal-Perinatal Medicine, Dallas, Texas, USA
[6]Department of Anesthesiology, Östersund Hospital, Östersund, Jämtland, Sweden
[7]Department of Neonatology, Landspitali National University Hospital of Iceland, Reykjavik, Iceland

Correspondence to
Dr Kolbrun Gunnarsdottir;
kolbrun.gunnarsdottir@ki.se

Received 4 April 2024
Accepted 26 August 2024
Published Online First
6 September 2024

To cite: Gunnarsdottir K, Stenson BJ, Foglia EE, *et al*. *Arch Dis Child Fetal Neonatal Ed* 2025;**110**:F213–F218.

ABSTRACT

Background T-piece is recommended for respiratory support during neonatal stabilisation. Bench studies have shown a delay >30 s in achieving changes in fraction of inspired oxygen (FiO_2) at the airway when using the T-piece. Using a face mask adds dead space (DS) to the patient airway. We hypothesised that adding face mask to T-piece systems adversely affects the time required for a change in FiO_2 to reach the patient.

Methods Neopuff (Fisher and Paykel, Auckland, New Zealand) and rPAP (Inspiration Healthcare, Croydon, UK) were used to ventilate a test lung. DS equivalent to neonatal face masks was added between the T-piece and test lung. Additionally, rPAP was tested with nasal prongs. Time course for change in FiO_2 to be achieved at the airway was measured for increase (0.3–0.6) and decrease (1.0–0.5) in FiO_2. Primary outcome was time to reach FiO_2+/−0.05 of the set target. One-way analysis of variance was used to compare mean time to reach the primary outcome between different DS volumes.

Results In all experiments, the mean time to reach the primary outcome was significantly shorter for rPAP with prongs compared with Neopuff and rPAP with face mask DS ($p<0.001$). The largest observed difference occurred when testing a decrease in FiO_2 with 10 mL tidal volume (TV) without leakage (18.3 s for rPAP with prongs vs 153.4 s for Neopuff with face mask DS). The shortest observed time was 13.3 s when increasing FiO_2 with 10 mL TV with prongs with leakage and the longest time was 172.7 s when decreasing FiO_2 with 4 mL TV and added face mask DS without leak.

Conclusion There was a delay in achieving changes in oxygen delivery at the airway during simulated ventilation attributable to the mask volume. This delay was greatly reduced when using nasal prongs as an interface. This should be examined in clinical trials.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Previous bench studies have shown a delay in achieving changes in fraction of inspired oxygen (FiO_2) at the airway when using the T-piece for positive pressure ventilation.

WHAT THIS STUDY ADDS

⇒ We found that the delay in changes of FiO_2 to reach the patient's airway during simulated ventilation is largely related to the interface dead space (DS) added to the respiratory circuit. This delay can be greatly reduced by using nasal prongs as the interface. The differences in mean time between different DS volumes ranged from twofold to eightfold.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These results raise questions about whether or not the face mask is the optimal interface for neonatal stabilisation.

INTRODUCTION

While most newborn infants breathe spontaneously at birth,[1] many require respiratory support to establish regular breathing.[2] This is more common in preterm infants and reaches 100% for the smallest preterm infants. Positive pressure ventilation (PPV) is delivered with devices such as conventional and variable flow T-pieces and self-inflating and flow-inflating bags.[3] During stabilisation, supplemental oxygen is adjusted to maintain the desired oxygen saturation (SpO_2) based on recommended targets.[4 5] Both hypoxia and hyperoxia can be potentially harmful[6] and recommendations for initial oxygen concentration during neonatal stabilisation have changed considerably during the last 20 years.[7 8]

Previous studies have shown clinically important delays (>30 s) in the time required for changes in fraction of inspired oxygen (FiO_2) at the blender to reach the patient's airway in simulated PPV tested with T-piece devices.[9 10] Those studies focused on different gas flow rates and leakages but no reasonable explanation was identified as a cause for this delay. The use of face masks during neonatal stabilisation is well-established.[11] However, providing PPV with a face mask can be challenging and ventilation can be compromised by leaks and airway obstruction.[12 13] Using a face mask as the interface substantially increases dead space (DS) outside the patient's airway. Nasal prongs are an alternative interface with very low DS. We hypothesised that the added DS of the airway interface (mask or prongs) would significantly affect the time taken for changes in FiO_2 at the blender to reach the patient's airway.

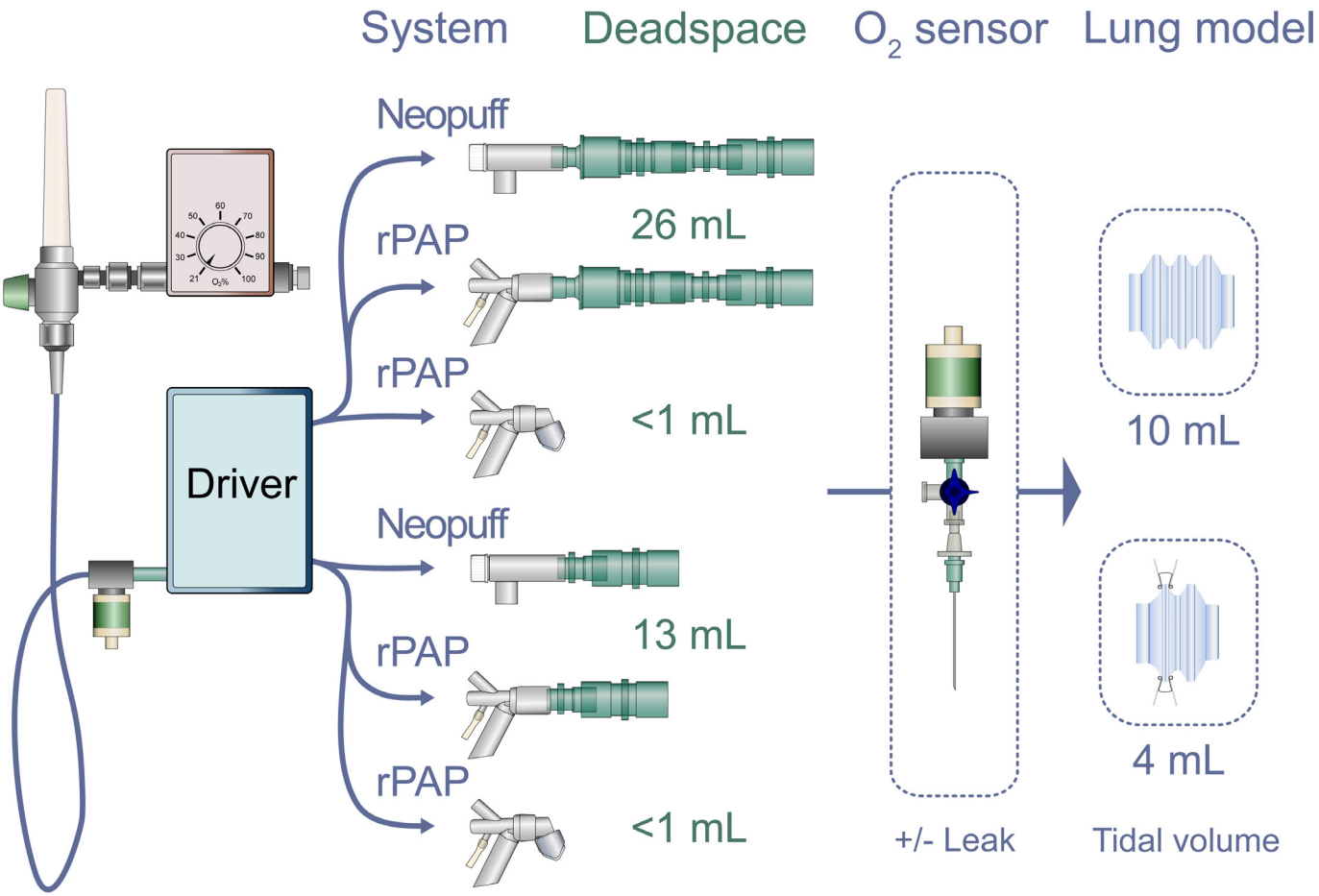

Figure 1 The equipment setup used for the experiment. Fresh gas flow was set to 10 litres per minute. FiO_2 was adjusted with a blender. Dead space was added by connecting straight cylinders to the Neopuff and rPAP. The respiratory system was connected to an O_2 sensor and directly to a 50 mL Dräger Bellows test lung. Tests were performed at two levels of tidal volumes which were altered by applying or removing clamps to the test lung. Measurements were done with and without leaks. FiO_2, fraction of inspired oxygen.

METHODS

The experimental setup is shown in figure 1. The primary outcome was time to reach a FiO_2 0.05 from the set target. For the two starting points, FiO_2 0.30 and 1.0, this was the time to reach FiO_2 of 0.55. The FiO_2 0.05 was similar to the 5% margin between the two sensors used by Dekker *et al*.[9] The respiratory support systems tested were Neopuff (Fisher and Paykel, Auckland, New Zealand) and rPAP (Inspiration Healthcare, Croydon, UK). The DS of the face mask was simulated by connecting straight 15 mm connectors to the T-piece. The inner space of Laerdal face masks (Laerdal Global Health, Stavanger, Norway) size 00 and 0 was measured by injecting water into the masks. The volume was 18 mL for size 00 and 31 mL for size 0. To make the simulation more clinically relevant, we decreased the estimated added mask DS by 5 mL for each mask on the basis that parts of the face will protrude into the face mask and compression of the face mask for seal may reduce the volume. The DS added was 13 mL and 26 mL to represent the volume of the size 00 and 0 masks respectively. The medium short binasal prongs used with the rPAP had an estimated volume of less than 1 mL. The respiratory support device and added interface DS/rPAP prongs were connected leak-free to a custom-built three-dimensional printed connector for the O_2 sensor (5 mL DS) and this was connected directly to a 50 mL Dräger Bellows MP20050 (Dräger, Lübeck, Germany). (online supplemental figure 1). There was no humidification circuit.

To simulate clinical problems with leakage during mask ventilation, the tests were performed both with and without leakage. Leakage between the resuscitation system and the oxygen sensor was generated through a 0.80*50 mm steel needle (21G Sterican, Braun, Melsungen, Germany) that could be turned on using an intravenous line valve. Tidal volumes (TVs) and leaks were measured by a respiratory function monitor (RFM), Monivent Neo100 (Monivent, Gothenburg, Sweden). With the leak activated, the relative leak for 10 mL TV was 29.9% (SD 1.8, for 12 inflations) and for 4.0 mL 47.5% (SD 5.8, 12 inflations). The absolute leakage was the same for both TVs. The Monivent connector piece was removed before the experiments were started to avoid introducing DS to the circuit.

All tests were performed using PPV at 60 breaths per minute with a peak inspiratory pressure (PIP) of 24 cm H_2O and positive end-expiratory pressure (PEEP) of 6 cm H_2O. Fresh gas flow was set to 10.0 L/min. All flows and pressures were calibrated using Fluke VT650 Gas Flow Analyser (Fluke, Washington, USA). Tests were performed at two levels of TVs which were altered by applying or removing clamps to the test lung to restrict movement and reduce compliance. The experiments were performed at 4 mL and 10 mL TV. These volumes represent the TV used to ventilate infants of appropriate weight for Laerdal face mask sizes 00 and 0, delivering 6 mL/kg per inflation for infants weighing 750 g and 1750 g respectively. The 13 mL DS was used for the 4 mL TV and 26 mL for the 10 mL TV. The less clinically

Table 1 Time until reaching FiO_2 0.05 from the set target when decreasing FiO_2 from 1.0 to 0.5 and increasing from 0.3 to 0.6. One-way ANOVA for comparison. * Post hoc test Bonferroni

							One-way ANOVA Mean difference (p value*)		
FiO_2 change	Leak	Tidal volume	System	Dead space	Mean time sec		rPAP mask	Neopuff mask	rPAP prongs
1.0–>0.5	Yes	4 mL	rPAP	13 mL	66.7	One-way ANOVA	NA	2.9 (<0.001)	34.4 (<0.001)
			Neopuff	13 mL	69.6		2.9 (<0.001)	NA	37.3 (>0.001)
			rPAP	Prongs	32.3		34.4 (<0.001)	37.3 (>0.001)	NA
		10 mL	rPAP	26 mL	83.0	One-way ANOVA	NA	4.1 (<0.001)	64.6 (<0.001)
			Neopuff	26 mL	78.9		4.1 (<0.001)	NA	60.5 (<0.001)
			rPAP	Prongs	18.3		64.6 (<0.001)	60.5 (<0.001)	NA
	No	4 mL	rPAP	13 mL	154.6	One-way ANOVA	NA	18.1 (<0.001)	121.3 (<0.001)
			Neopuff	13 mL	172.7		18.1 (<0.001)	NA	139.4 (<0.001)
			rPAP	Prongs	33.3		121.3 (<0.001)	139.4 (<0.001)	NA
		10 mL	rPAP	26 mL	143.8	One-way ANOVA	NA	9.6 (<0.001)	125.5 (<0.001)
			Neopuff	26 mL	153.4		9.6 (<0.001)	NA	135.1 (<0.001)
			rPAP	Prongs	18.3		125.5 (<0.001)	135.1 (<0.001)	NA
0.3–>0.6	Yes	4 mL	rPAP	13 mL	47.1	One-way ANOVA	NA	4.3 (<0.001)	23.3 (<0.001)
			Neopuff	13 mL	51.4		4.3 (<0.001)	NA	27.6) (<0.001)
			rPAP	Prongs	23.8		23.3 (<0.001)	27.6<0.001)	NA
		10 mL	rPAP	26 mL	56.2	One-way ANOVA	NA	0.7 (0.01)	42.9 (<0.001)
			Neopuff	26 mL	55.5		0.7 (0.01)	NA	42.2 (<0.001)
			rPAP	Prongs	13.3		42.9 (<0.001)	42.2 (<0.001)	NA
	No	4 mL	rPAP	13 mL	113.1	One-way ANOVA	NA	24.5 (<0.001)	88.1<0.001)
			Neopuff	13 mL	137.6		24.5 (<0.001)	NA	112.6 (<0.001)
			rPAP	Prongs	25.0		88.1 (<0.001)	112.6 (<0.001)	NA
		10 mL	rPAP	26 mL	103.7	One-way ANOVA	NA	11.9 (<0.001)	88.9 (<0.001)
			Neopuff	26 mL	115.6		11.9 (<0.001)	NA	100.8 (<0.001)
			rPAP	Prongs	14.8		88.9 (<0.001)	100.8 (<0.001)	NA

ANOVA, analysis of variance; FiO_2, fraction of inspired oxygen.

relevant combinations (13 mL DS with 10 mL TV and 26 mL DS with 4 mL) are available as supplement (online supplemental table 1).

FiO_2 was adjusted from 0.30 to 0.60 and from 1.00 to 0.50. FiO_2 was adjusted manually using a blender and the time was set to zero when FiO_2 deviated from baseline at an oxygen sensor positioned after the blender. FiO_2 was measured using chemical sensors (R-17MED, Teledyne Analytical Instruments, California, USA). Data was collected until equilibrium was reached at the patient interface or a maximum of 3 min. Data was acquired using NI NI-9205 and LabVIEW 2015 (National Instruments, Austin, Texas, USA) at 100 Hz.

Each experiment was repeated three times to ensure a low variance of the measuring method. Data were compiled and analysed in SPSS (IBM, Armonk, New York, USA). One-way analysis of variance (ANOVA) was used to compare means in seconds to reach FiO_2 0.55 for all combinations of TV, presence of a leak or not and upwards and downwards titration of oxygen. This resulted in eight ANOVA tests. Post hoc comparisons to reveal within group difference were done using Bonferroni. Assumptions were checked with normal probability plots and the assumption of equality of variance was tested with Levene's test. Statistical significance was set to $p<0.05$.

RESULTS

Mean time to reach FiO_2 within 0.05 of the set target was significantly shorter for rPAP with prongs compared with Neopuff and rPAP with higher DSs representing facemask volumes. This was seen in all measurements, in both set TVs and with or without leakage (table 1). The largest difference was found when testing the decrease in FiO_2 with 10 mL TV without leakage where it took 18.3 s for rPAP with prongs compared with 153.4 s for Neopuff with face mask DS ($p<0.001$, 95% CI 134.4 to 135.7) (table 1). This difference was mainly related to the interface DS and not the type of resuscitation device.

There was a delay of >10 s in reaching the set oxygen concentration at the patient interface in every measurement (table 1, figures 2 and 3). Comparisons between different DS volumes, for both TVs, both T-piece devices, with and without leakage, were all statistically significant, p=<0.001, in one-way ANOVA, post hoc analysis with Bonferroni. Statistical analyses and 95% CI are available as a supplement (online supplemental tables 2,3).

DISCUSSION

This bench study shows that with current equipment used for neonatal stabilisation at birth there is a substantial time delay between when FiO_2 is adjusted at the blender and when the new intended FiO_2 is achieved at the patient interface. This is particularly prolonged with the system DS of a commonly used face mask interface and much reduced with a low DS nasal prong interface. Our results indicate that during PPV in the smallest infants, when changing the O_2 concentration at the blender from 30% to 60%, the concentration may reach 40% first after 30 s and 50% after almost 1.5 min to only come close to the target concentration of 60% nearly 3 min after adjustment. The same is likely to apply for downward titration from 100% to 50% where the O_2 concentration may be at 80% 30 s after changes made at the blender and at 60% after approximately 2 min. Two previous

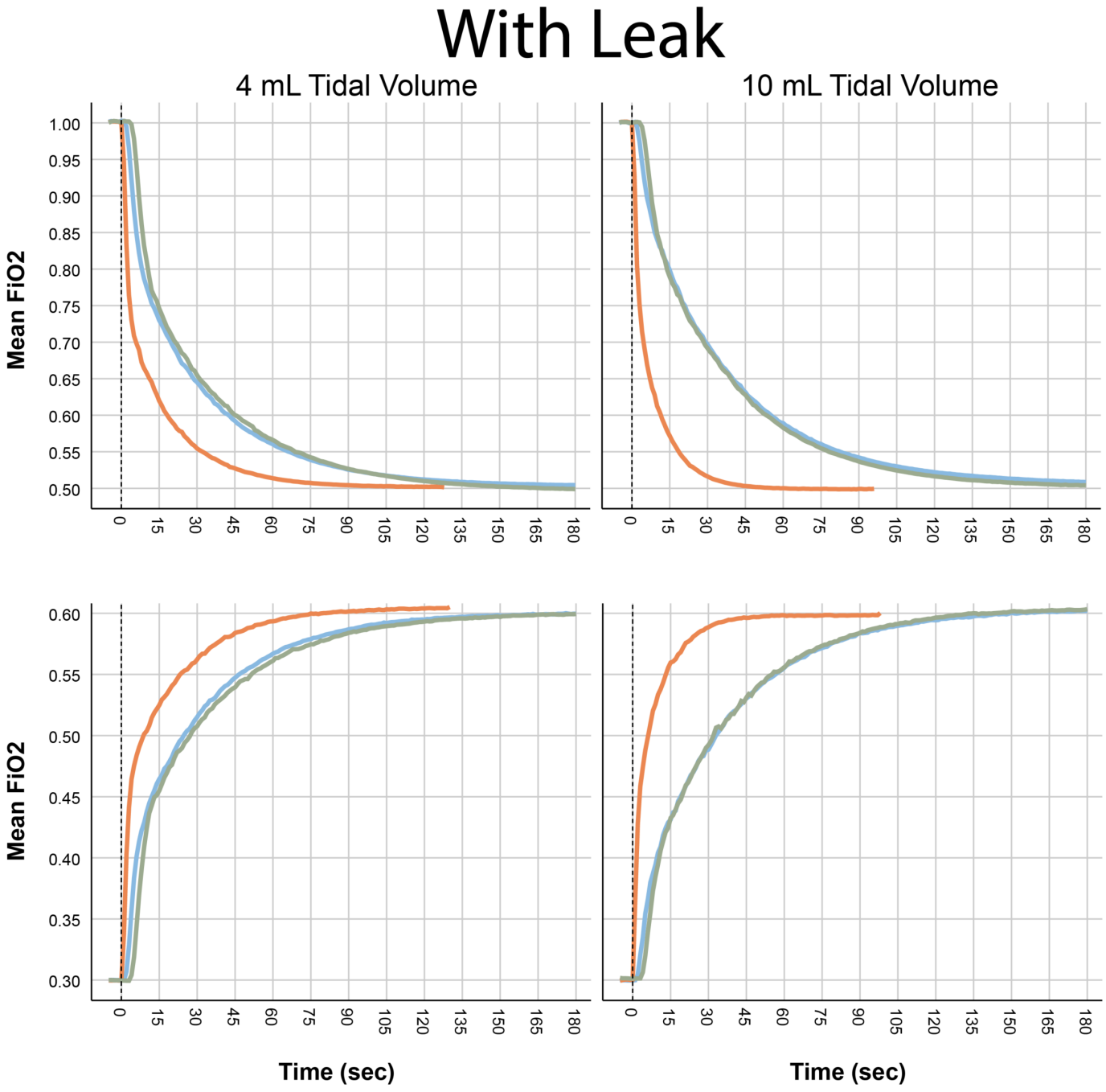

Figure 2 Oxygen measured at the patient interface for the first 90 s after adjustments from FiO_2 1.0 to 0.5, downward titration and from FiO_2 0.3 to 0.6, upward titration. On the left simulations with tidal volume 4 mL and dead space 13 mL: On the right simulations with tidal volume 10 mL and dead space 26 mL. Orange line; rPAP with prongs (<1 mL dead space). Blue line; rPAP with 13 mL and 26 mL added dead space. Green line; Neopuff with 13 mL and 26 mL added dead space. Measurements with leaks. FiO_2, fraction of inspired oxygen.

studies identified a time lag in oxygen adjustments[8 9] but did not measure the additional substantial effect of the mask DS in the set-up. These time delays are clinically important because they are a lot longer than clinicians manually titrating FiO_2 against SpO_2 or automated oxygen adjustment systems would allow between FiO_2 changes.[9 14] These time delays may explain the observation that clinicians are frequently undershooting and later overshooting the target SpO2 in the delivery room. This may result in unnecessary oxygen exposure which in turn may contribute to hyperoxia in the first few minutes of life. This may also explain why many preterm infants are not able to achieve SpO_2 of 80% at 5 min after birth. SpO_2 <80% at 5 min is associated with death and severe intraventricular hemorrhage (IVH) in preterm infants <32 weeks gestational age (GA).[15] The results also highlight the potential value of further clinical studies comparing different interfaces for respiratory support during initial stabilisation.

The reason we opted to use the time to reach a FiO_2 0.05 from the set target as the primary outcome is that a change in FiO_2 over time is exponential in our setup. That means that the final few percent of change takes a long time with the majority of change occurring earlier. This is also in harmony with methods used earlier.[9]

In a study from 2017, Hishikawa *et al* reported delayed oxygen titration during face mask CPAP in term infants. Their

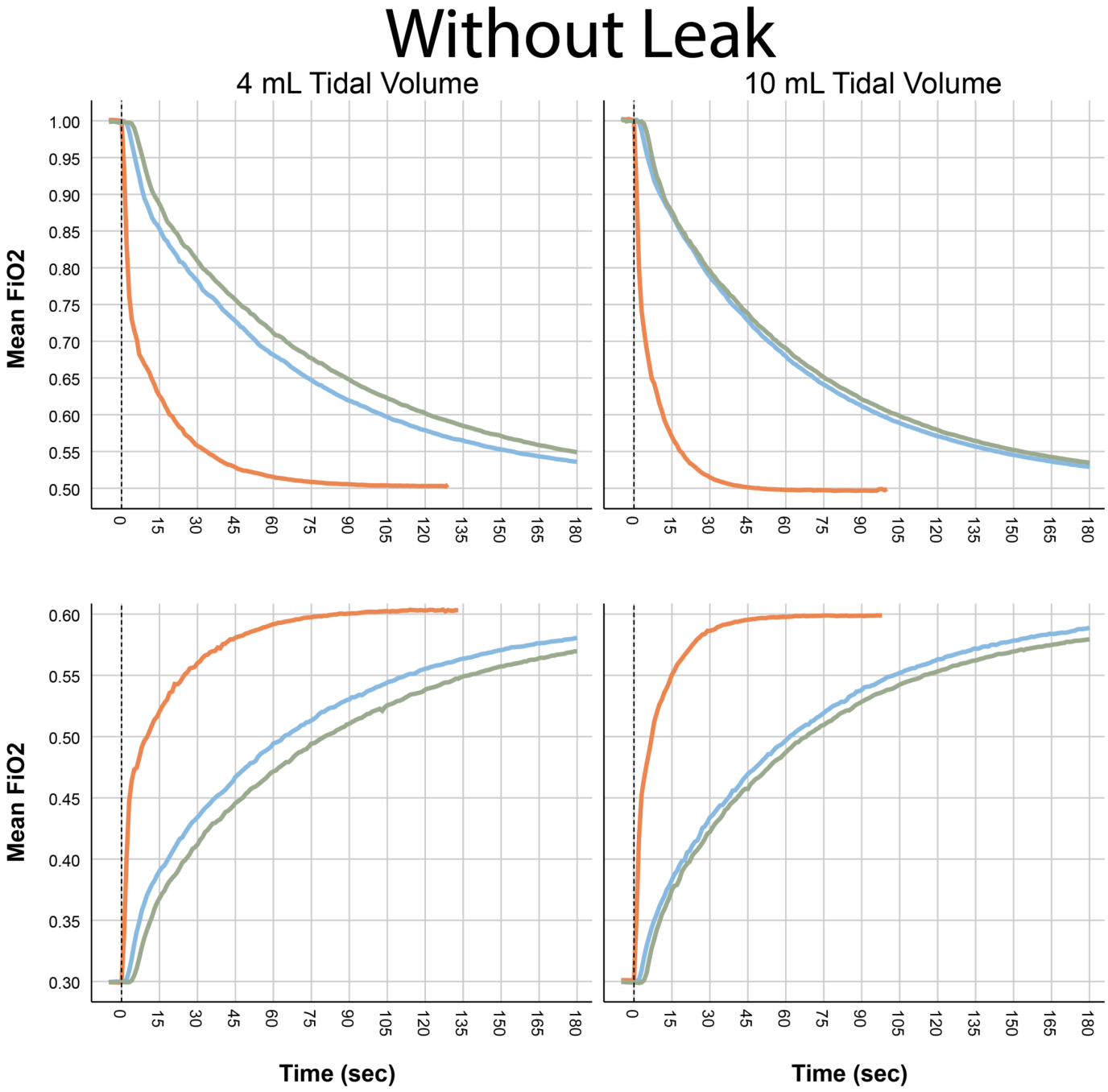

Figure 3 Oxygen measured at the patient interface for the first 90 s after adjustments from FiO_2 1.0 to 0.50, downward titration and from FiO_2 0.3 to 0.6, upward titration. On the left simulations with tidal volume 4 mL and added dead space 13 mL: On the right simulations with tidal volume 10 mL and added dead space 26 mL. Orange line; rPAP with prongs (<1 mL dead space). Blue line; rPAP with 13 mL and 26 mL added dead space. Green line; Neopuff with 13 mL and 26 mL added dead space. Measurements without leaks. FiO_2, fraction of inspired oxygen.

explanation was that due to DS in the face mask, ventilation was less efficient. When leaks were added to their model by making holes in the face mask, oxygen titration time was shorter.[16] Similar results were reported by Dekker *et al* where leaks reduced the time needed to achieve the desired FiO_2 after adjustments using the T-piece system during PPV.[9] This concurs with our results on the shorter time needed when leaks were introduced in the model compared with measurements without leaks. Studies on PPV with face mask have shown that leakage is common and is often very large.[12 13] However, with the increasing use of RFM during stabilisation the users get feedback on the leak in real time which leads to less leakage.[17] This facilitates stable PEEP and the establishment of functional residual capacity (FRC). However, reduced leaks will increase the delay of accurate oxygen delivery to the patient after adjustments.

The ratio between DS and TV (DS/TV) in mechanically ventilated preterm infants has been shown to be around 0.4–0.8.[18] Placing a face mask on the infant during stabilisation adds DS volume to the anatomical DS. The DS of the neonatal face mask greatly exceeds the anatomical DS making the DS/TV ratio during face mask ventilation for the infants unfavourable. The smallest infants with respiratory distress syndrome (RDS) and non-compliant lungs will have a reduced TV before surfactant is given. FRC will also be low initially and will then gradually

increase. All of these factors may influence oxygen delivery after adjustments.

In all the experiments performed, we used ventilation rates of 60 with an inspiratory to expiratory (I:E) ratio of 1:1 and a PEEP of 6 cm H_2O. If lower inflation rates were used, which are included in some international guidelines,[4] the oxygen adjustment time may be longer. The delay in change in FiO_2 due to DS will also apply when providing PEEP/CPAP to a spontaneously breathing infant with a face mask. The delay could be different compared with the presented PPV results depending on spontaneous respiratory rate, lower mask leakage and wash out of DS. Furthermore, the titration frequency and increments will affect the oxygen concentration at the airway level. All of the above should be investigated in future research, preferably in clinical settings.

Limitations

This study reflects the delay observed in vitro. These results need to be confirmed in a clinical study. The added DS in our respiratory circuit model was a straight cylinder and not in the face mask shape. Different types and brands of face masks will have different volumes. However, the experiment was only designed to show the relationship between added DS and TV and the effect that this has on oxygen delivery time after adjustments. In the clinical setting leakage, inflation rate, I:E ratio, TV, PEEP, glottic closure, intermittent spontaneous breathing and FRC will be variable and this could not be accounted for in our lab settings.

Conclusion

There is a substantial delay in the time taken for changes in FiO_2 made at the blender to reach the patient's airway during simulated ventilation when face mask DS is added to the respiratory circuit used for neonatal stabilisation. This should be recognised in guidelines and research protocols. Using nasal interfaces with low DS might be more appropriate for infants to minimise the risk for hypo-oxygenation and hyper-oxygenation during initial stabilisation.

X Vishal Kapadia @kapadianeo

Acknowledgements Mathilda Stenmark, MD, helped with designing and producing figure 1.

Contributors KG: Study design, data collection, data and statistical analysis, manuscript writing and review. BJS, EEF, VK: Study design, manuscript writing and review. TD: Study design, data collection, equipment development, manuscript writing and review. SD: Study design, manuscript writing and review. Study guarantor.

Funding The study was funded by Region Stockholm ALF agreement, clinical research appointment (2020-0302).

Competing interests TD is one of the designers of the original rPAP respiratory support system.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
Kolbrun Gunnarsdottir http://orcid.org/0000-0003-2000-2006
Thomas Drevhammar http://orcid.org/0000-0002-4038-2221

REFERENCES

1 Niles DE, Cines C, Insley E, *et al*. Incidence and characteristics of positive pressure ventilation delivered to newborns in a US tertiary academic hospital. *Resuscitation* 2017;115:102–9.
2 Bjorland PA, Øymar K, Ersdal HL, *et al*. Incidence of newborn resuscitative interventions at birth and short-term outcomes: a regional population-based study. *BMJ Paediatr Open* 2019;3:e000592.
3 Donaldsson S, Drevhammar T, Taittonen L, *et al*. Initial stabilisation of preterm infants: a new resuscitation system with low imposed work of breathing for use with face mask or nasal prongs. *Arch Dis Child Fetal Neonatal Ed* 2017;102:F203–7.
4 Madar J, Roehr CC, Ainsworth S, *et al*. European Resuscitation Council Guidelines 2021: Newborn resuscitation and support of transition of infants at birth. *Resuscitation* 2021;161:291–326.
5 Wyckoff MH, Wyllie J, Aziz K, *et al*. Neonatal Life Support 2020 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Resuscitation* 2020;156:A156–87.
6 Marseglia L, D'Angelo G, Granese R, *et al*. Role of oxidative stress in neonatal respiratory distress syndrome. *Free Radic Biol Med* 2019;142:132–7.
7 Sotiropoulos JX, Vento M, Saugstad OD, *et al*. The quest for optimum oxygenation during newborn delivery room resuscitation: Is it the baby or is it us? *Semin Perinatol* 2022;46:151622.
8 Gottimukkala SB, Sotiropoulos JX, Lorente-Pozo S, *et al*. Oxygen saturation (SpO2) targeting for newborn infants at delivery: Are we reaching for an impossible unknown? *Semin Fetal Neonatal Med* 2021;26:101220.
9 Dekker J, Stenning FJ, Willms LJFB, *et al*. Time to achieve desired fraction of inspired oxygen using a T-piece ventilator during resuscitation of preterm infants at birth. *Resuscitation* 2019;136:100–4.
10 Follett G, Cheung P-Y, Pichler G, *et al*. Time needed to achieve changes in oxygen concentration at the T-Piece resuscitator during respiratory support in preterm infants in the delivery room. *Paediatr Child Health* 2015;20:e10–2.
11 Tribolet S, Hennuy N, Rigo V. Ventilation devices for neonatal resuscitation at birth: A systematic review and meta-analysis. *Resuscitation* 2023;183:S0300-9572(22)00754-7.
12 Kaufman J, Schmölzer GM, Kamlin COF, *et al*. Mask ventilation of preterm infants in the delivery room. *Arch Dis Child Fetal Neonatal Ed* 2013;98:F405–10.
13 O'Currain E, O'Shea JE, McGrory L, *et al*. Smaller facemasks for positive pressure ventilation in preterm infants: A randomised trial. *Resuscitation* 2019;134:91–8.
14 Kapadia V, Oei JL. Optimizing oxygen therapy for preterm infants at birth: Are we there yet? *Semin Fetal Neonatal Med* 2020;25:101081.
15 Oei JL, Finer NN, Saugstad OD, *et al*. Outcomes of oxygen saturation targeting during delivery room stabilisation of preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2018;103:F446–54.
16 Hishikawa K, Fujinaga H, Ito Y. Increased dead space in face mask continuous positive airway pressure in neonates. *Pediatr Pulmonol* 2017;52:107–11.
17 O'Currain E, Thio M, Dawson JA, *et al*. Respiratory monitors to teach newborn facemask ventilation: a randomised trial. *Arch Dis Child Fetal Neonatal Ed* 2019;104:F582–6.
18 Williams E, Dassios T, Dixon P, *et al*. Physiological dead space and alveolar ventilation in ventilated infants. *Pediatr Res* 2022;91:218–22.