Automated Oxygen Control via Nasal High Flow Cannulae for Preterm Babies: A Randomised-controlled Crossover Study

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BACKGROUND

A recent meta-analysis from the NeoProm Collaboration confirmed that a lower SpO₂ range was associated with a higher risk of death and necrotising enterocolitis¹. As a result, many neonatal units, including our own, target a higher range of SpO₂, e.g. 90-95%.

Avoiding hypoxia and hyperoxia are both important goals². Whilst additional training improves compliance³, manual maintenance of the target range 90-95% may only be achieved less than 50% of the time⁴.

Improved targeted SpO₂ can be achieved using automated control of inspired oxygen concentration (FiO₂) in babies requiring both invasive and non-invasive ventilation (NIV)⁵.

This study evaluates a new device (IntelloO₂™, Vapotherm, USA) which uses a closed loop algorithm to control the Precision Flow™ (Vapotherm) delivering nasal High Flow (HF).

We hypothesised that, for preterm babies on HF, the IntelloO₂ would maintain a SpO₂ target range of 90-95% for a greater percentage of time compared to standard (manual) practice.

Our study was a prospective, 2-centre, order-randomised, crossover trial, conducted in the Neonatal Intensive Care Units (NICU) at St. Peter's Hospital, Surrey UK, and Oxford University Hospitals NHS Foundation Trust, Oxford UK. Patients were eligible to participate if they were preterm and receiving HF at FiO₂ ≥25%, and requiring at least 12 FiO₂ adjustments in the 24-hr study periods.

METHODS

The primary outcome was the time in target SpO₂ range 90-95% (90-100% if FiO₂=21%) by pulse oximetry. A sample requirement of 30 patients was needed to provide 90% power, and 0.05 significance (two-sided) to show difference of 19% in time spent within target SpO₂ range. Each subject acted as their own control. Study approvals were obtained from the MHRA Devices Division and Research Ethics Committee (London-Chelsea 16/LO/1272). The study was registered at ClinicalTrials.gov NCT02074774.

RESULTS

Table 1 shows the patient demographics, Table 2 shows the primary outcomes and Table 3 the secondary outcomes. Figure 1 shows percentage of time spent in SpO₂ ranges.

Patient Demographics

Patient characteristics	Median (IQR)	[Range]
Gestation age at birth (weeks)	26 (24 - 27)	[23 - 32]
Birth weight (grams)	793 (606 - 918)	[378 - 2100]
Age at time of study (days)	29 (18 - 53)	[5 - 109]
Weight at time of study (grams)	1080 (959 - 1443)	[576 - 2318]
Males, n (%)	13 (43%)	---

Data presented as median (IQR) & range [min - max], except for gender, for N=30

Figure 1. The frequency of SpO₂ values denote the total time in the associated 1% range for each bar. Bars are paired as automated (grey) and manual (black) control. Target SpO₂ range (90-95%) illustrated by shaded region.

Primary Outcomes

Oxygen Saturation Range Compliance			
Category	Automated Control	Manual Control	p value*
Target SpO ₂ Range **			
Episodes / hour (counts)	41 (32 - 52)	38 (32 - 46)	0.0387
Avg. episode duration (sec)	70 (49 - 99)	48 (31 - 61)	< 0.0001
Percent time in range (%)	80 (70 - 87) %	49 (40 - 57) %	< 0.0001
Data presented as median (IQR) for N=30.			
*Statistical analysis comprised Wilcoxon Signed Rank test.			
**Target range defined as SpO ₂ ≥90% if FiO ₂ =21% or SpO ₂ 90-95% if FiO ₂ >21%.			

Secondary Outcomes

Category	Automated Control	Manual Control	p value*
SpO ₂ > 95% §			
Episodes / hour (counts)	37 (30 - 46)	18 (13 - 25)	< 0.0001
Avg. episode duration (sec)	12 (9.5 - 14)	48 (34 - 68)	< 0.0001
Percent time in range (%)	12 (8.9 - 16) %	23 (15 - 41) %	< 0.0001
SpO ₂ > 98% §			
Episodes / hour (counts)	4.5 (1.8 - 8.5)	5.5 (1.9 - 14)	0.572
Avg. episode duration (sec)	6.4 (5.1 - 7.0)	24 (20 - 32)	< 0.0001
Percent time in range (%)	0.68 (0.29 - 1.4) %	3.7 (1.2 - 9.9) %	< 0.0001
SpO ₂ < range			
Episodes / hour (counts)	27 (22 - 30)	24 (21 - 26)	0.082
Avg. episode duration (sec)	17 (15 - 21)	42 (29 - 50)	< 0.0001
Percent time in range (%)	12 (8.8 - 17) %	28 (17 - 36) %	< 0.0001
SpO ₂ < 80% for ≥60 seconds			
Total Number of Episodes †	0 (0 - 1.3)	5 (2.8-14)	< 0.0001
Avg. episode duration (sec) ‡	0 (0 - 69)	119 (97 - 148)	< 0.0001
§Data for above range categories reported for FiO ₂ >21%			
†Range [min - max] = [0 - 10] for automated and [1 - 38] for manual control			
‡Range [min - max] = [0 - 118] s for automated and [60 - 191.3] s for manual control			

<80% for 60 seconds or more), which has previously been identified as a risk factor for a poorer outcome⁶.

DISCUSSION POINTS AND CONCLUSIONS

Babies on automatic mode spent 31% more time in the target range, 11% less time above target range &16% less time below target range. They were less likely to have saturations >98% when in oxygen and spend less time at SpO₂ <80%. Every baby showed an improvement in their SpO₂ targeting although we did not identify why some showed greater improvements than others. The overshoot episodes may represent FiO₂ oscillations due to the algorithm; their effect at tissue/organ level is not known. A larger study is needed to determine if the improved targeting achieved using the IntelloO₂ device would lead to improved clinical outcomes.

Patients were more likely to “overshoot” (hyperoxia arising after a period of hypoxia) under automatic control: Overshoot % time (13 [6 – 18] % (auto) vs. 8 [3– 19] % (manual); p=0.021). Number of overshoot episodes/hr was (20 [11 – 2.7] /hour (auto) vs. 5 [3 – 16] /hour (manual) ; p<0.0001). We noted a significant reduction in hypoxic episodes (SpO₂

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