Oxygen titration and compliance with targeting oxygen saturation in preterm infants

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Chapter 7

The effect of implementing an automated oxygen control on hypoxaemic events in preterm infants

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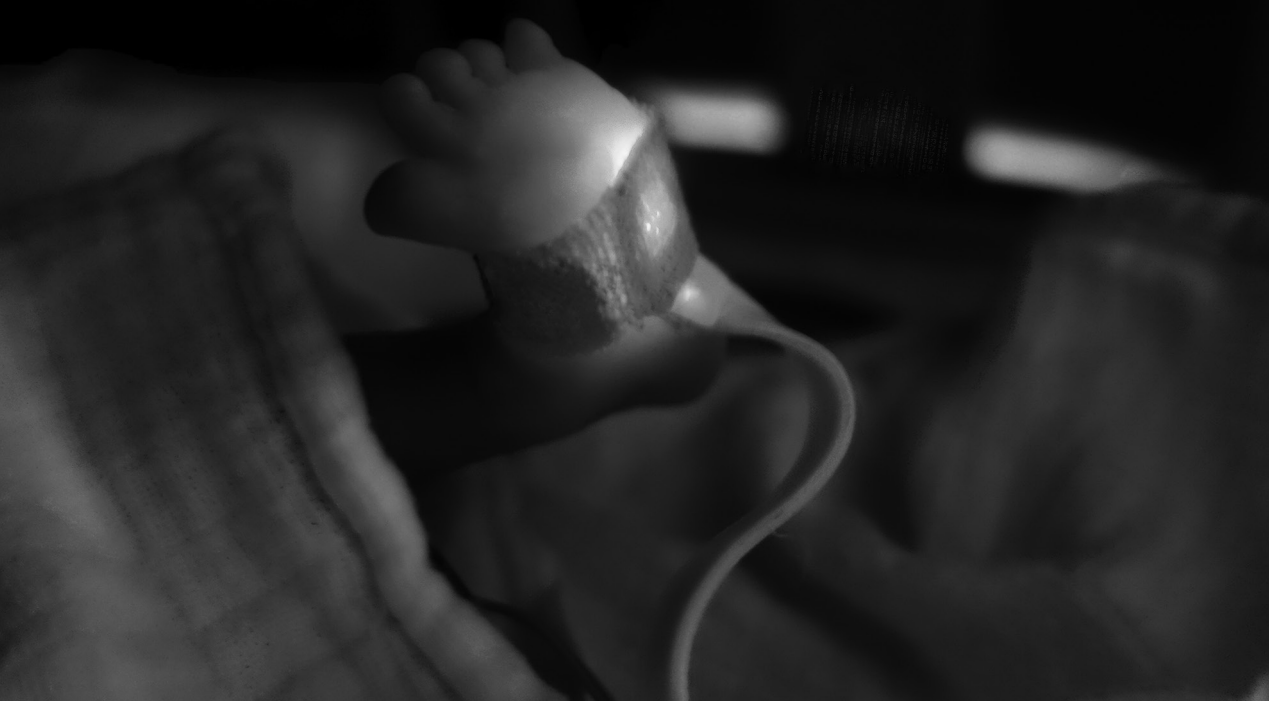

ABSTRACT

Objective: To study the effect of automated versus manual titration on apnoea, bradycardia, cyanosis (ABC) and oxygen therapy in preterm infants.

Methods: Preterm infants born <30 weeks of gestation and admitted to the neonatal unit of the Leiden university medical centre (LUMC) between May and December 2015 before and after implementation of the automated fraction of inspired oxygen (FiO_2) system were retrospectively compared. Oxygen saturation (SpO_2), heart rate and respiratory rate were collected every minute and included for analysis when infants received supplemental oxygen. The count of minute values is used to express duration and the lowest minute value is used to express depth of SpO_2 and heart rate. ABCs where oxygen therapy was given were identified and analysed.

Results: 12/21 (57%) infants admitted during the manual period vs 12/21 (57%) infants during the automated period had ABCs (61 vs 252;p=0.004) during non-invasive respiratory support and where supplemental oxygen was given. In the automated period the duration of hypoxaemia (SpO_2<80%) during ABC was reduced (2(1-3) min vs 1(1-2) min;p<0.05), but not the depth (68(50-73)% vs (68(56-75)%;ns). Hyperoxaemia (SpO_2 >95%) occurred less often (83.6% vs 67.3%;p<0.05) and lasted shorter (5(3-11)min vs 2(1-4)min;p<0.001).

Conclusion: Implementing automated oxygen control for preterm infants led to a shorter duration of hypoxaemia and hyperoxaemia during and after ABCs. Nurses should stay alert for hypoxaemic events related to apnoeas.

INTRODUCTION

Manual titration of oxygen in order to maintain the oxygen saturation (SpO_2) within the target range (TR) has been shown to be quite challenging, especially during apnoea, combined with bradycardia and cyanosis (ABC).[10 24] We recently demonstrated that manual titration of oxygen therapy in preterm infants during ABCs, unintendedly led to occurrence of hyperoxaemia (SpO_2 >95%).[24] Both hypoxaemia and hyperoxaemia have been associated with prematurity related short and long term consequences (impaired growth, bronchopulmonary dysplasia, retinopathy of prematurity, cerebral injury) and mortality. Reducing the periods of hypoxaemia and hyperoxaemia has the potential to improve survival and neurodevelopmental outcome.[9-13 15 34]

Randomised trials comparing automated fraction of inspired oxygen (FiO_2) systems with manual titration for short periods, demonstrated an increase in the proportion of time spent with SpO_2 within TR and a decrease in hyperoxaemia.[35 36 38 39] However, how hypoxaemic events (ABC) are handled when automated oxygen control is used has not been investigated. In the neonatal intensive care unit in Leiden University Medical Centre (LUMC) an automated oxygen control (Closed loop of inspired Oxygen, $CliO_2$, Avea, Carefusion, Yorba Linda, California) was implemented and routinely used since August 2015 in order to improve the SpO_2 targeting during oxygen therapy. We performed a prospective study in preterm infants to evaluate the automated FiO_2 control when it was used as standard care and for a longer period. The aim was to compare the effect on ABC and oxygen therapy when oxygen was titrated automatically or manually.

METHODS

A prospective pre-post implementation study was performed in the neonatal intensive care unit (NICU) of the LUMC, which is a tertiary level perinatal centre in the Netherlands with an average of 650 intensive care admissions per year. In the Netherlands, no ethical approval is required for anonymised studies with medical charts and patient data that were collected and noted for standard care. The LUMC Medical Ethics Committee provided a statement of no objection for obtaining and publishing the anonymised data. All preterm infants born <30 weeks of gestation (GA) admitted to the NICU before and after the implementation of the automated FiO_2 device in August 2015 (May 2015 - January 2016) receiving (non-) invasive respiratory support using the AVEA ventilator (Carefusion, Houten, The Netherlands) were included. Preterm infants with major congenital heart disease were excluded, since different oxygen saturations and guidelines are followed for this group.

Patient basic characteristics, as well as clinical parameters of each infant and ventilator settings (including FiO_2 and SpO_2) were standardly collected and stored every minute in the patient data management system (PDMS) (Metavision; IMDsoft, Tel Aviv, Israel). The data of clinical parameters and ventilator settings of each infant were analysed until the infants reached a GA of 32 weeks. After 32 weeks most infants are transferred to the post IC in our unit or regional hospital, where no automated FiO_2 system was available.

During the manual and the automated oxygen control period, SpO_2 was measured using a neonatal pulse oximeter (Masimo Radical, Masimo Corporation, Irvine CA, USA) integrated into the ventilator. During the manual FiO_2 control period the nurses titrated the supplemental oxygen following local guidelines manually. During the automated oxygen control period, an automated oxygen control system integrated in the ventilator was used ($CliO_2$; Avea, Carefusion, Yorba Linda, California). The $CliO_2$ function is a closed-loop controller designed to regulate FiO_2 levels for preterm infants receiving support and oxygen from a mechanical ventilator. The FiO_2 will be automatically adjusted to maintain the SpO_2 within the TR set by the clinician.[33] In this study, the SpO_2 TR was set from 90% to 95%. The alarm was activated if SpO_2 was below 90% or above 95%. During the manual control period the intended TR and alarms were the same. All preterm infants received, as part of standard care, a loading dose of 10mg/kg caffeine base followed by 5 mg/kg/day. Dopram (2 mg/kg/hr) was added in case of refractory apnoeas.

ABCs during non-invasive ventilation were manually identified in PDMS and analysed starting at the occurrence of an ABC until the oxygen supplied returned to the baseline before the ABC occurred. ABC was defined as apnoea (respiratory pause >20 seconds (or shorter when this pause is combined with hypoxaemia and/or bradycardia), accompanied with bradycardia (<80 beats per minutes (bpm)) and cyanosis (SpO_2 < 80%). As data is sampled every minute, every ABC where supplemental oxygen was titrated was evaluated by documenting the following characteristics: lowest stored minute value (depth) and count in low minute values (duration) of HR <80 bpm, lowest stored minute value (depth) and the count in low minute values (duration) of SpO_2 <80%, baseline FiO_2 and additional oxygen given, the count in minute values with additional oxygen, occurrence and count in minute values with SpO_2 >95%. Hypoxaemia was defined as SpO_2 <80% and hyperoxaemia as SpO_2 >95%.

Statistical analyses

Quantitative data are presented as median (IQR), mean ± SD or number (percentage) where appropriate. The Mann-Whitney-U test was used to compare the frequency, duration, and depth of each ABC in each group. A Chi-square test was used to analyse discrete variables. If one of the cells had an expected count of less than five, the Fisher's exact test was used. Statistical analyses were performed by IBM SPSS Statistics version 23.

RESULTS

During non-invasive respiratory support 61 hypoxaemic events followed by supplemental oxygen occurred in 12/21 (57%) infants in the manual period and 252 events in 12/21 (58%) infants in the automated period. Infants in the manual period had a higher gestational age when compared to the automated period, but this was not significantly different (28+3 (26+2 – 28+6) weeks vs 26+4 (26+0-28+0)weeks;*p* =0.09) Further patient characteristics were not different between the two periods (Table 1). The amount of ABCs per day during respiratory support and supplemental oxygen was higher during the automated period, but this was not significantly different (Table 2). During ABCs, the depth and duration of bradycardia were not different between the two periods. Also no differences were observed in the depth of hypoxaemia (68 (50-73)% vs 68 (56-75)%; ns). However, the duration was shorter in the automated period (2 (1-3) vs 1 (1-2) minute values;*p*<0.05). The occurrence of hyperoxaemia after an ABC significantly reduced (83.6% vs 67.3%;*p*<0.05) and lasted shorter (5 (3-11) vs 2 (1-4) minute values;*p*<0.001) (Table 1). There were no differences in the duration of titrating FiO_2 back to baseline FiO_2, but the amount of supplemental FiO_2 given during an ABC was non-significantly higher after implementation of the automated oxygen control. The baseline FiO_2 before an ABC was slightly higher in the automated period (0.24 (0.21-0.27) vs 0.27 (0.25-0.31);*p*<0.001)(Table 2).

Table 1. Patient characteristics with ABCs

	Manual period N= 12	Automated period N= 12	*p*-value
Gestational age at birth (weeks), Median (IQR)	28+3 (26+2–28+6)	26+4 (26 –28)	0.09[a]
Birthweight (grams). Median (IQR)	901 (806-1299)	855 (708–948)	0.2 [a]
Male sex, no (%)	6 (50)	8 (77)	0.4[b]
Caesarean delivery, no (%)	6 (50)	3 (25)	0.4[c]
Singletons, no (%)	8 (66)	3 (25)	0.09[b]
Apgar at 5 min, Median (IQR)	7 (6-9)	8 (6-9)	0.25[a]

[a] Independent samples Mann-Whitney U test
[b] Chi-square test
[c] Fisher's exact

Table 2. Comparison of ABCs: manual vs automated

ABC characteristics	Manual N= 61	Automated N=252	p Value 0.004[a]
Number of ABC/24h, n,	0.18 (0-0.74)	0.31 (0-2.26)	*ns*[b]
Lowest minute value during bradycardia, bpm (depth)	67 (61-72)	69 (60-74)	*ns*[a]
Count minute values with bradycardia, min (duration) Median (IQR)	1 (1-1)	1 (1-1)	*ns*[a]
Lowest minute value during SpO_2 <80%, % (depth)	68 (50-73)	68 (56-75)	*ns*[a]
Count minute values SpO_2 <80%, min (duration)	2 (1-3)	1 (1-2)	< 0.03[a]
Baseline FiO_2,	0.24 (0.21-0.27)	0.27 (0.25-0.31)	<0.001[a]
Maximum increase FiO_2,	0.20 (0.19-0.46.5)	0.30 (0.18-0.50)	*ns*[a]
Count minute values of FiO_2 titration to baseline oxygen concentration, min	3 (2-6)	3 (2-4)	*ns*[a]
Hyperoxaemia, n(%)	51 (83.6)	171 (67)	< 0.03[b]
Count minute value with SpO_2 >95%, min	5 (3-11)	2 (1-4)	<0.001[a]

[a] Independent samples Mann-Whitney U test
[b] Chi-square test
ABC, apnoea, bradycardia, cyanosis; SpO_2, pulse oxygen saturation; FiO_2, fraction of inspired oxygen.

DISCUSSION

This study demonstrated the impact of routine use of an automated oxygen control during respiratory support and oxygen therapy of preterm infants admitted in a neonatal intensive care unit. During ABCs, we observed that the automated oxygen control had no effect on the depth of SpO_2 and heartrate, but the duration of hypoxaemia was reduced with 50%. Although the duration of supplemental oxygen titration did not change and the maximum FiO_2 given after an ABC was higher, the occurrence and duration of SpO_2 >95% decreased. This discrepancy is likely the result of a faster and more diligent titration when this is regulated automatically. It is possible that responding automatically to a hypoxaemic event with a higher FiO_2 than would have been given manually led to a shorter duration of hypoxaemia. Likewise, the more frequent correction of FiO_2 when SpO_2 was measured above TR probably led to the reduction in hyperoxaemia.

An unexpected finding was the increase in ABCs with oxygen therapy during the automatic period. This is in contrast with the findings of a previous study comparing manual and automated oxygen titration, where a reduction in hypoxaemic episodes was observed,[85] however, it is difficult to compare our results with their findings. The TR was wider (88-96%

vs 90-95%), and hypoxaemic events were defined as SpO_2 <88% instead of <80%, and not combined with bradycardia <80 bpm as in our study.[85] Our study was not randomized and an unbalance between the groups could not be avoided. Indeed, the infants in the automatic period were younger and could have been more unstable. Similarly, the observation that the infants in the automatic period spent more time in the 80-89% could be a reflection of this instability instead that this was an effect of the automatic control. Likewise, infants in the manual period could have been more stable as they spent more time in higher SpO_2 values and desaturations are less likely to occur.[74] In contrast, when the more frequent desaturation in the 80-89% region would have been an effect of the automated titration, using a higher and more narrow TR could improve this. However, we could not confirm this in a recent randomized trial.

The difference in the amount of ABCs could also be explained by the fact that nurses performed other routines before increasing the fraction of inspired oxygen during manual control, resulting in less intervention with oxygen. Nurses often already responded to ABC before our criteria of noting an ABC were met. This could be repositioning CPAP prongs/ mask, tactile stimulation, and/or suctioning whereas automatic oxygen controllers can only rely on one intervention to a single input parameter (SpO_2): increasing the oxygen. It is obvious that solely increasing the oxygen is not adequate enough when an apnoea occurs and more interventions such as tactile stimulation are needed. Therefore, automatic oxygen control does not decrease the need for manual intervention when an apnoea occurs and the nurses should stay attentive to these events.

We did not adjust for the contribution of the amount of ABCs of each patient, but we considered every ABC as an independent event because all ABCs are handled the same for each infant. However, we could only use a 1-minute time interval for sampling parameters, which is less frequent than reported in other studies.[14 85] It is possible that in both groups we missed hypoxaemic or hyperoxamic events that were resolved within one minute. These limitations indicate that the results have to be interpreted with caution.

In conclusion, after implementing automated oxygen control, during ABC in preterm infants the occurrence hypoxaemia did not decrease but lasted shorter. The duration of oxygen titration was not shorter, but less hyperoxaemia occurred. When oxygen is titrated automatically, nurses should stay alert for hypoxaemic events related to apnoeas.