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REVIEW ARTICLE

Automated oxygen control in preterm infants: a new frontier in neonatal respiratory care. A review

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Abstract

Maintaining optimal oxygen saturation (SpO_2) in preterm infants remains a critical yet challenging aspect of neonatal intensive care. Manual adjustment of inspired oxygen (FiO_2) is both labor-intensive and prone to human error, often resulting in significant fluctuations in oxygen levels that may increase the risk of complications such as retinopathy of prematurity (ROP), bronchopulmonary dysplasia (BPD), and long-term neurodevelopmental impairment. Emerging evidence indicates that automated oxygen control (AOC) systems enhance the stability of SpO_2, reduce the frequency of hypoxic and hyperoxic episodes, and minimize the need for manual FiO_2 adjustments. Despite these promising physiological improvements, high-certainty evidence demonstrating a positive impact on short- and long-term clinical outcomes remains lacking. Current data on mortality, severe ROP, BPD, and neurodevelopmental outcomes are limited and often of low certainty. AOC technology shows significant potential to improve oxygen management in preterm infants by maintaining target saturation ranges more consistently. However, robust, high-quality multicenter trials are essential to confirm its clinical benefits, assess its feasibility in various healthcare settings, and assess cost-effectiveness. This review synthesizes the current evidence surrounding the use of AOC in preterm infants, with a focus on its efficacy, safety profile, and potential role in advancing neonatal respiratory care.

Keywords: Automated oxygen control. Hyperoxia. Hypoxia. Neonatal intensive care. Oxygen saturation. Preterm infants.

Controlo automatizado do oxigénio em recém-nascidos pré-termo: uma nova fronteira nos cuidados respiratórios neonatais. Revisão

Resumo

Manter a saturação periférica de oxigénio (SpO_2) na faixa desejada em recém-nascidos prematuros permanece um aspeto crítico, porém desafiador, dos cuidados intensivos neonatais. O ajuste manual do oxigénio inspirado (FiO_2) é trabalhoso e suscetível a erros humanos, e resulta, frequentemente, em flutuações significativas na SpO_2, o que pode aumentar o risco de complicações como a retinopatia da prematuridade (ROP), displasia broncopulmonar (DBP) e compromisso do desenvolvimento neurológico a longo prazo. Evidências emergentes indicam que os sistemas de controlo automatizado de oxigénio (CAO) melhoram a estabilidade da SpO_2, reduzem a frequência de episódios de hipóxia e hiperóxia e minimizam a necessidade de ajustes manuais da FiO_2. Apesar das melhorias fisiológicas promissoras, ainda faltam evidências de qualidade que demonstrem um impacto positivo nos desfechos clínicos de curto e longo prazo. Os dados atuais sobre mortalidade, ROP grave, DBP e efeitos no neurodesenvolvimento são limitados e, muitas vezes, de baixa qualidade. A tecnologia CAO demonstra um potencial significativo para melhorar o manejo do oxigénio em prematuros, mantendo os intervalos-alvo de saturação

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de forma mais consistente. No entanto, são necessários ensaios multicêntricos robustos e de alta qualidade para confirmar seus benefícios clínicos, avaliar sua viabilidade em diferentes contextos clínicos e analisar sua relação custo-benefício. Esta revisão sintetiza as evidências atuais sobre o uso do CAO em recém-nascidos prematuros, com foco em sua eficácia, perfil de segurança e potencial papel no avanço dos cuidados respiratórios neonatais.

Palavras-chave: Controlo automatizado de oxigénio. Hiperóxia. Hipóxia. Cuidados intensivos neonatais. Saturação de oxigénio. Recém-nascidos prematuros.

What is known
- It is well established that maintaining optimal oxygen saturation in preterm infants is a major challenge due to frequent fluctuations between hypoxia and hyperoxia.
- Automated oxygen control (AOC) systems have been shown to improve the stability of SpO_2 and reduce the frequency of both hypoxemic and hyperoxemic episodes compared with manual control.
- Despite these physiological benefits, current evidence remains insufficient to confirm improvements in key clinical outcomes.

What is added
- This review compiles and critically analyzes the most recent evidence on AOC systems in preterm infants, highlighting their efficacy, safety, and practical implications for neonatal care.
- It identifies existing research gaps, including the need for large multicenter randomized trials to establish the clinical benefits and cost-effectiveness of AOC.
- The review also outlines future research priorities aimed at optimizing control algorithms, improving sensor technology, and integrating AOC into routine NICU practice worldwide.

Introduction

The vast majority of extremely preterm infants require oxygen therapy in their early days of life due to pulmonary immaturity.[1] Maintaining peripheral oxygen saturation (SpO_2) within the desired range in preterm newborns receiving invasive or non-invasive mechanical ventilation is a challenge in neonatal care, particularly during the first days of life.[2] This difficulty is due to several factors, notably the respiratory instability related to the severity of respiratory distress syndrome (RDS) and the relentless work of nurses in the neonatal unit, which prevents them from adjusting the fraction of inspired oxygen (FiO_2) manually in a timely manner.[2]

The European Consensus for the treatment of RDS in preterm neonates recommends maintaining SpO_2 within the 90-94% range.[3] Several important studies have shown that extremely preterm infants receiving oxygen frequently spend time outside the target SpO_2 range, experiencing frequent episodes of both hypoxemia and hyperoxemia.[4-7]

Intermittent hypoxemia (IH) events in preterm infants have been linked to various morbidities, including retinopathy of prematurity (ROP), necrotizing enterocolitis (NEC), sleep-disordered breathing, neurodevelopmental impairment, and even mortality.[8-10] Additionally, these infants are especially vulnerable to oxidative stress because of their insufficient enzymatic and non-enzymatic antioxidant defenses, making them more susceptible to the detrimental effects of hyperoxemia, including the development of bronchopulmonary dysplasia (BPD).[11-13] Furthermore, severe ROP has been associated with prolonged exposure to high FiO_2 levels and iatrogenic hyperoxemia, particularly in infants with extremely low birth weight, despite the efforts to titrate FiO_2 more frequently.[14]

In an attempt to overcome the difficulty of maintaining FiO_2 within the desired values, especially during the first days of life in preterm neonates under oxygen therapy, systems of closed-loop automated control (CLAC) of FiO_2 were developed, and have been increasingly used in neonatal intensive care units (NICUs).[15]

The objective of this review is to compile and analyze the available evidence on automated oxygen control (AOC) in preterm infants, focusing on its advantages, limitations, and clinical impact. For this purpose, a review was conducted in the PubMed database, with no time limit and up until April 25, 2025, searching for articles on the topic. The search used the following keywords: automated oxygen control, closed loop automated oxygen control, manual oxygen control, hyperoxia, normoxia, hypoxia, and preterm infant.

Manual method of FiO_2 adjustment

Traditionally, FiO_2 was manually adjusted based on clinical observation of the neonate's SpO_2 levels. This process involves continuous monitoring of SpO_2 and adjusting FiO_2 on ventilators or oxygen therapy devices accordingly. Healthcare providers, including doctors and nurses, are responsible for frequently adjusting the ventilator settings or oxygen systems based on SpO_2

readings, clinical signs (such as respiratory rate and effort), and the perceived needs of the patient. The goal is to maintain SpO_2 within the desired range. A study by Lim K. et al., involving 45 infants with a gestational age of 30 weeks (IQR: 27-32) receiving nasal continuous positive airway pressure (NCPAP), demonstrated that FiO_2 adjustments were required a median of 25 times per day (interquartile range: 16-41).[16] This number of adjustments is difficult to achieve with precision in units caring for extremely preterm infants due to the high number of tasks nurses are in charge of.[2] Additionally, the nurse-to-infant ratio also affects the effectiveness of manual control.[16]

There are several disadvantages to the manual FiO_2 control. Preterm infants often experience rapid changes in oxygen saturation, and manual control cannot respond immediately to these fluctuations.[2] This increases the risk of both hypoxemia and hyperoxemia.[2] Manual adjustment requires continuous attention from healthcare providers, especially nurses, who often manage multiple tasks simultaneously in the NICU.[2] This can lead to delays in FiO_2 adjustment or even missed interventions. Also, continuously adjusting SpO_2 levels can result in overcorrection, potentially leading to unintended hyperoxia.[2] The high-pressure clinical environment, combined with fatigue or competing demands, can result in inaccurate or inconsistent FiO_2 titration, increasing the likelihood of errors.[2] FiO_2 adjustments can vary between caregivers and across shifts, leading to inconsistent care and fluctuations in oxygen exposure.[2] Continuous monitoring of SpO_2 and frequent manual FiO_2 adjustments add significantly to the workload of clinical personnel, potentially diverting attention from other critical aspects of neonatal care.[2] Finally, studies have proven that with manual control, preterm infants often spend a significant amount of time outside the recommended SpO_2 range, which can range between 18% and 68%.[1,17] On the contrary, NICUs that implemented AOC reported that the children spent less time with saturations outside the target range, ranging from 9% to 60%, depending on the system used and the infant's clinical condition.[1,18]

Automatic control of FiO_2

The AOC is currently used in the NICU for infants receiving invasive mechanical ventilation, non-invasive ventilation (nasal CPAP, nasal IPPV), and high-flow nasal cannula. The closed loop AOC is a technology used automatically adjust the amount of oxygen delivered to neonates, usually preterm infants, based on their continuously monitored SpO_2 levels. A sensor continuously measures the baby's SpO_2, and an automated system compares this value to a predefined target range (e.g.: 90-94%). These systems use software algorithms that automatically adjust the FiO_2 in response to fluctuations in the infant's SpO_2, aiming to maintain a predetermined target oxygen saturation range. If the SpO_2 is outside the target range, the system automatically adjusts the FiO_2, increasing or decreasing the oxygen being carried.[19]

Currently available algorithms include CLiO™$_2$ (Closed Loop inspired Oxygen) integrated into the Avea® infant ventilator; CLAC (Closed Loop Automatic Oxygen Control), incorporated into the Leoni plus® ventilator; IntellO$_2$™, part of the Oxygen Assist Module in the Vapotherm® Precision Flow; VDL 1.1 OxyGenie on the SLE6000® ventilator; PRICO (Predictive Intelligent Control of Oxygenation) on the Fabian® Acutronic ventilators; and SPOC on the Sophie® neonatal ventilator (MEDACX).[1,20-21] Each algorithm has a different design for processing the input and computing adjustments in FiO_2.[21] Fathabadi et al. described the main characteristics of algorithms developed for automated FiO_2 control in preterm infants and classified them into four categories: rule-based (fuzzy or non-fuzzy), proportional-integral-derivative (PID), adaptive, and robust, though the latter is not currently available in clinical practice.[22] Among the most widely used systems, PRICO® employs a rule-based, non-fuzzy control algorithm; the OxyGenie® system uses a PID algorithm; and the AVEA™-CLiO$_2$™ system utilizes an adaptive algorithm.[1,21] It is important to emphasize that the clinical outcomes of systems for AOC in preterm infants can vary depending on several factors such as the study population, the type of respiratory support, and the chosen target range, as well as the effectiveness of the algorithm itself.[1,21] Also, the experience of the medical team, the available ventilation technology, and the specific clinical needs are crucial factors influencing the outcome. Although there are minor differences in the functioning of the algorithms, the most effective is currently unknown. All algorithms proved to maintain FiO_2 more consistently and accurately within the desired range by continuously adjusting oxygen levels based on real-time measurements, minimizing fluctuations, and ensuring optimal oxygenation.[21]

AOC systems can minimize the need for frequent manual adjustments by continuously monitoring and adjusting oxygen levels in real time. This, in turn, becomes a technology that supports and facilitates the work of nurses. However, it is important to emphasize that the AOC does not replace the nurse's work and, moreover, it itself needs to be supervised by the nurse,

since in the event of a technical issue, they shall ensure the control of the oxygen. Despite the advantages, technological and financial challenges remain significant obstacles to the widespread implementation of these systems. The high cost of advanced monitoring equipment, coupled with limited access to such technologies in certain NICUs, can impede their adoption, particularly in resource-limited environments.[21]

A commonly mentioned limitation of AOC is the possibility of masking a clinical deterioration in the patient.[21] This aspect is usually detected more quickly with manual adjustment. However, this limitation may be mitigated by implementing protocols that include periodic assessment of the FiO_2 delivered by the ventilator, or by setting an upper FiO_2 limit that facilitates early detection of increasing oxygen requirements in the patient.[21] With the continued use of AOC, caregivers become more familiar with both the technique and the assessment of the clinical status of the patient receiving this AOC, making the masking of clinical deterioration no longer a real issue.[2,21]

Results of studies comparing automatic FiO_2 control with manual control

Since the 1950s, studies have emphasized the detrimental impact of excessive oxygen supplementation and hyperoxia in preterm infants.[23,24] The most evident condition associated with this practice is ROP, which develops as a result of the exposure of the immature retinal vasculature to high oxygen concentrations.[23-25] In subsequent years, studies showed that the preterm lung condition of chronic lung disease (CLD) was associated with prior exposure to higher concentrations of oxygen.[26-28] Also, the harmful effects of hypoxia in preterm infants became evident when prolonged periods of low oxygen were found to increase the risk of death or neurological impairment.[29,30]

The introduction of transcutaneous oxygen electrodes in the 1970s to measure partial pressure of oxygen (PaO_2), followed by the development of pulse oximetry in the 1980s, enabled clinicians to titrate oxygen therapy based on non-invasive assessments of oxygenation.[31,32] Pulse oximetry is now the standard method for monitoring oxygenation in NICUs. To prevent both hypoxia and hyperoxia, maintaining SpO_2 within an admissible range has become a widely accepted practice. However, the optimal target range for preterm infants continues to be a topic of ongoing debate.[30]

In routine clinical practice, NICU personnel – typically nurses – manage oxygen therapy by manually adjusting the fraction of inspired oxygen (FiO_2) or the flow rate based on fluctuations in the infant's SpO_2. However, this manual approach can be challenging due to the numerous factors that influence its effectiveness.[2,33]

The implementation of AOC in neonatal care began in the 1970s.[34-36] Since then, advancements in ventilation technology led to the development of the first AOC systems, designed to enhance the precision of oxygen delivery to newborns, particularly preterm infants.[37]

Over the past two decades, many studies have assessed the effectiveness of AOC in the care of preterm infants. Meanwhile, systematic reviews and meta-analyses have already been conducted using several of these studies. A systematic review by Hummler H et al. in 2014, wich included nine studies, found that AOC allows SpO_2 to remain within the target range for longer periods, reduces the number of episodes of hyperoxemia and severe hypoxemia, and decreases nurses' manual workload.[38] Additionally, a systematic review and meta-analysis by Mitra S et al. up to December 2016, published in 2018, including ten studies, also concluded that AOC improves the maintenance of target oxygen saturations.[17] Another systematic review and meta-analysis by Denault MH et al., conducted in 2018 and published in 2019, included seven studies in preterm infants and two in adults, and reached the same conclusion: AOC allows for a greater percentage of time within the target saturation range.[39] Also, a systematic review by Abdo M et al., conducted in December 2020 and published in 2022, included 13 studies and 343 preterm infants on respiratory support. It concluded that AOC is fast and effective in regulating SpO_2 and may be used to reduce nurses' workload.[40]

A recent Cochrane systematic review, published on January 23, 2023, aimed to assess the benefits and harms of AOC systems (integrated into ventilators or oxygen delivery devices) for preterm infants with respiratory dysfunction requiring respiratory support or supplemental oxygen therapy.[41] This review included 18 studies that enrolled a total of 457 infants, of which 13 studies (339 infants) contributed data to meta-analyses.[15,37,42-57] The included studies were randomized controlled trials and randomized cross-over trials that compared AOC versus manual oxygen delivery, or that compared different automated oxygen delivery systems head-to-head. Seventeen studies involved preterm infants of both genders, with an average gestational age at birth between 25 and 29 weeks (ranging from 23 to 36 weeks), and birth weights ranging from 350 g to 2460 g. One study (Kaltsogianni, 2023) included late preterm or term infants born after 34 weeks of gestation.[47] Across studies, the mean age

at enrolment varied between eight and 33 days postbirth. The duration of the period in which AOC was used ranged from 90 minutes to 24 hours, except in one study (Nair 2023)[56] in which the infants remained on AOC while being ventilated. Three main comparisons were made: one (1) AOC versus standard manual delivery; two (2) AOC versus enhanced manual delivery with additional personnel (a dedicated research nurse or research assistant adjusting FiO_2 to provide a level of care beyond routine practice); and three (3) comparisons between different AOC systems. The results indicated that AOC, compared to routine manual administration, likely increases the percentage of time that SpO_2 remains within the target range (mean difference 13.54%; 95% CI: 11.69-15.39; I^2 = 80%; 11 studies, 284 infants; moderate-certainty evidence). No studies assessed in-hospital mortality. Regarding the risk of severe ROP, AOC may have little or no effect compared to routine manual administration (risk ratio 0.24; 95% CI: 0.03-1.94; one study, 39 infants; low-certainty evidence). No studies assessed neurodevelopmental outcomes. When compared with enhanced manual oxygen delivery, AOC may show no clear increase in the time spent within the target SpO_2 range (mean difference 7.28%; 95% CI: –1.63-16.19; I^2 = 0%; two studies, 19 infants; low-certainty evidence). No studies reported on in-hospital mortality, severe ROP, or neurodevelopmental outcomes. A comparison was also made between AOC algorithms: CLACfast, which allows up to 120 automated adjustments per hour, and CLACslow, which allows up to 20 adjustments per hour. CLACfast may result in little or no increase in the percentage of time within the target SpO_2 range compared to CLACslow (mean difference 3.00%; 95% CI: –3.99-9.99; one study, 19 infants; low-certainty evidence). Again, no studies mentioned in-hospital mortality, severe ROP, or neurodevelopmental outcomes. The authors' conclusion was that AOC likely increases the amount of time that preterm infants on respiratory support spend within the target SpO_2 range when compared with routine manual delivery (with an average increase of 13.54%). However, it remains uncertain whether this improvement translates into meaningful clinical benefits. The available evidence on outcomes such as CLD and severe ROP is of low certainty, with minimal or no differences observed between interventions. Current data are also insufficient to draw firm conclusions regarding comparisons between AOC and enhanced manual delivery, or between different automated systems.

At our center, we conducted a prospective study over a three-year period (2020-2023), enrolling preterm infants born at less than 33 weeks' gestation who required supplemental oxygen within the first 24 hours of life and received either invasive or non-invasive respiratory support.[58] The closed-loop AOC system used was the PRICO feature integrated into Fabian® ventilators. Infants were randomized into two groups: one receiving combined automatic and manual FiO_2 control, and the other receiving standard manual control. The study included 89 patients: 45 received combined automatic and manual FiO_2 control, while 44 received routine manual control. Compared to the manual control group, the combined control group required fewer manual FiO_2 adjustments [median 0 (range 0-4) versus 4 (range 0-12), $p < 0.001$], had fewer episodes of hypoxemia [median 0 (range 0-4) versus 2 (range 0-8), $p < 0.001$] and hyperoxemia [median 0 (range 0-0) versus 1 (range 0-6) ($p < 0.001$)], and spent significantly more time within the target SpO_2 range [median (min - max), in minutes: 1440 (1424-1440) versus 1406 (936-1440), $p < 0.001$]. After adjusting for potential confounders, the time spent in normoxemia remained significantly higher in the combined control group (β = 81.5; 95% CI: 47.9-115.2; $p < 0.001$). The use of AOC was feasible and was associated with fewer episodes of both hypoxia and hyperoxia, resulting in longer periods of SpO_2 within the target range. Furthermore, its use was associated with a reduction in the need for manual FiO_2 adjustments.

Several other studies are currently underway.[41] Their results will be available soon, potentially providing more relevant information.

A related study was that of Dani C. et al. which assessed the impact of the PRICO system on cerebral (rSO_2 C) and splanchnic (rSO_2 S) oxygenation in a cohort of 20 preterm infants (< 32 weeks gestational age) experiencing frequent desaturation episodes.[59] The infants were randomly assigned in sequence to 12 hours of either automated or manual FiO_2 adjustment. Throughout this period, continuous monitoring was conducted using near-infrared spectroscopy (NIRS). While AOC with the PRICO® system did not improve cerebral or splanchnic oxygenation compared to manual control, it reduced SpO_2 fluctuations and shortened the duration of both hypoxemia (% of time SpO_2 < 80%: 1.6 ± 0.9 vs 3.0 ± 2.9, p = 0.46) and hyperoxemia (% of time SpO_2 > 95%: 17.6 ± 12 vs 30.9 ± 18.9, p = 0.014). The total percentage of time in normoxemia (SpO_2 90-95%) was significantly higher with AOC (66.0 ± 14.1% vs. 50.0 ± 20.6%, p = 0.009).

Assessing the clinical potential of automated oxygen control in neonatal care

Most studies have shown that AOC allows neonates to spend more percentage of time within the target SpO_2 range, although this period of time varies among studies, ranging from 40% to 91% with automatic control and from 32% to 82% with manual control[1]. Also, the width of the SpO_2 target range does not seem to have influence on the effectiveness of AOC[1]. Additionally, some studies showed that the AOC performs less favorably with hypoxia than with hyperoxia[1]. It should be noted, however, that while AOC can respond to hypoxia, it cannot prevent it[1].

Although current evidence suggests that AOC in preterm infants results in longer time spent within the target SpO_2 range, fewer episodes of hypoxemia and hyperoxemia, and reduced need for manual FiO_2 adjustments, several important questions remain before this technology can be widely adopted in NICUs.

It remains unclear whether improved oxygen saturation control translates into better clinical outcomes. The studies conducted to date have predominantly employed crossover designs rather than randomized controlled trials, are highly heterogeneous, and lack sufficient statistical power to assess the impact of AOC versus manual oxygen control on neonatal morbidities. Further studies are necessary to assess the effect of AOC on key short and long-term outcomes, including mortality, BPD, severe ROP, intraventricular hemorrhage, and long-term neurodevelopmental outcomes. The FiO_2-C study group trial (www.ClinicalTrials.gov: NCT03168516) is ongoing and will address questions related to neonatal outcomes and neurodevelopment at 24 months of corrected age, ensuring an appropriate assessment of safety and efficacy before AOC can be implemented as standard therapy[60].

Most existing trials compare AOC with routine manual adjustment. Evidence is still lacking on how AOC systems perform against enhanced manual protocols involving well-trained personnel and standardized oxygen management strategies.

The safety and effectiveness of AOC in different clinical settings and patient subgroups – such as those receiving invasive versus non-invasive respiratory support – require further exploration.

Before widespread adoption, comprehensive analyses of cost-effectiveness are needed. Additional considerations include equipment compatibility, training requirements, and the availability of technical support.

Standardized guidelines and regulatory frameworks must be developed to ensure its safe and consistent implementation across institutions. Validation of AOC systems across different ventilators and NICU environments is essential.

To support clinical decision-making and guideline development, larger and higher-quality multicenter randomized controlled trials are necessary to provide more robust evidence of effectiveness and safety.

Until these gaps are addressed, the routine use of AOC in NICUs should be approached with caution and guided by ongoing research findings.

Suggestions for future research

Future research in preterm infants should prioritize the inclusion of both short- and long-term clinical outcomes, including mortality, BPD, ROP, patent ductus arteriosus (PDA), intraventricular hemorrhage, periventricular infarction, sepsis, necrotizing enterocolitis, duration of mechanical ventilation, and time on oxygen therapy, as well as neurodevelopmental outcomes at two years of corrected age. To allow meaningful comparisons between clinical outcomes and physiological parameters such as SpO_2, researchers should favor parallel-group randomized controlled trial designs over crossover approaches. Moreover, these studies should involve large patient cohorts and clearly defined nosocomial groups. Finally, clinical trials are necessary to assess and compare the effectiveness of different oxygen regulation algorithms.

Conclusion

AOC in neonatology represents a significant advancement in care, with growing evidence indicating improved oxygen targeting, fewer episodes of hypoxia and hyperoxia, and reduced workload for clinicians. While the results to date are promising, current AOC systems still face important challenges, including individual patient variability, sensor limitations, and difficulties in integrating these technologies into routine clinical workflows. Future research should prioritize the optimization of control algorithms, the development of more accurate and reliable sensors, and the execution of large-scale parallel-group randomized clinical trials to assess long-term outcomes. These efforts will be essential to determine whether AOC systems should become the standard of care. As neonatal intensive care continues to evolve, investing in and refining these technologies will be critical to improving both the safety and effectiveness of care for preterm infants.

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Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

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References

1. Dani C. Automated control of inspired oxygen (FiO_2) in preterm infants: Literature review. Pediatr Pulmonol 2019;54(3):358-363.
2. van Zanten HA, Tan RN, van den Hoogen A, Lopriore E, te Pas AB. Compliance in oxygen saturation targeting in preterm infants: a systematic review. Eur J Pediatr 2015;174(12):1561-72.
3. Sweet DG, Carnielli VP, Greisen G, Hallman M, Klebermass-Schrehof K, Ozek E, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update. Neonatology 2023;120(1):3-23.
4. Schmidt B, Whyte RK, Shah PS, Abbasi S, Bairam A, Harrold J, et al; Canadian Oxygen Trial (COT) Group. Effects of Targeting Higher or Lower Oxygen Saturations in Centers with More Versus Less Separation between Median Saturations. J Pediatr 2016;178:288-291.e2.
5. BOOST-II Australia and United Kingdom Collaborative Groups; Tarnow-Mordi W, Stenson B, Kirby A, Juszczak E, Donoghoe M, Deshpande S, et al. Outcomes of Two Trials of Oxygen-Saturation Targets in Preterm Infants. N Engl J Med 2016;374(8):749-60.
6. BOOST II United Kingdom Collaborative Group; BOOST II Australia Collaborative Group; BOOST II New Zealand Collaborative Group; Stenson BJ, Tarnow-Mordi WO, Darlow BA, Simes J, Juszczak E, Askie L, et al. Oxygen saturation and outcomes in preterm infants. N Engl J Med 2013;368(22):2094-104.
7. SUPPORT Study Group of the Eunice Kennedy Shriver NICHD Neonatal Research Network; Carlo WA, Finer NN, Walsh MC, Rich W, Gantz MG, Laptook AR, et al. Target ranges of oxygen saturation in extremely preterm infants. N Engl J Med 2010;362(21):1959-69.
8. Di Fiore JM, MacFarlane PM, Martin RJ. Intermittent Hypoxemia in Preterm Infants. Clin Perinatol 2019 ;46(3):553-565.
9. Bancalari E, Claure N. Respiratory Instability and Hypoxemia Episodes in Preterm Infants. Am J Perinatol 2018;35(6):534-536.
10. Kaplina A, Kononova S, Zaikova E, Pervunina T, Petrova N, Sitkin S. Necrotizing Enterocolitis: The Role of Hypoxia, Gut Microbiome, and Microbial Metabolites. Int J Mol Sci 2023;24(3):2471.
11. Lakshminrusimha S, Steinhorn RH, Wedgwood S, Savorgnan F, Nair J, Mathew B, et al. Pulmonary hemodynamics and vascular reactivity in asphyxiated term lambs resuscitated with 21 and 100% oxygen. J Appl Physiol (1985) 2011;111(5):1441-7.
12. Saugstad OD, Oei JL, Lakshminrusimha S, Vento M. Oxygen therapy of the newborn from molecular understanding to clinical practice. Pediatr Res 2019;85(1):20-29.
13. Buczynski BW, Maduekwe ET, O'Reilly MA. The role of hyperoxia in the pathogenesis of experimental BPD. Semin Perinatol 2013;37(2):69-78.
14. Srivatsa B, Hagan JL, Clark RH, Kupke KG. Oxygenation Factors Associated with Retinopathy of Prematurity in Infants of Extremely Low Birth Weight. J Pediatr 2022;247:46-52.e4.
15. Urschitz MS, Horn W, Seyfang A, Hallenberger A, Herberts T, Miksch S, et al. Automatic control of the inspired oxygen fraction in preterm infants: a randomized crossover trial. Am J Respir Crit Care Med 2004;170(10):1095-100.
16. Lim K, Wheeler KI, Gale TJ, Jackson HD, Kihlstrand JF, Sand C, et al. Oxygen saturation targeting in preterm infants receiving continuous positive airway pressure. J Pediatr 2014;164(4):730-736.e1.
17. Mitra S, Singh B, El-Naggar W, McMillan DD. Automated versus manual control of inspired oxygen to target oxygen saturation in preterm infants: a systematic review and meta-analysis. J Perinatol 2018;38(4): 351-360.
18. Van Zanten HA, Kuypers KLAM, Stenson BJ, Bachman TE, Pauws SC, Te Pas AB. The effect of implementing an automated oxygen control on oxygen saturation in preterm infants. Arch Dis Child Fetal Neonatal Ed 2017;102(5):F395-F399.
19. Stewart L, MacVicar S. Narrative review of closed loop automated oxygen systems. J Neonatal Nurs 2023; 29 (2): 229-234.
20. Nair V, Loganathan P, Lal MK, Bachman T. Automated Oxygen Delivery in Neonatal Intensive Care. Front Pediatr 2022;10:915312.
21. Salverda HH, Cramer SJE, Witlox RSGM, Dargaville PA, Te Pas AB. Automated oxygen control in preterm infants, how does it work and what to expect: a narrative review. Arch Dis Child Fetal Neonatal Ed 2021;106(2):215-221.
22. Fathabadi OS, Gale TJ, Dargaville PA. Automated control of inspired oxygen for preterm infants: What we have and what we need. Biomed Signal Process Control 2016;28:9-18.
23. Kinsey VE. Retrolental fibroplasia; cooperative study of retrolental fibroplasia and the use of oxygen. AMA Arch Ophthalmol 1956;56(4):481-543.
24. Campbell K. Intensive oxygen therapy as a possible cause of retrolental fibroplasia; a clinical approach. Med J Aust 1951;2(2):48-50.
25. Saugstad OD, Aune D. Optimal oxygenation of extremely low birth weight infants: a meta-analysis and systematic review of the oxygen saturation target studies. Neonatology. 2014;105(1):55-63.
26. Flynn JT, Bancalari E, Bawol R, Goldberg R, Cassady J, Schiffman J, et al. Retinopathy of prematurity. A randomized, prospective trial of transcutaneous oxygen monitoring. Ophthalmology 1987;94(6):630-8.
27. Supplemental Therapeutic Oxygen for Prethreshold Retinopathy Of Prematurity (STOP-ROP), a randomized, controlled trial. I: primary outcomes. Pediatrics 2000;105(2):295-310.
28. Askie LM, Henderson-Smart DJ, Ko H. Restricted versus liberal oxygen exposure for preventing morbidity and mortality in preterm or low birth weight infants. Cochrane Database Syst Rev 2009;2009(1):CD001077.
29. Cross KW. Cost of preventing retrolental fibroplasia? Lancet 1973;2(7835):954-6.
30. Mamidi RR, McEvoy CT. Oxygen in the neonatal ICU: a complicated history and where are we now? Front Pediatr 2024;12:1371710.
31. Flynn JT, Bancalari E, Snyder ES, Goldberg RN, Feuer W, Cassady J, et al. A cohort study of transcutaneous oxygen tension and the incidence and severity of retinopathy of prematurity. N Engl J Med 1992;326(16): 1050-4.
32. Hay WW. History of pulse oximetry in neonatal medicine. NeoReviews 2005;6(12):e533-8.
33. Clucas L, Doyle LW, Dawson J, Donath S, Davis PG. Compliance with alarm limits for pulse oximetry in very preterm infants. Pediatrics 2007;119(6):1056-60.
34. Beran AV, Taylor WF, Ackerman BD, Sperling DR, Strauss J. An automatic oxygen control system for infants. Pediatrics 1971;48(2):315-8.
35. Beddis IR, Collins P, Levy NM, Godfrey S, Silverman M. New technique for servo-control of arterial oxygen tension in preterm infants. Arch Dis Child 1979;54(4):278-80.
36. Collins P, Levy NM, Beddis IR, Godfrey S, Silverman M. Apparatus for the servocontrol of arterial oxygen tension in preterm infants. Med Biol Eng Comput 1979;17(4):449-52.
37. Claure N, Gerhardt T, Everett R, Musante G, Herrera C, et al. Closed-loop controlled inspired oxygen concentration for mechanically ventilated very low birth weight infants with frequent episodes of hypoxemia. Pediatrics 2001;107(5):1120-4.
38. Hummler H, Fuchs H, Schmid M. Automated adjustments of inspired fraction of oxygen to avoid hypoxemia and hyperoxemia in neonates - a systematic review on clinical studies. Klin Padiatr 2014;226(4):204-10.
39. Denault MH, Péloquin F, Lajoie AC, Lacasse Y. Automatic versus Manual Oxygen Titration in Patients Requiring Supplemental Oxygen in the Hospital: A Systematic Review and Meta-Analysis. Respiration 2019; 98(2):178-188.
40. Abdo M, Hanbal A, Asla MM, Ishqair A, Alfar M, Elnaiem W, et al. Automated versus manual oxygen control in preterm infants receiving respiratory support: a systematic review and meta-analysis. J Matern Fetal Neonatal Med 2022;35(25):6069-6076.

41. Personnelord IG, Lai NM, Tan K. Automated oxygen delivery for preterm infants with respiratory dysfunction. Cochrane Database Syst Rev 2023;11(11):CD013294.
42. Claure N, D'Ugard C, Bancalari E. Automated adjustment of inspired oxygen in preterm infants with frequent fluctuations in oxygenation: a pilot clinical trial. J Pediatr 2009;155(5):640-5.e1-2.
43. Claure N, Bancalari E, D'Ugard C, Nelin L, Stein M, Ramanathan R, et al. Multicenter crossover study of automated control of inspired oxygen in ventilated preterm infants. Pediatrics 2011;127(1):e76-83.
44. Dijkman KP, Mohns T, Dieleman JP, van Pul C, Goos TG, Reiss IK, et al. Predictive Intelligent Control of Oxygenation (PRICO) in preterm infants on high flow nasal cannula support: a randomised cross-over study. Arch Dis Child Fetal Neonatal Ed 2021;106(6):621-626.
45. Gajdos M, Waitz M, Mendler MR, Braun W, Hummler H. Effects of a new device for automated closed loop control of inspired oxygen concentration on fluctuations of arterial and different regional organ tissue oxygen saturations in preterm infants. Arch Dis Child Fetal Neonatal Ed 2019;104(4):F360-F365.
46. Hallenberger A, Poets CF, Horn W, Seyfang A, Urschitz MS; CLAC Study Group. Closed-loop automatic oxygen control (CLAC) in preterm infants: a randomized controlled trial. Pediatrics 2014;133(2):e379-85.
47. Kaltsogianni O, Dassios T, Harris C, Jenkinson A, Lee RA, Sugino M, et al. Closed-loop oxygen system in late preterm/term, ventilated infants with different severities of respiratory disease. Acta Paediatr 2023; 112(6):1185-1189.
48. Lal M, Tin W, Sinha S. Automated control of inspired oxygen in ventilated preterm infants: crossover physiological study. Acta Paediatr 2015;104(11):1084-9.
49. Reynolds PR, Miller TL, Volakis LI, Holland N, Dungan GC, Roehr CC, et al. Randomised cross-over study of automated oxygen control for preterm infants receiving nasal high flow. Arch Dis Child Fetal Neonatal Ed 2019;104(4):F366-F371.
50. Salverda HH, Cramer SJE, Witlox RSGM, Gale TJ, Dargaville PA, Pauws SC, et al. Comparison of two devices for automated oxygen control in preterm infants: a randomised crossover trial. Arch Dis Child Fetal Neonatal Ed 2022;107(1):20-25.
51. Schwarz CE, Kidszun A, Bieder NS, Franz AR, König J, Mildenberger E, et al. Is faster better? A randomised crossover study comparing algorithms for closed-loop automatic oxygen control. Arch Dis Child Fetal Neonatal Ed 2020;105(4):369-374.
52. Sturrock S, Ambulkar H, Williams EE, Sweeney S, Bednarczuk NF, Dassios T, et al. A randomised crossover trial of closed loop automated oxygen control in preterm, ventilated infants. Acta Paediatr 2021;110(3):833-837.
53. van Kaam AH, Hummler HD, Wilinska M, Swietlinski J, Lal MK, te Pas AB, et al. Automated versus Manual Oxygen Control with Different Saturation Targets and Modes of Respiratory Support in Preterm Infants. J Pediatr 2015;167(3):545-50.e1-2.
54. Waitz M, Schmid MB, Fuchs H, Mendler MR, Dreyhaupt J, Hummler HD. Effects of automated adjustment of the inspired oxygen on fluctuations of arterial and regional cerebral tissue oxygenation in preterm infants with frequent desaturations. J Pediatr 2015;166(2):240-4.e1.
55. Wilińska M, Bachman T, Swietlinski J, Wasko A, Jakiel G. Quicker response results in better SpO_2 control - a comparison of 3 FiO_2-titration strategies in ventilated preterm infants. Ann Agric Environ Med 2015;22(4):708-12.
56. Nair V, Kannan Loganathan P, Lal MK, Pringleton H, Bachman TE, Brodlie M, et al. Automatic oxygen control for reducing extremes of oxygen saturation: a randomised controlled trial. Arch Dis Child Fetal Neonatal Ed 2023;108(2):136-141.
57. Zapata J, Gómez JJ, Araque Campo R, Matiz Rubio A, Sola A. A randomised controlled trial of an automated oxygen delivery algorithm for preterm neonates receiving supplemental oxygen without mechanical ventilation. Acta Paediatr 2014;103(9):928-33.
58. Rocha G, Soares P, Flor-de-Lima F, Amaral R. Automated Adjustment of the Fraction of Inspired Oxygen (FiO_2) and the Time Spent in Normoxemia in Preterm Infants. Acta Med Port 2025;38(4):208-216.
59. Dani C, Pratesi S, Luzzati M, Petrolini C, Montano S, et al. Cerebral and splanchnic oxygenation during automated control of inspired oxygen (FiO_2) in preterm infants. Pediatr Pulmonol 2021;56(7):2067-2072.
60. Maiwald CA, Niemarkt HJ, Poets CF, Urschitz MS, König J, Hummler H, et al; FiO_2-C Study Group. Effects of closed-loop automatic control of the inspiratory fraction of oxygen (FiO_2-C) on outcome of extremely preterm infants - study protocol of a randomized controlled parallel group multicenter trial for safety and efficacy. BMC Pediatr 2019;19(1):363.