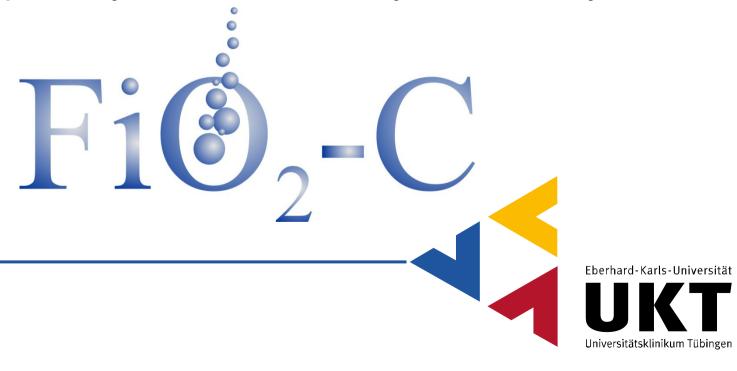
Effects of closed-loop automatic control of the inspiratory fraction of oxygen (FiO₂-C) on outcome of extremely preterm infants -

a randomized controlled parallel group multicenter trial for superiority to evaluate safety and efficacy



Conflict of interest statement



- No conflict of interest in the context of FiO₂-C
- The group of Tübingen was involved in the development of the CLAC controller (Leonie-plus).





Frequency and timing of intermittant hypoxemic episodes in ELGAN infants



Graph deleted

DeFiore et al. J. Peds 2010



Association of intermittant hypoxemic episodes with Laser-ROP

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DeFiore et al. J. Peds 2010



Association of intermittant hypoxemic episodes with adverse long-term outcome

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Poets et al. JAMA 2015



Background I: Hypoxemic Episodes



- Preterm infants suffer from intermittant hypoxemic episodes.
- These intermittant hypoxemic episodes are associated with long-term NDI.
- More prolonged episodes and episodes occuring at a later postnatal age seem to be particularly associated with adverse outcome.
- Role of (,overshoot'-) hyperoxemic episodes is less well studied and remains unclear



The invention of closed-loop FiO₂-Controllers UKT

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The invention of closed-loop FiO₂-Controllers UKT

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Background II



Closed-loop automated control of FiO₂ (FiO₂-C) reduces:

- spontaneous hypoxemic episodes due to respiratory instability
- time in hyperoxemia due to inappropriately high FiO₂

and increases:

time in SpO₂ target range



Effect of closed-loop automated control of FiO₂ on %-time in SpO₂-target range

Graph deleted



Poets CF, Franz AR ADC 2016 accepted



Polish contribution to the field of closed-loop automated control of FiO₂



- 2 groups from Poland (Poznan and Warzaw) contributed to the RCT trial published by vanKaam
 [J Peds 2015]
- The use of CLiO₂ resulted in significantly decreased time with SpO₂ at SpO₂ extremes if compared to ,attentive or ,observative manual adjustments [Wilinska M., Ann Agric Environ Med. 2015]
- M. Wilinska reported ,routine use of CLIO₂ in
 121 mechanically ventilated preterm infants for up to 9 days.
 [Wilinska M., Dev Period Med 2015]



Problems to date



- ➤ To date all randomised FiO₂-C studies have been:
 - a) very short-term (maximum time on FiO₂-Controller: 24h)
 - b) cross-over
 - c) outcome variables were %-time in SpO₂-target range etc.
- ➤ No conclusion can be made with regard to:
 - a) effects on longer-term, clinically relevant outcomes
 - b) safety during long-term application (weeks & months), during weaning from FiO2 and from positive pressure support

Hypothesis



Closed-loop automated control of FiO₂ (FiO₂-C) will reduce the incidence of:

- → Death or
- > severe retinopathy of prematurity, or
- → bronchopulmonary dysplasia, or
- → necrotizing enterocolitis until discharge from hospital as well as the incidence of:
- → Death or
- → cognitive or language delay, or
- → CP, hearing or visual impairment at 24 months corrected age

Design



- ELGAN infants
- randomly assigned to FiO₂-C + manual control or to manual control of FiO₂ only
- within 48h after birth
- until 32 (-36) weeks PMA (depending on need for CPAP)



FiO₂-C



- AVEA with CLiO₂ (Carefusion)
- FABIAN with PRICO (Acutronic)
- LEONIE with CLAC (Heinen & Löwenstein)
- SOPHIE with SPOC (Stephan)
- other FiO₂-Controller could also be used
 The support of the companies is appreciated!



Concomittant therapy



- ➤ SpO₂-target range at the discretion of each center but within the range of 85-95%
- SpO₂-alarms should activate right outside the targets
- Caffeine citrate early (5)-10-(20) mg/kg/d



Recruitment



We aim:

- > to involve 40-60 study centers in Europe
- > to screen 3350 ELGANs
- > to recruit 2340 ELGANs
- to assess at least 2220 ELGANs at discharge within 3 years



Challenges for FiO₂-C



- Centers use HFNC or Infant-flow-type CPAP early (before the relevant hypoxemic episodes even start)
- Potential Solution:
 Accutronic may have a flow generator with Pricco within 1 year

Graph deleted



Summary



- •The FiO₂-C study presents great challenges but eventually may help to improve the outcome of the preterm infants and also the preformance of the FiO₂-C devices.
- •We would greatly appreciate your contribution / participation in the study!
- Thank you for coming and listening!



