Optimization Of Oxygen Titration and Weaning With FreeO$_2$: Update On Clinical Evaluation In More Than 700 subjects

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Introduction

The first goal of oxygen therapy is to avoid hypoxemia. However, excessive oxygen flow rate may be detrimental through toxicity and prolonged oxygen therapy. Oxygen toxicity was described by Lavoisier himself in 1783 with acute respiratory failure occurring in guinea pigs with pure oxygen within few days (1). Lorrain Smith and other authors confirmed this direct pulmonary toxicity (2). Hyperoxia-induced hypercapnia in severe COPD patients (3) and proliferative retinopathy (4) are known for almost 70 years. Beyond this well-known toxicity, a global and systemic toxicity of oxygen related to diffuse arterial vasoconstriction (5) and inflammation is now well described. A recent meta-analysis confirmed the impact on mortality (6) and dose effect of oxygen toxicity seems well demonstrated (7). The recommendations concerning oxygen administration are well defined: titration of oxygen to maintain SpO_2 within a accurate range 88-92% in COPD and hypercapnic patients and 94-98% in other patients with close monitoring (8). These recommendations are not followed and automated oxygen titration may be useful. We developed and evaluated a new device developed to automatically titrate oxygen flowrate based on SpO_2 target set by the clinicians (FreeO$_2$, Oxynov, Canada). We present an update of the clinical evaluation of this device.

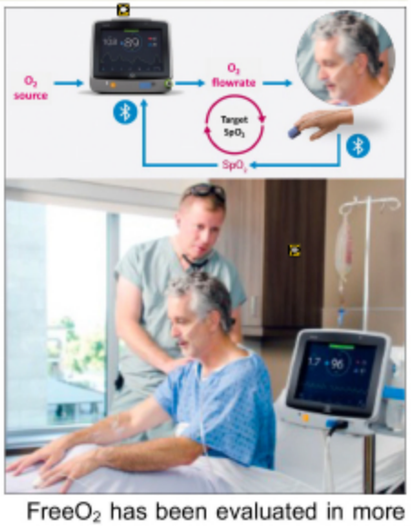
References: 1- Lavoisier 1783. 2- Lorrain Smith 1899. 3- Davis Lancet 1949 4- Terry Am J Ophthalmology 1942 5- Poder BMJ open 2018. 6- Chu Lancet 2018. 7- Helmerhorst CCM 2017 8- O'Driscoll BTS guidelines 2017

Methods

FreeO$_2$ is an automated system which automatically adjusts the administered O_2 flow using a closed-loop algorithm, based on physiological data (mainly SpO_2 measured every second) and provides continuous monitoring of cardio-respiratory parameters.

A proportional integral controller adjusts the oxygen flow delivered by a mass-flow controller from 0 to 20 L/min (accuracy 0.1 L/min), with the aim of maintaining the SpO_2 within a predefined target that can be set by the clinicians.

FreeO$_2$ was compared to usual administration of O_2, in randomized controlled studies, with two parallel arms or with a cross over design.



FreeO$_2$ has been evaluated in more than 700 patients, only completed studies are presented here.

Results

n	Population	Study design = RCT	Main results with FreeO$_2$
10	Healthy Subjects[1] Spont. Breathing	FreeO$_2$ vs. Air vs. continuous O_2	↑ time in SpO_2 target, ↓ hypoxemia, ↓ hyperoxia ↓ induced tachycardia
10	Healthy Subjects SB, CPAP, NIV	FreeO$_2$ vs. Air vs. continuous O_2	↑ time in the SpO_2 target, ↓ hypoxemia, ↓ hyperoxia ↓ workload with FreeO$_2$
16	COPD *Rehabilitation*[2]	FreeO$_2$ vs. Air vs. continuous O_2	↑ time in SpO_2 target, ↓ hypoxemia, ↓ hyperoxia ↑exercise tolerance vs. air (p<0.05) and vs. O_2 (trend p=0.22)
12	Severe COPD on LTOT *Rehabilitation*[3]	FreeO$_2$ vs. continuous O_2	↑ time in SpO_2 target, ↓ hypoxemia, ↓ hyperoxia ↑exercise tolerance vs O_2 (p=0.02), no induced hypercapnia
50	COPD *Hospitalization for AE*[4]	FreeO$_2$ vs. continuous O_2 (manual setting)	FreeO$_2$ well accepted by caregivers and patients ↑ time in SpO_2 target, ↓ hypoxemia, ↓ hyperoxia 30% reduction in hospital LOS (p=0.051)
47	COPD *Hospitalization for AE*[5]	Economic evaluation Cost analysis and ICERs	-20.7% /patient costs reduction(-Can$ 2,959.71; p=0.13) ICERs = -Can$ 96.91 per % point in the target SpO_2
190	ARF in the ED[6]	FreeO$_2$ vs. continuous O_2 (manual setting)	↑ time in SpO_2 target, ↓ hypoxemia, ↓ hyperoxia ↑ Patients O_2 weaned, ↓ hospital LOS
60	Acute coronary syndrome[7]	FreeO$_2$ (target 92%) FreeO$_2$ (target 96%) vs. manual O_2 setting	↑ time in SpO_2 target, ↓ hypoxemia, ↓ hyperoxia Less ventricular arythmias
60	Bronchiolitis ARF[8]	FreeO$_2$ vs. manual O_2 setting	↑ time in SpO_2 target, ↓ hypoxemia, ↓ hyperoxia, ↓ hospital LOS

Table references: 1- Lellouche & L'Her. Respiratory Care 2012;57(8):1254-62. 2- Lellouche et al. Respiratory care 2016;61:1456-64. 3- Vivodtzev et al. European Respiratory Journal 2016;48:1567 4- Lellouche et al. International journal of chronic obstructive pulmonary disease 2016;11:1983-90 5- Poder et al. BMJ open 2018;8:e018835. 6- L'Her et al. Eur Respir J. 2017 Jul 20;50(1). 7- Huynh Ky et al AJRCCM 2017;195:A3766 8- Barzic et al. Thesis 2016

Conclusions

The main findings of these studies can be summarized as follow:

- ➔ Optimized oxygenation [1,2,3,4, 5,6,7,8]:
  - (1) increase of the time within SpO_2 target (above 80% of the time with FreeO$_2$ compared to about 50% with manual titration. In the pediatric study, the time in the target was 95%
  - (2) Reduction of the time with hypoxemia
  - (3) Reduction of the time with hyperoxia
- ➔ Automated weaning of oxygen → Reduced oxygen therapy duration [4,5,6]
- ➔ Reduced length of the hospital stay (-30%) associated with a reduction of the costs during acute exacerbation of COPD [4,5]
- ➔ Automated triage (at the emergency department)
- ➔ Increased exercise tolerance: in COPD patients, oxygenation was improved (less hypoxemia and less hyperoxia with automated oxygen titration)[2,3] walking distance was increased[3] and there was no worsening of hypercapnia in most severe patients despite much higher oxygen flow with FreeO$_2$

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