Computer Methods and Programs in Biomedicine 146 (2017) 101–108

Contents lists available at ScienceDirect

Computer Methods and Programs in Biomedicine

journal homepage: www.elsevier.com/locate/cmpb

Physiological closed-loop control in intelligent oxygen therapy: A review

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ARTICLE INFO

Article history:
Received 3 March 2017
Revised 5 May 2017
Accepted 26 May 2017

Keywords:
Oxygen therapy
Oxygen
COPD
Long-term oxygen therapy
Closed-loop control
Oximetry

ABSTRACT

Background and Objective: Oxygen therapy has become a standard care for the treatment of patients with chronic obstructive pulmonary disease and other hypoxemic chronic lung diseases. In current systems, manually continuous adjustment of O_2 flow rate is a time-consuming task, often unsuccessful, that requires experienced staff. The primary aim of this systematic review is to collate and report on the principles, algorithms and accuracy of autonomous physiological close-loop controlled oxygen devices as well to present recommendations for future research and studies in this area.
Methods: A literature search was performed on medical database MEDLINE, engineering database IEEE-Xplore and wide-raging scientific databases Scopus and Web of Science. A narrative synthesis of the results was carried out.
Results: A summary of the findings of this review suggests that when compared to the conventional manual practice, the closed-loop controllers maintain higher saturation levels, spend less time below the target saturation, and save oxygen resources. Nonetheless, despite of their potential, autonomous oxygen therapy devices are scarce in real clinical applications.
Conclusions: Robustness of control algorithms, fail-safe mechanisms, limited reliability of sensors, usability issues and the need for standardized evaluating methods of assessing risks can be among the reasons for this lack of matureness and need to be addressed before the wide spreading of a new generation of automatic oxygen devices.

1. Introduction

Oxygen is essential for sustaining human life. Oxygen performs hundreds of tasks in the body, but the two most important are detoxification and energy production. Many diseases affect the lung's ability to transfer of oxygen from the outside air to the bloodstream.

Oxygen therapy has become a standard care for the treatment of patients with chronic obstructive pulmonary disease (COPD) and other hypoxemic chronic lung diseases. Oxygen supplementation is also widely used in adult intensive care patients and during pre-hospital transport. The goal of oxygen therapy is to maintain an adequate oxygenation while avoiding hypoxemia and hyperoxemia. However, although supplemental oxygen is valuable in many clinical situations, inappropriate supplemental oxygen can be detrimental [1].

Hypoxemia is frequently present in patients with COPD. In these patients, long-term oxygen therapy (LTOT) has been found to improve outcomes and reduce mortality [2]. It has been reported that many patients with COPD that were hospitalized because of moderate acute respiratory failure were poorly oxygenated during significant periods of time [3]. It is accepted that the oxygen flow, usually delivered in fixed flows to patients under oxygen therapy, is not always optimal [4]. In this context, adjustment of oxygen flow according to daily living activities is generally prescribed. However, this task poses a burden on patients that often affects therapy compliance.

Although the risks of hypoxemia are well known, there is also increasing evidence that excessive oxygen flow can be harmful. Hyperoxia, when compared with either hypoxia or normoxia, has been associated with increased in-hospital mortality among patients admitted to the intensive care units (ICU) following

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http://dx.doi.org/10.1016/j.cmpb.2017.05.013
0169-2607/

resuscitation from cardiac arrest [5]. Hyperoxia may be especially problematic in patients with COPD in acute phase of exacerbation because of: (a) its association with hypercapnia [6,7]; (b) the adverse clinical outcomes [8] and (c) the potential risks due to the possible masking of the onset of worsening in lung function by induced hyperoxemia [9]. In addition, emerging concerns are rising about the theoretical possibility of toxicity caused by hyperoxia in some patients with COPD receiving LTOT [10].

Notwithstanding the above-mentioned body of facts, there are clear evidences that the appropriate use of supplemental oxygen therapy is an important factor that may influence outcomes [11]. Consequently, tailoring oxygen therapy to patients' requirements appears as a key challenge. The adjustment of supplemental oxygen delivery should meet several objectives, namely:

i. The optimization of therapy and safety by minimizing the number of episodes of desaturation while avoiding periods of hyperoxia. The primary goal during oxygen supplementation is to target normoxemia, avoiding both hypoxemia and hyperoxemia. Clinicians suggest potential benefits of titrating supplemental oxygen therapy to target oxygen saturations instead of setting high fractions of inspired oxygen (FiO_2) independently of the arterial oxygen levels [8].
ii. The personalization of the oxygen flow to patients' needs. In patients receiving LTOT, oxygen flow is generally selected for maintaining a target oxygenation range. However, existing oxygen delivery methods may be insufficient when patient activity, and accordingly demand, increases [12].
iii. The optimization of oxygen consumption. Consumption of oxygen resources is a concern. Prescribed LTOT is frequently coupled with physical rehabilitation and physiotherapy in patients with COPD. These patients' adequate mobility and exercise is highly motivated. Therefore, smaller and lighter portable oxygen devices with more autonomy are desired new developments [4].

In traditional flow oxygen delivery, the amount of administered oxygen is generally adjusted manually by selecting the level of oxygen flow. The manual adjustment of oxygen flow is carried out by health professionals or by patients themselves to meet their changing needs. In the case of LTOT, the prescribed oxygen flow rate depends on the patient profile, him/her mobility, the adequate correction of SpO_2 during stand and exercise, and other related factors.

However, manually continuous adjustment of O_2 flow rate is a time-consuming task, often unsuccessful, that requires experienced staff. In the specific case of in-hospital oxygen therapy, clinicians, more concerned with oxygen desaturation than with hyperoxia, may be potentially lead to provide higher oxygen flow rates than required [13–15]. In home oxygen therapy, the correct use of oxygen in all domestic situations has been associated to the effective use of this treatment [16]. These limitations convert systems for the automatic oxygen flow rate control in a desirable achievement.

Recent advances in control system engineering are supporting emerging applications in the field of bioengineering. A physiological close-loop controlled (PCLC) medical device has been defined as a device that uses one or more physiological sensors to automatically manipulate a physiological variable through a therapy designed by a clinician [17]. In the field of respiratory care, the search for autonomous PCLC medical devices is leading to the development of new oxygen delivery methods able to automate simple medical tasks like manual adjustments during oxygenation. Recently, novel closed-loop oxygen delivery systems are being developed. These devices have the potential to optimize oxygen therapy, reduce workload of health professionals, diminish medical error, reduce health care costs and improve mortality and morbidity [4,18,19]. In most of the approaches, SpO_2 measured using a pulse-

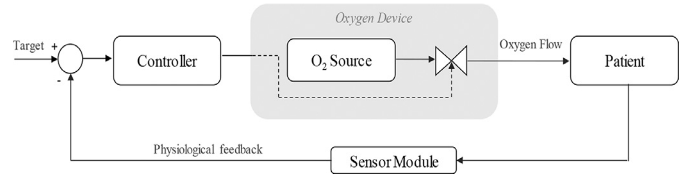

Fig. 1. Architecture of close loop controlled oxygen therapy devices.

oximeter is selected as process variable for the control algorithm. A target value of SpO_2, customized for the patients' specific needs, is provided as a reference by the physician. Fig. 1 illustrated the general architecture of a closed-loop controlled oxygen therapy device. Automatic flow rate control systems comprise a sensor module to feedback one or more physiological parameters, a control algorithm implemented on a controller hardware and an oxygen delivery device. The controller receives the physiological parameters continuously and compares them to the set value. Then, the controller calculates the appropriate flow-rate at a fixed rate (i.e. once per second).

Control system engineering have generated a plethora of control strategies. Common control strategies include proportional, integral and derivative (PID) control. Expert control (i.e. fuzzy control), optimal control (i.e. model-predictive control), robust control, adaptive control and neural control are among advanced control algorithms. Key aspects on the selection of the control strategy are the ability of the controller to manage disturbances arising from model (patient) variabilities and the versatility to handle events leading to system failure (e.g., sensor or actuator failure) [20].

Nonetheless, despite of their potential, PCLC oxygen therapy devices are not generally found in real clinical applications. Robustness of control algorithms, fail-safe mechanisms, limited reliability of sensors, usability issues and the need for standardized evaluating methods of assessing risks can be among the reasons for this lack of matureness [20]. In this regards, interdisciplinary collaboration between engineers and clinicians is essential to reach expected clinical and technical outcomes.

Automated closed-loop systems to control oxygen flow rate in infants have been developed and evaluated [13,14,21–24]. The clinical studies that evaluated these systems in premature infants have been recently reviewed [25]. However, to our knowledge, automated PCLC oxygen therapy devices in adults have yet to be systematically collated and reviewed. The primary aim of this systematic review is to collate and report on the principles, algorithms and accuracy of these automated devices as well to present recommendations for future research and studies in this field.

2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used as a basis for reporting this systematic review [26]. The search aimed to identify studies about oxygen therapy devices that incorporated physiological closed-loop controllers in adults. Inclusion criteria included English-language publications in a peer-reviewed journals. Non-original articles (e.g., editorials and review papers), regularly issued conference proceedings as well as abstracts of communications were excluded from this review. Nevertheless, their reference list was screened closely.

A systematic search of medical database MEDLINE, engineering database IEEE-Xplore and wide-raging scientific databases Scopus and Web of Science was undertaken in the period from June to December 2016 (DS and OO). The search aimed to identify the evidence from the literature on oxygen therapy experiences about the study of novel PCLC oxygen delivery devices. A combination of