International Journal of Applied Engineering Research ISSN 0973-4562 Volume 14, Number 3 (2019) pp. 694-702

A Survey of Control Algorithms Used In Physiological Closed Loop Control for Oxygen Therapy

S.Shree Vidhya[1,*], K.Keerthana[2], M.Janaki[3], J.Kanimozhi[4]

[1,2,3,4] Department of Computer Science and Engineering,
Sri Manakula Vinayagar Engineering College, Puducherry, India.

*(*Corresponding Author: Shree Vidhya)*

Abstract

For individuals requiring long term oxygen therapy for chronic obstructive lung disease (COPD) or similar respiratory distress syndromes resulting in hypoxia, the maintenance of a constant inflow of oxygen during oxygen therapy is of paramount importance not only for efficient functioning but also to maintain a healthy oxygen saturation in order to prevent complications resulting from hypoxia or hyperoxemia. In most clinical setups, flow rates are regulated by clinical staff as and when necessary. This technique is both inefficient and time-consuming. In recent years, various techniques have been developed to automate this process and several studies have been conducted on various populations to determine the efficiency of automated titration. Although the final outcome is to deliver a constant supply of oxygen and to maintain a constant oxygen saturation level by adjusting the supply of oxygen, the techniques, hardware and control algorithms to facilitate closed loop control is subject to considerable variations across the studies. In this survey, we discuss the various control algorithms used in closed loop oxygen therapy across several studies.

Keyword: Oxygen, Closed-loop control, Oxygen titration, Hypoxia, Hyperoxia, control algorithms, Flow control, COPD.

I. INTRODUCTION

Oxygen is one of the most essential gases required for survival. Although it performs several tasks in the body, one of the most important tasks include cellular respiration through which energy is produced for carrying out various activities [1]. Without oxygen, cellular respiration cannot proceed beyond the initial phase and this in turn results in cellular depletion. Although cells can survive for short periods without oxygen, constant deprivation leads to cell death which in turn causes the death of the organism [1, 2].

Healthy individuals receive the required oxygen through the regular process of respiration [3]. However, for individuals suffering from hypoxemia-inducing conditions such as chronic obstructive pulmonary disease (COPD) and cystic fibrosis or for those in trauma who are unable to breathe without assistance, oxygen has to be administered artificially though oxygen therapy [4]. Oxygen therapy has become widespread in the treatment of COPD, sufferers of which often have to take on long term oxygen therapy (LTOT) [5, 6, 7].

Oxygen therapy has become commonplace in hospitals and clinics alike, be it short term or long term. The aim of oxygen therapy is to endure that a steady supply of oxygen is supplied to the patient whilst also ensuring that the blood oxygen saturation (SpO_2) stays within the required limit (94-98%) which can vary between individuals depending on various indications (including the existence of hypoxia inducing lung conditions) without causing hypoxia or hyperoxia [8,9]. The delivery of oxygen can be facilitated through a nasal cannula [1, 10], a face mask or a hyperbaric chamber and supply of the gas can be through a fixed/portable source such a cylinder, a flow regulator or a mechanical ventilator. Although oxygen therapy has become a fairly common and safe method of treatment, if not administered properly, it can cause further complications and deterioration. During titration, strict precautions have to be taken to ensure that the SpO2 stays within the required level [11]. If the SpO2 falls below the lower threshold, hypoxia will set in causing cyanosis, hypercapnia, disorientation, tachycardia, and shortness of breath and in extreme cases, brain death. Conversely, increase in SpO2 beyond the safe limit can cause onset of hyperoxia (increased oxygen saturation) which causes tracheal irritation, tightness of the chest and lung injury due to increase in alveolar pressure [8, 11, 12].

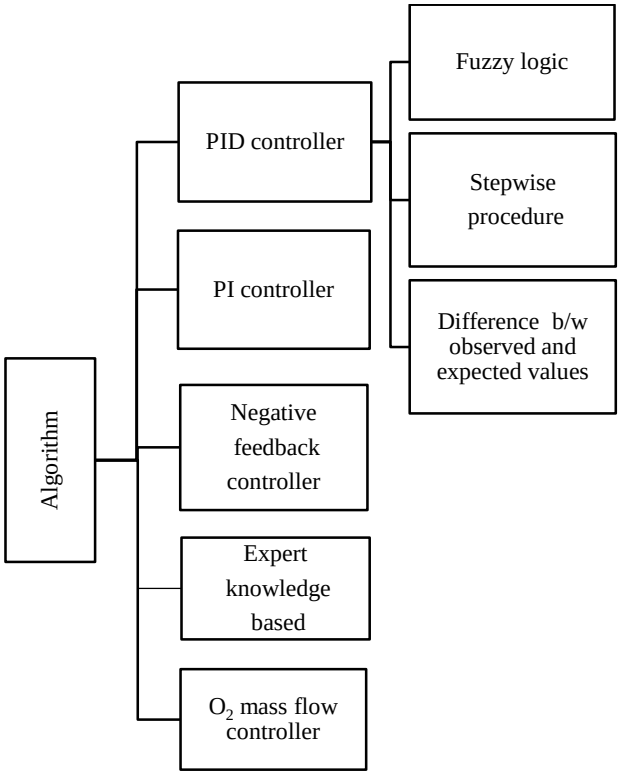

Figure 1. Various algorithms used in automated oxygen titrations.

In order to prevent these occurrences, a pulse oximeter is used to monitor the patients' SpO_2. Once the SpO_2 is found to fall below the optimal limit, intervention is required by the medical staff wherein the flow valve of the oxygen source is adjusted accordingly to bring the SpO_2 back to normal [1]. In cases where the patient isn't hospitalized, self-adjustment is done, which is not recommended by clinicians [18].

The above techniques are not only time-consuming [12], but require greater recovery time form hypoxic events, require more intervention and are risky if not addressed properly.

In recent years, various techniques have been introduced to automate this process, to bring about closed loop systems in which the oxygen supply is automatically adjusted in accordance with the patients' oxygen saturation levels ensuring speedy recovery from hypoxia and fewer interventions on the part of the clinician [5, 13-23]. Such systems have also been developed and evaluated for preterm infants [2, 4, 12, 24-28] and to control SpO_2 levels under general anesthesia [29].

Figure 1. gives a classification of the various algorithms used in physiological closed loop control devices. However, despite the evolving techniques to facilitate automated oxygen titration, such devices have yet to be used in clinical setups due to various factors including uncertainty on reliability of control algorithms, reliability of sensors and usability issues. In this survey, we review the various studies conducted on automated, closed-loop oxygen therapy in patients suffering from COPD [15-21] and those on mechanical ventilation as a result of trauma [8,22,23]. Specifically, we discuss the various control algorithms and hardware used in the implementation of these systems and their efficiency in maintaining the target SpO_2 in comparison to the manual technique.

II. MATERIALS AND METHODS

In this segment, the various control algorithms that have been used in various studies to facilitate automated oxygen titration during oxygen therapy are discussed. Although several studies have used a PID controller algorithm as a means of regulating oxygen supply, several other studies have also used PID in combination with other techniques and a few more studies have used a different algorithm altogether.

Across the studies, the algorithms and their implementation were found to differ in 1.) SpO_2 set point, 2.) Target population 3.) Control hardware. The algorithms used across the studies are listed below:

a. PID controller algorithms
   i. PID in combination with fuzzy logic
   ii. PID in combination with a stepwise procedure
   iii. PID based on difference between observed and expected saturation values
b. PI controller
c. Negative feedback controller in combination with a rule-based system
d. Expert knowledge based
e. O_2 mass flow controller algorithm

a. PID controller algorithms

i. PID used in computer simulation

Iobbi et al evaluated a closed-loop, flow-rate control method for patients undergoing treatment with LTOT. In this study, the feedback from a pulse oximeter was used to maintain a target SpO2 of 91% by changing the oxygen flow-rate to the patient. The closed-loop control scheme was simulated using Simulink software. The system consists of two important components one is the controller and the other is the patient model [20].

The controller uses arterial oxygen saturation measurement from pulse oximetry to automatically regulate oxygen flow-rate during treatment. Feedback from the pulse oximeter is used to maintain the patient SpO2 within an ideal range. The controller was evaluated using a model to approximate the patient's arterial oxygen saturation response, including hypoxic events from artificial disturbances as well as recorded patient oximetry data. The controller uses arterial oxygen saturation measurement from pulse oximetry to automatically regulate oxygen flow-rate during treatment. [20].

Algorithm description

The controller computes the error (E) between the target set point and measured oximetry value and based on this, it determines the oxygen flow-rate output to the patient. The patient saturation is modeled as a composite value, dependent

on the oxygen flow rate and a local disturbance. The controller computes the error (E) between the target set point and measured oximetry value. It then determines the oxygen flow-rate output to the patient. The patient saturation is modeled as a composite value which depends on the oxygen flow rate and a local disturbance. The simulation also accounts for the discrete sampling from the pulse oximeter which is assumed to have a sampling rate of 1 Hz. The controller is based around the well-known PID algorithm whose function is given in the equation below, where E is the input error (difference between actual and target SpO2), K_P, K_I, K_D are the proportional, integral and derivative parameters and U is the resultant oxygen flow rate expressed in L/min [20].

$$U(t) = K_T E(t) + K_I \sum E(t)\,dt + K_D\, d\,E(t)/dt$$

In order to prevent hazardous events, lower and higher threshold values are set. As a result, the flow rate can range only from 0-5 L/min. Thus, only the values within the given range can be generated as an output to the flow controller [20].

ii. PID in combination with fuzzy logic

El Adawy et al used a combination of PID (proportional-integral-derivative) and Fuzzy logic control (FLC) for supplying supplemental oxygen for patients having sub-acute respiratory diseases by maintaining a healthy blood oxygen level. This was done by controlling the dosage of oxygen in response to the patients' actual blood oxygen level automatically [16].

Attempts were made to keep the neonatal models at the target level but more emphasis is made on keeping the patient in normoxemia (PaO_2 85-110 mm Hg) condition to prevent any neurocognitive dysfunction in survivors. The systems and methods used in this study targeted patients receiving oxygen therapy in acute respiratory environment. The neuro fuzzy logic control was another control algorithm which was suggested for future implementation in this study to maintain the target oxygen concentration level which was mentioned as a complex process [16].

Algorithm description

This algorithm uses the difference between the patients' actual blood oxygen level and target blood oxygen level including the trends in blood oxygen level. It was inferred from the study that both the controllers produced good results but the fuzzy logic algorithm was the best. In this study, commercial software was used to implement the cardiovascular model, respiratory model, air-oxygen blender (cylinder) model and the pulse-oximeter model. The adult cardiovascular system model was implemented in this study. The pulse-oximeter model was represented by a sensor using the MATLAB software [16].

Fuzzy logic has emerged as a simple tool for controlling complex processes and is based on fuzzy logic. The fuzzy logic control also simplifies and reduces the development cycle in design and ease of implementation. This study developed three controllers: manual, PID and fuzzy logic. The manual mode was used to represent the normal clinical oxygen therapy with the aim of keeping the patient under normoxemia instead at a specific target. A non-linear fuzzy logic controller uses two inputs: error and error rate to formulate a single output. The performance is measured by the percentage of duration for which the model stays in normoxemia [16].

iii. PID in combination with a stepwise procedure

A fine PID controller in tandem with a fast-stepwise procedure was used for automated control of the fraction of inspired oxygen (FiO_2) and post end expiratory pressure (PEEP) in individuals on mechanical ventilation to prevent hypoxemia and hyperoxemia and to enable quick recovery should any deviations in oxygen saturation occur. The system starts off with using the PID controller but reverts to the stepwise procedure in case the SpO_2 value rapidly drops.

The designed closed loop system consisted of a finger pulse-oximeter, which recorded the patient's oxygen saturation level (SpO_2). The signal from the oximeter was passed through an analog to digital converter before being passed to a microprocessor. In addition to SpO_2, the microprocessor also received a signal from the ventilator which indicated the value of PEEP.

Based on the above input signals, the microprocessor calculated the subsequent FiO_2 and PEEP values to be used by the system. Both the FiO_2 and PEEP signals were passed through a digital to analog convertor before transmission; the FiO_2 signal was passed to an air-oxygen mixer which was used to control the volume of oxygen to admit into the mixer. The mixer then supplies oxygenated air to the ventilator which in turn supplies it to the ventilated patient. The PEEP signal from the microcontroller is fed to the ventilator [22].

Algorithm description

The algorithm consists of a PID controller used along with a stepwise controller. The purpose of the stepwise procedure is to rapidly stabilize the oxygen saturation levels in case of any hypoxia. The PID controller is used for the fine control of FiO_2 when the SpO_2 stabilizes [22].

Initially, the set point for arterial partial pressure of oxygen PaO_2 and the threshold values for SpO_2 are specified. Four threshold levels of SpO_2 are set in order to enable rapid stabilization of oxygen saturation by the stepwise controller in case of hypoxic events. The patient's oxygen saturation is read by the pulse oximeter and from this value, the PaO_2 is calculated. This value is then compared to a lower threshold value to detect any artifacts [22].

If the PaO_2 level is found to be less than the required threshold value, an artifact is assumed to exist and subsequently, a warning is raised. The current SpO_2 value is discarded and previous values of SpO_2 and PaO_2 are resumed. Otherwise, if the PaO_2 is greater than or equal to the required threshold value, then no artifact is detected and the measured values are taken into account [22].

The SpO_2 is then compared to a minimum threshold value, and if found to be less than the required limit, or if the FiO_2 was calculated in the previous cycle of the algorithm by the stepwise procedure, then control is transferred back to the stepwise procedure in order to rapidly stabilize the values of SpO_2.The procedure steadily raises the FiO_2 in order to ensure that an

optimal supply of oxygen is received by the patient and is subsequently reduced once saturation levels stabilize [22].

The stepwise procedure compares the patients SpO_2 with that of four threshold values with each step, and, if found to increase with time, it gradually reduces the FiO_2 in order to prevent hyperoxemia. Once the SpO_2 rises to the fourth threshold level, the control is transferred back to exercise finer control of FiO_2 in order to ensure that the SpO_2 stays within the specified range [22].

iv. PID based on difference between observed and expected saturation values

In a comparison study on $AccuO_2$ Oximetry-Driven Oxygen-Conserving Device and Fixed-Dose Oxygen Devices conducted by Kathryn L Rice, the patients were originally prescribed LTOT to achieve a target SpO_2 of 90 – 92%. Most LTOT (Long-term oxygen therapy) systems provide a continuous and fixed flow of oxygen. The prescribed O2 flow is usually based on a single measurement and aimed at maintaining the oxygen saturation greater than or equal to 90%. The aim of this study was to maintain a flow of 1-3 L/min for 18 –24 hours per day. It was conducted for both the cases including in-home testing and in-clinic testing. The following hardware was used during the study: oxygen conserving device (CR-50) which were added to the portable LTOT system to reduce the O_2 waste, pulse-oximeter, portable computer, nasal cannula, respiration sensor and a microcontroller [5].

In the case of fixed-dose system, the oxygen was delivered via nasal cannula at a flow rate previously prescribed for that patient to maintain $SpO_2 \geq 90\%$. Whereas the $AccuO_2$ was designed to maintain SpO_2 at a desired value at all times. This was made possible by the continuous monitoring of pulse-oximeter readings and the respiration sensor outputs by a microcontroller. Thus, the $AccuO_2$ maintained a clinically acceptable SpO_2 level with less SpO_2 variation and lower oxygen consumption than fixed-dose oxygen system. But the performance of $AccuO_2$ under more clinical varied circumstances is not known [5].

Algorithm description

In $AccuO_2$, the volume of oxygen to be delivered is calculated by a proportional integral differential control algorithm. This is based on the difference between the observed and desired SpO_2 values and the trend in that difference. Oximeter data and oxygen pulse/bolus size are measured and updated every second. When the patient's SpO_2 is stable at the target, the $AccuO_2$ begins increasing the oxygen dose on the first inhalation. The oximeter's output includes error flags for a detached sensor, low-perfusion state, and heart rates of 40 beats/min and 180 beats/min. If an error condition occurs, the $AccuO_2$ continues to deliver oxygen during every inhalation at the same level administered prior to the error condition for 15 seconds. If the error condition persists for 15 seconds, the $AccuO_2$ defaults to a standard fixed-bolus (33 mL/breath bolus). The maximum oxygen bolus was set at 66 mL/breath. All the oxygen used in this study was in E-size cylinders [5].

The Mean SpO_2 was the lowest with $AccuO_2$, because the $AccuO_2$ is designed to maintain the SpO_2 as close as possible to 90%, consistent with the therapeutic goal of the Nocturnal Oxygen Therapy Trial, in which patients with a baseline Po_2 55 mm Hg were given supplemental oxygen to achieve a Po_2 range of 60 mm Hg (which approximately corresponds to an SpO_2 of 90%) to 80 mm Hg. Based on the results of that trial, there is general consensus that the SpO_2 goal of LTOT should be greater than or equal to 90% [5].

The primary advantage of oximetry-driven oxygen delivery is maintaining the SpO_2 at or near 90% while reducing oxygen waste. The mean conservation ratio with the $AccuO_2$ was more than 3 times that with the CR-50 and 9 times that with fixed-dose flow. The difference in oxygen savings between the AccuO2 and standard O2 delivery devices might be smaller if standard O_2-conserving devices were more tightly set to achieve SpO_2 of 90%, although the practicality of that approach is questionable. Almost 50% of patients on LTOT for COPD are reported to experience substantial nocturnal desaturation with standard O_2 delivery systems. In patients who are hospitalized for COPD exacerbation, pulse oximetry-driven oxygen delivery could be used to avoid the high SpO_2 values that have been associated with acute CO_2 retention [5].

a. PI controller

Lellouche et al used a PI controller in two studies conducted on automated oxygen flow titration on patients with COPD using the $FreeO_2$ automated oxygen titrating device the prototype of which was developed by the authors in the first study [18]. Another study was conducted after proper development to test the devices' safety and usability in a clinical setting [19]. This device uses a closed-loop algorithm that is capable of monitoring the patients' respiratory variables including the end-tidal CO_2, respiratory rate, SpO_2, heart rate and respiratory rate. In particular the SpO_2 which is monitored by a pulse oximeter having a sampling rate of 1s. A predefined target range is set by the clinician prior to administration. The $FreeO_2$ device makes use of a PI controller to regulate the patients' oxygen supply and maintain the target SpO_2 [18]. The device was tested on 10 healthy individuals in a state of induced hypoxia in the first study [18] and a study was conducted on 50 hospitalized patients in the second study [19]. Target SpO_2 was set as 94% and 90% in respective studies [18, 19].

Algorithm description

The FreeO2 system automatically adjusts oxygen flow rates administered via nasal cannula or non-occlusive mask, using a closed-loop algorithm based on physiological data. The algorithm used is a PI controller which alters the oxygen flow rate in response to the patients' oxygen saturation based on the difference between the measured SpO_2 value and the target value set by the clinician [19]. The primary input to the algorithm is the SpO_2 value which is fed through the pulse oximeter. The PI controller is capable of regulating the flow rate from 0 to 20 L/min [18].

Among the other respiratory data monitored by the algorithm are the end-tidal CO_2 and the respiratory rate which serve as indicators of respiratory distress and hypoxia and can be used to generate warnings id needed [18,19].

c. Negative feedback controller in combination with a rule-based system

Jay A. Johannigman proposed a system for the autonomous control of inspired oxygen saturation for ventilated patients in a combat zone. Notable concerns that were reported regarding the conservation of resources due to the absence of the provision for adequate oxygen supplies were also taken into account. As a result, the Autonomous control of oxygen concentration resulted in the overall reduction of the load [8].

A study was made to evaluate ventilated patients requiring oxygen concentration greater than 0.35. The study consisted of two 4-hour periods of observation for a total duration of 8 hours. The patients randomized to consecutive 4-hour periods of autonomous control or standard care. The following hardware was required to setup the autonomous control. It consisted of a ventilator, oximeter, and a portable computer. The mobile computer contained the control algorithm and it the ventilator settings and the oxygen saturation (SpO_2) values were collected for every five seconds for analysis. The controller goal was to maintain SpO_2 at 94% ± 2% via discrete changes of 1% to 5% [8].

Algorithm description

The autonomous control algorithm is a modified negative feedback controller which uses information regarding current FiO_2, current SpO_2, and trend in SpO_2, and recent FiO_2 changes to maintain a target SpO_2 of 94% ± 2%. This information allows the controller to manipulate Fio_2 in 1% to 5% increments every 30 seconds to 60 seconds. A rule-based system controls algorithm behavior during periods of hypoxemia (defined as SpO_2 88% lasting 10 seconds). Under these conditions the increase in FiO_2 is more rapid with an increase to 1.0 if hypoxemia persists [8]. Endpoints Study included both safety and efficacy variables. Efficacy endpoints were to determine the amount of oxygen conserved with closed-loop control of FiO_2 and the ability of the controller to maintain the desired SpO_2 94% ±2%. Oxygen utilization in liter per minute was calculated from set FiO_2 and current minute ventilation (V_E) using the equation $(Fio_2 - 0.21) / 0.79 \times VE$ [8].

The endpoints included the prevention of hyperoxia (where $SpO_2 \geq 97\%$) and hypoxemia (where $SpO_2 \leq 88\%$). Fifteen patients were enrolled in this study. Oxygen saturation was maintained in the 92% to 96% saturation range 33% ± 36% of the time during clinician control versus 83% ± 21% during autonomous control. Oxygen usage was reduced by 44% during autonomous control [8]. Computerized analysis was used to calculate the mean SpO_2 and the number of and duration of episodes of hypoxemia. The percentage of time during each study period with a SpO_2 of 97%, 92% to 96%, 89% to 91%, and 88% was determined for each patient. Within participant comparisons using a two-tailed, paired t test were used when appropriate. A p value of 0.05 was considered significant [8].

d. Expert knowledge based

This technique focuses upon the support of the syndrome ARDS and reduce cardiac surgery patients. Closed-loop control ventilation refers to the use of a feedback signal to adjust the ventilator outputs in order to meet individual patient's needs. IntelliVent-ASV is a recently released development of ASV that automatically adjusts both ventilation and oxygenation parameters. In short, minute volume is adjusted according to end tidal CO2 (ETCO2) information in passive breathing patients and oxygenation is adjusted according to SpO2 information [23].

The first clinical experience of IntelliVent-ASV in ICU patients, the objective was to include passive stable patients with moderate severity acute respiratory failure. Exclusion criteria were increased intracranial pressure, severe ARDS requiring a permissive hypercapnia strategy, chronic respiratory failure receiving long-term oxygen therapy and/or home non-invasive ventilation, severe cardiac arrhythmia, therapeutic hypothermia, brain-dead patients, pregnancy and bronchopleural fistula. Patients were orally intubated and mechanically ventilated using an S1 ventilator with IntelliVent-ASV software [23].

Algorithm description

In this system the closed loop automatically controls both oxygenation and ventilation parameters. And the volume is adjusted according to the End Tidal value of co2 (ETCO2). Information in passive breathing patients and oxygenation is adjusted according to the SpO2 information.

The basic process includes the ventilation and maximum inspiratory pressure that were adjusted to keep tidal volume below 10ml/Kg of predicted body weight. On the basis of ETCO2 information derived from a mainstream sensor positioned at the Y piece of the ventilator circuit, MV is automatically adjusted to target ranges of ETCO2 between 35 and 41 mmHg. These ETCO2 target ranges can be manually adjusted by users and are more permissive when inspiratory pressure (PINSP) increases above 25 cmH2O [23].

If ETCO2 and SpO2 information is lost, the controllers automatically pause and an alarm is sounded. In addition, FiO2 is automatically increased to 100 % if SpO2 is below 85 %, and 100 % FiO2 manual bypass is still available. On the basis of SpO2 information derived from a pulse oximetry, FiO2 and positive end-expiratory pressure (PEEP) are adjusted automatically to keep SpO2 within target ranges of 93 to 97 % [23].

These ranges are adjustable by users and are more permissive when PEEP is above 8 cmH2O. The combination of FiO2 and PEEP is determined by a PEEP–FiO2 table derived from the ARDS Network publications and the user can also adjust the maximum peep [23].

e. O_2 mass flow controller algorithm

Cirio et al conducted a pilot study of a new device, the O_2 mass flow controller, to test its safety and efficiency in managing hypoxic events and maintaining the target SpO_2 in comparison with the manual titration method in patients with Chronic Obstructive Pulmonary Disease (COPD). The O_2 flow regulator is automated oxygen that regulates the oxygen flow to the patient based on recorded SpO_2 values. The device is

used as an intermediary between the patient and the O_2 source [15].

For this study, 18 patients with COPD requiring long term oxygen therapy (LTOT) were selected as test subjects. The criteria for the selection were that the patients' PaO_2 be less than 55 mm Hg. The SpO_2 was monitored via a pulse oximeter and 3 lead electrocardiograms. The subjects underwent two standardized 15-minute cycling tests. In one of the tests, the manual titration method was used, with a clinician intervening when required. In this test, the time taken to set up the various devices and the number of interventions were observed. In the other test, the O_2 flow regulator controlled the titration with the required SpO_2 set beforehand by a clinician [15].

The O_2 mass flow controller uses an algorithm that controls the flow valve on the oxygen source in response to the patient's saturation level. The aim of the algorithm is to maintain a constant level of oxygen saturation, the value of which is set beforehand by a respiratory therapist [15].

Algorithm description

Initially, the set point for the oxygen saturation is specified by the respiratory therapist. In this study, the target oxygen saturation value of the patient was set at 94%. The patients SpO_2 is read by a pulse oximeter. The signal from the oximeter is continuously monitored by a microprocessor. The flow is increased or decreased according to the rise or fall in saturation levels [15].

If the SpO_2 falls short of the required target, rapid opening of the flow valve is initiated at the rate of 2L/30s, thus increasing supply to the patient and facilitating rapid recovery from hypoxemia should that be the case. If the SpO_2 crosses the set point, the valve is gradually closed at a rate of 0.5L/30s, thus reducing the flow of oxygen, effectively preventing hyperoxemia. If SpO_2 is maintained within the target range, no changes are made to the flow; the current flow rate is maintained [15].

III. RESULT ANALYSIS

A common performance metric used across all the studies was the percentage of time that the patient remained below the target in the automatic mode of titration when compared to the manual mode. The results proved an overall decrease in the percentage of time that the patient remained in a hypoxic state with the difference between manual and automatic modes. The percentage of time spent in a hypoxemic state ranged from 0.2% to 19% with automatic control in contrast with 2.3% to 67% with the manual method. Corresponding results for hyperoxemia ranged from 1.5% to 47% as opposed to 4.1% to 75% with manual adjustment. Physiological closed loop control has also been reported to reduce the oxygen utilization and to aid in O_2 conservation.

Table 1: Performance measure comparison for automatic and manual method

First author	Control hardware	Control Algorithm	% time below threshold	
			Manual	Automatic
Lellouche (2012) [18]	$FreeO_2$ automated titration device	PI controller	67%	17%
Cirio (2011) [15]	O_2 mass flow controller	O_2 Mass flow controller algorithm	38%	19%
Johannigman (2009) [8]	Computer	Negative feedback controller with rule-based system	1.9%	1.0%
Arnal (2012) [23]	Intellivent ASV Ventilator	Expert Knowledge based	19%	2%
Lellouche (2016) [19]	Free O_2 automated oxygen titration device	PI controller	23%	0.2%
Rice (2011) [5]	$AccuO_2$ oximetry driven Oxygen conservation device	PID controller based on the difference between observed and expected values	23.5%	22%

Table 1 depicts the differences in the percentage of time reported between manual and automated titration across the various studies. Across the studies, although percentage of time that the patient remained in a hypoxic state was the standard metric, a few studies [5, 8, 18, 19, 23] also took into consideration the percentage of time spent within the specified range and percentage of time spent in hyperoxia. However, the primary focus has been on hypoxic events, since this is the major drawbacks of the current practice. The improvement in percentage time across the studies varied from 12% to 46%. Overall, all findings reported a significant difference between manual and automatic titration with automatic titration resulting in reduced time spent under hypoxia and hyperoxemia.

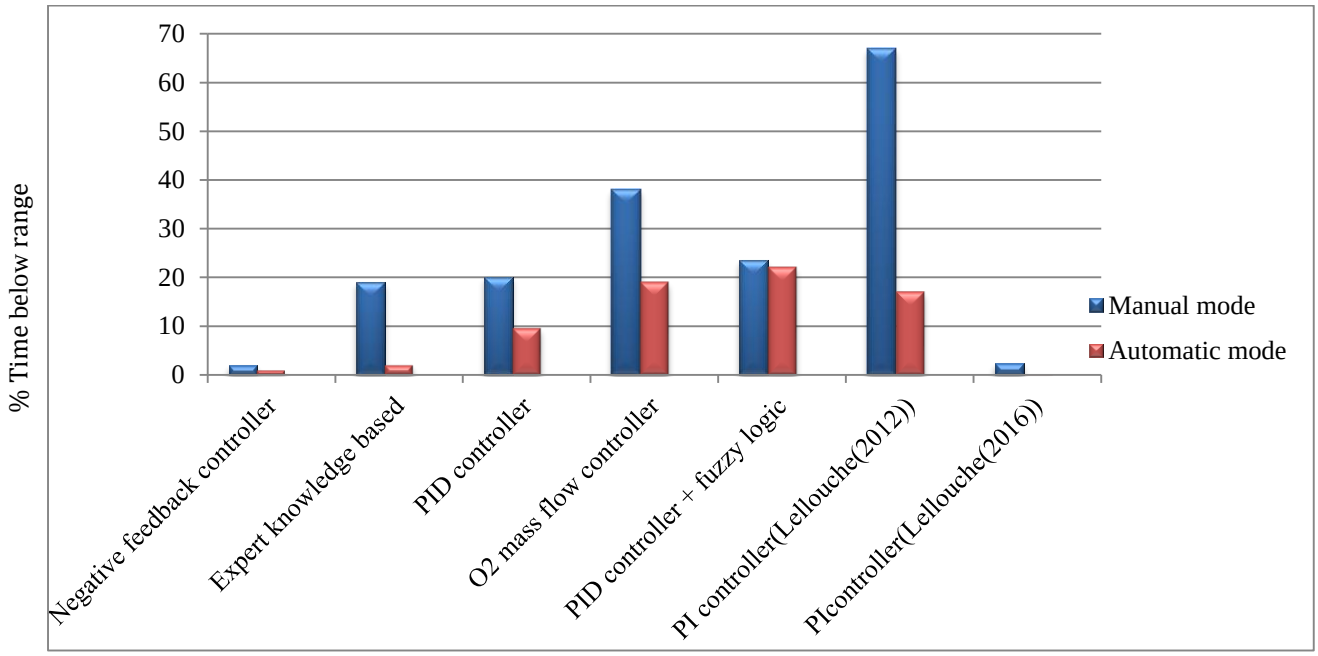

Figure 2. Comparison between manual and automated titration algorithms across various studies

The comparison between automated titration and manual method is given in Figure 2. Although these algorithms have shown a marked improvement in efficiency when compared to the manual method, they use only a pulse oximeter a means of input which may not always be reliable in clinical practice. The oximeter is used as a primary means of sensory input to the algorithm in the automated systems whereas in clinical practice, several parameters are observed in addition to oxygen saturation including respiratory rate and other respiratory parameters. Hence, the development of different sensors to keep track of all respiratory parameter simultaneously remains to be seen. Since the algorithm relies on the input of the sensor to function, an unreliable sensor yields an unreliable algorithm. On the other hand, these algorithms focus on one approach only, whereas, multiple modalities need to be adapted for proper monitoring.

IV. CONCLUSION

In this survey, the various control hardware and algorithms are compared in order to determine which algorithm and control technique was more efficient when compared to the manual mode. Although all algorithms have proved to reduce the time under target as far as hypoxia and hyperoxemia are concerned, in addition to this, the studies have also varied according to the technology used, the hardware and performance comparison. Overall, the outcomes of the studies show that automatic titration improves patient safety since the time taken for desaturation is reduced. It has also been shown to maintain a higher patient SpO_2 and conserve O_2 usage.

Automated oxygen titration is still a relatively new area in respiratory medicine and although various techniques have been devised, several issues have prevented these devices from being implemented in clinical setups the reasons being sensor reliability, algorithm reliability and appropriately skilled clinicians. Hence, to enable these devices to be used in clinal settings, further studies have to be undertaken in order to ensure their safety and efficacy in maintaining optimal oxygen saturation.

REFERENCES

[1] Abraham, V. J., Le, X., Al-Mharib, Y. W., Santacroce., J. F., Dow, D. E., and Donnel, B. E., 2015, “Automatic regulator for supplemental oxygen therapy”, EAI International Conference on Bio-Inspired Information and Communications Technologies (BICT), pp. 5-8.

[2] Chanyagorn, P., and Kiratiwudhikul, P., 2015, "Automation control algorithms in gas mixture for preterm infant oxygen therapy", 2015 IEEE International Conference on Consumer Electronics - Taiwan, ICCE-TW 2015, pp. 236–237.

[3] Jacono, F. J., 2013, "Control of ventilation in COPD and lung injury", Respiratory Physiology and Neurobiology, 189(2), 371–376.

[4] Claure, N., and Bancalari, E., 2013, "Automated Closed Loop Control of Inspired Oxygen Concentration", Respiratory Care, 58(1), pp. 151-161.

[5] Rice, K. L., Schmidt, M. F., Buan, J. S., Lebahn, F., and Schwarzock, T. K., 2011, "AccuO2 Oximetry-Driven Oxygen-Conserving Device Versus Fixed-Dose Oxygen Devices in Stable COPD Patients", Respiratory Care, 56(12), pp. 1901–1905.

[6] Dijemeni, E., and Roberts, D., 2014, "Desktop based real time oxygen auto-ventilation and gas monitoring system for homecare respiratory application", International Conference on Applied Electronics, 2015–January (January), pp. 67–70.

[7] Doorduin, J., Sinderby, C. A., Beck, J., van der Hoeven, J. G., and Heunks, L. M. A., 2014, "Automated patient-ventilator interaction analysis during neurally adjusted non-invasive ventilation and pressure support ventilation in chronic obstructive pulmonary disease", Critical Care, 18(5), pp. 1–8.

[8] Gangidine, M. M., Blakeman, T. C., Branson, R. D., and Johannigman, J. A., 2016, "System Design Verification for Closed Loop Control of Oxygenation with Concentrator Integration", Military Medicine, 181(5S), pp.177–183.

[9] Memar, M. Y., Yekani, M., Alizadeh, N., and Baghi, H. B., 2019, "Hyperbaric oxygen therapy: Antimicrobial mechanisms and clinical application for infections", Biomedicine and Pharmacotherapy, 109(October 2018), pp. 440–447

[10] Di mussi, R., Spadaro, S., Stripoli, T., Volta, C. A., Trerotoli, P. Pierucci, and P. Grasso, S., 2018, "High-flow nasal cannula oxygen therapy decreases postextubation neuroventilatory drive and work of breathing in patients with chronic obstructive pulmonary disease", Critical Care, 22(1), pp. 1–11.

[11] Hoiland, R. L., Mladinov, S., Barak, O. F., Willie, C. K., Mijacika, T. and Stembridge., 2018, "Oxygen therapy improves cerebral oxygen delivery and neurovascular function in hypoxaemic chronic obstructive pulmonary disease patients", Experimental Physiology, 103(8), pp. 1170–1177.

[12] Hallenberger, A., Poets, C. F., Horn, W., Seyfang, A., and Urschitz, M. S., 2014, "Closed-Loop Automatic Oxygen Control (CLAC) in Preterm Infants: A Randomized Controlled Trial", Pediatrics, 133(2), pp. e379–e385.

[13] Chatburn, R. and Mireles-Cabodevila, E., 2011, "Closed-Loop Control of Mechanical Ventilation: Description and Classification of Targeting Schemes", Respiratory Care, 56(1), pp.85-102.

[14] Wenstedt, E. F. E., De Bie Dekker, A. J. R., Roos, A. N., Verberne, J. J. M., Korsten, H. H. M., Schultz, M. J., and Bindels, A. J. G. H., 2017, "Current practice of closed-loop mechanical ventilation modes on intensive care units – A nationwide survey in the Netherlands", Netherlands Journal of Medicine, 75(4), pp. 145–150.

[15] Cirio, S., and Nava, S., 2011, "Pilot Study of a New Device to Titrate Oxygen Flow in Hypoxic Patients on Long-Term Oxygen Therapy", Respiratory Care, 56(4), pp. 429–434.

[16] El Adawi, M. I., El-garhy, A. M., and Sawafta, F. O., 2012, "Design of Fuzzy Controller for Supplying Oxygen in Sub-acute Respiratory Illnesses", International Journal of Computer Science Issues, *9*(3), pp.192–206.

[17] Alzoubi, K., Alguraan, Z., and Ramahi, O. M., 2016, "Portable Automated Oxygen Administration System for hypoxaemic patients", SpringerPlus, *5*(1), pp. 1-18.

[18] Lellouche, F., and L'Her, E., 2012, "Automated Oxygen Flow Titration to Maintain Constant Oxygenation", Respiratory Care, *57*(8), 1254–1262.

[19] Bouchard, P., Roberge, M., Simard, S., and Her, E. L., 2016, "Automated oxygen titration and weaning with FreeO 2 in patients with acute exacerbation of COPD: a pilot randomized trial", International Journal of COPD, (NA), pp.1983–1990.

[20] Iobbi, M. G., Simonds, A. K., and Dickinson, R. J., 2007, "Oximetry feedback flow control simulation for oxygen therapy", Journal of Clinical Monitoring and Computing, 21, pp. 115–123.

[21] Pennycott, A., Hunt, K. J., Coupaud, S., Allan, D. B., and Kakebeeke, T. H., 2010, "Feedback control of oxygen uptake during robot-assisted gait", IEEE Transactions on Control Systems Technology, 18(1), pp. 136–142.

[22] F.T Tehrani., 2012, "A closed –loop system for the control of the fraction of inspired oxygen and the positive end expiratory pressure in mechanical ventilation", Comput.Biol. Med. ,42, pp. 1150-1156.

[23] J.M. Arnal, M. Wysocki, D. Novotni, D. Demory, R. Lopez, S. Donati, I. Granier, G. Corno and J. Durand-Gasselin., 2012, "safety and efficacy of a fully closed-loop control ventilation in sedated ICU patients with acute respiratory failure: a prospective randomized cross-over study", Intensive Care Med., 38, pp. 781-787.

[24] Mitra, S., Singh, B., El-Naggar, W., and McMillan, D. D.,2018, "Automated versus manual control of inspired oxygen to target oxygen saturation in preterm infants: A systematic review and meta-analysis", Journal of Perinatology, 38(4), pp. 351–360.

[25] Van den Heuvel, M. E. N., van Zanten, H. A., Bachman, T. E., te Pas, A. B., van Kaam, A. H., and Onland, W.,2018, "Optimal Target Range of Closed-Loop Inspired Oxygen Support in Preterm Infants: A Randomized Cross-Over Study", Journal of Paediatrics, 197, pp. 36–41.

[26] Van Zanten, H. A., Kuypers, K. L. A. M., Stenson, B. J., Bachman, T. E., Pauws, S. C., and Te Pas, A. B., 2017, "The effect of implementing an automated oxygen control on oxygen saturation in preterm infants", Archives of Disease in Childhood: Fetal and Neonatal Edition, 102(5), pp. F395–F399.

[27] Zapata, J., Gõmez, J. J., Araque Campo, R., Matiz Rubio, A., and Sola, A., 2014, "A randomised controlled trial of an automated oxygen delivery algorithm for preterm neonates receiving supplemental oxygen without mechanical ventilation", Acta Paediatrica, International Journal of Paediatrics, 103(9), 928–933.

[28] Weiss, B., and Kaplan, L. J., 2017, "Oxygen Therapeutics and Mechanical Ventilation Advances", Critical Care Clinics, 33(2), pp. 293–310.

[29] Schädler, D., Miestinger, G., Becher, T., Frerichs, I., Weiler, N., and Hörmann, C., 2017, "Automated control of mechanical ventilation during general anaesthesia: Study protocol of a bicentric observational study (AVAS)", BMJ Open, 7(5), pp. 1–6.