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Evaluation of Three Automatic Oxygen Therapy Control Algorithms on Ventilated Low Birth Weight Neonates

Edmund P. Morozoff, *Member IEEE*, and John A. Smyth, MD

Abstract—**Neonates with under developed lungs often require oxygen therapy. During the course of oxygen therapy, elevated levels of blood oxygenation, hyperoxemia, must be avoided or the risk of chronic lung disease or retinal damage is increased. Low levels of blood oxygen, hypoxemia, may lead to permanent brain tissue damage and, in some cases, mortality. A closed loop controller that automatically administers oxygen therapy using 3 algorithms - state machine, adaptive model, and proportional integral derivative (PID) - is applied to 7 ventilated low birth weight neonates and compared to manual oxygen therapy. All 3 automatic control algorithms demonstrated their ability to improve manual oxygen therapy by increasing periods of normoxemia and reducing the need for manual FiO_2 adjustments. Of the three control algorithms, the adaptive model showed the best performance with 0.25 manual adjustments per hour and 73% time spent within target +/- 3% SpO_2.**

I. Introduction

Oxygen therapy is the process of administering an air/oxygen gas mixture to a patient in order to maintain adequate tissue oxygenation. Premature infants frequently require continuous oxygen therapy because of under-developed, or diseased lungs. For each infant, adjustment of the relative proportions of air and oxygen in the inspired gas mixture will supply the appropriate fraction of inspired oxygen (FiO_2). This is important to avoid the potentially adverse consequences of subjecting the infant to either too much or too little oxygen.

Arterial blood oxygen saturation (SaO_2), representing the percentage of hemoglobin bonded with oxygen, is used as a measure of tissue oxygenation. Pulse oximetry permits continuous, non-invasive determination of pulse oxygen saturation (SpO_2), which correlates well with SaO_2 [1], [2]. The ease of SpO_2 makes the technology attractive for the monitoring and administration of oxygen therapy. Medical staff use blood gas analysis to correlate existing arterial partial pressures of oxygen, PaO_2 (another indicator of tissue oxygenation), to current SpO_2. With this information, staff must then determine a safe range of SpO_2 for each infant. FiO_2 is generally manually regulated, using an air/oxygen blender, in response to changes in SpO_2. In practice, frequent and unpredictable changes in an infant's condition may make attainment of a target SpO_2 difficult.

Oxygen therapy may be life-saving in certain disease states, however, oxygen may also be harmful. The toxicity of oxygen is thought to be mediated by "oxygen free radicals" that react with cellular constituents causing cell damage or cell death. Oxygen toxicity is thought to play a part in two specific conditions affecting premature infants: retnopathy of prematurity (ROP) and bronchopulmonary dysplasia (BPD). ROP is characterized by disordered growth of blood vessels in the developing retina of the eye which may lead to scaring and, in some severe cases, blindness [3]. BPD is characterized by disordered lung structure and cellular injury leading to the development of a chronic lung condition [4].

Figure 1 is a generic system block diagram of the oxygen therapy process. The goal of neonatal oxygen therapy is to give enough oxygen to maintain normal physiological functions and minimize the risks of toxicity. The definition of "safe" levels of oxygenation in premature infants is controversial [5], [6]. Appropriate arterial blood oxygen levels have traditionally been defined in terms of PaO_2. Prescribed ranges of PaO_2 for premature infants are generally within the normal range for healthy infants breathing air, ranging between 45 and 100 mmHg. Because blood is fully saturated with oxygen at PaO_2 = 100 mmHg, SaO_2 or SpO_2 is relatively insensitive to hyperoxemia. However, in practice, SpO_2 in the range of 88-95% (defined as normoxemia), correlating to a PaO_2 range of 40-100 mmHg, has been shown to protect against both hypoxemia and hyperoxemia.

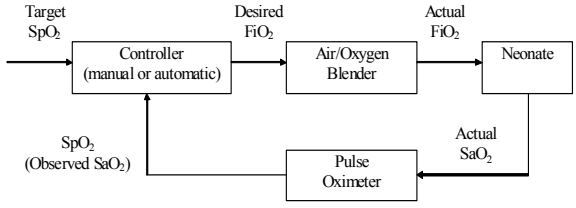

Fig. 1. System block diagram of the oxygen therapy process.

Manually administering oxygen therapy can be difficult and time consuming and the need for accurate full time oxygen therapy has been identified [7]. This paper describes the automation of oxygen therapy via three control algorithms and its clinical application to ventilated low birth weight neonates.

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Edmund P. Morozoff was with BC's Children's Hospital. He is now with Medtronic, 8200 Coral Sea Street NE, Mounds View, MN 55112 USA (phone: 763-526-1443; email: paul.p.morozoff@medtronic.com).

John A. Smyth, MD., is with Children's & Women's Health Centre of British Columbia, 4500 Oak Street, Vancouver, BC, Canada, V6H 3V4. (phone: 604-875-2345; email: jsmyth@cw.bc.ca)

II. Closed Loop Controller Development

A. Previous and Current Research

Oxygen therapy automation was first approached during WWII by Millikan and Pappenheimer who were tasked with preventing fighter pilots from losing consciousness during high altitude dogfights [8]. This work led to the further development of optical based oxygen sensors that eventually led to the refinement of the pulse oximeter. In the late 1970's, Beddis and Collins [9, 10] developed automated oxygen therapy using an invasive PaO_2 sensor. Taube used SpO_2 as an input to manage inspired oxygen for non-ventilated neonates using a proportional-integral-differential (PID) algorithm [11]. The authors developed closed loop SpO_2 controllers for ventilated low birth weight neonates using various algorithms [12]-[14]. Sun and Kohane [15] developed an open loop Fuzzy Logic controller in the mid 1990's. Since 2000, Urschlitz [16] and Claure [17] have also demonstrated promising results.

B. Device Design

The second generation controller designed by the authors for this study consists of 3 components – a generic graphical user interface, a central control unit, and a motorized air/oxygen blender. Its menu driven user interface accommodates algorithm selection, alarm management, data transfer, algorithm tuning, and SpO_2 trend display. The central control unit houses the main processor and is electrically tethered to the user interface and blender. A commercial air/oxygen blender was modified with a motor and clutching mechanism that supported manual override. The blender's gas lines were adapted to feed into a commercial ventilator. A commercial pulse oximeter is used to measure SpO_2. The system also has an FiO_2 sensor that is used as a trending mechanism and to support system alerts.

C. Challenges

Frequent and unpredictable changes in an infant's condition may make attainment of a target SpO_2 difficult. Rapid artificial and actual changes in reported SpO_2 values require intelligent filtering to determine if they warrant an FiO_2 adjustment. Valid rapid desaturations may be the result of a change in the neonate's physiology such as sinus bradycardia, right to left cardiac shunting, and poor pulmonary circulation. Artificial changes in presented SpO_2 may be the result of patient motion or weak signal. These fluctuations in the pulse oximeter's values may negatively impact traditional control algorithms.

D. State Machine Control Algorithm

SpO_2 error is defined in this paper as the target SpO_2 minus observed SpO_2. The state machine algorithm uses the error, its velocity, and acceleration as inputs into a state machine. A set of rules are then used to set an FiO_2 change that is actuated by the controller. Further details are described in our previous work [12], [13]. Although some researchers have stated that the work done in 1992 demonstrated that the controller had inadequate response during a preliminary clinical evaluation [15, 16, 17], they failed to cite the results of our 1993 randomized clinical study where the same controller demonstrated a statistically significant increase in time spent at normoxemia versus that time spent by the neonate under manual control [13].

E. PID Control Algorithm

Classical PID algorithms use the error (target – observed), its integration over time, and its velocity, to determine a new output. Weightings, known as gains, are applied to each of these three inputs and the new output is produced per (1). Some researchers have developed adaptive PID algorithms where the gains are automatically adjusted over time [18]. Our PID algorithm allowed the user to manually set each of the gain factors as a means of improving system response.

$$\text{New } FiO_2 = (k_p * e) + (k_i * \int\{e\}dt) + (k_d * de/dt) \qquad (1)$$

where: k_p = proportional gain; k_i = integral gain; k_d = differential gain; e = SpO_2 error

F. Adaptive Model Control Algorithm

Oxygen diffuses across the alveolar walls of the lungs into the pulmonary capillaries where only a small percentage dissolves in the blood. Over 98% of the oxygen is transported through the circulatory system bonded to hemoglobin. The percentage of total hemoglobin bonded with oxygen, $\%SaO_2$, is a function of the PaO_2 and is described by a non-linear relationship known as the oxygen dissociation curve - shown in Figure 2. Changes in patient physiology - temperature, amount of fetal hemoglobin, and pH - can affect the shape of this curve. A non-linear mathematical model, including the oxygen dissociation curve, was created to map FiO_2 at the patient's airway to SaO_2 at the tissue. This model had the capability of adapting to changing physiology using a supervisory loop that used the trends of the percentages of times at normoxemia, hypoxemia and hyperoxemia as inputs. At two or five minute periods, the controller would adjust its model of the FiO_2-SaO_2 relationship in an effort to maximize normoxemia. This model and its implementation are further described in a previous publication [14].

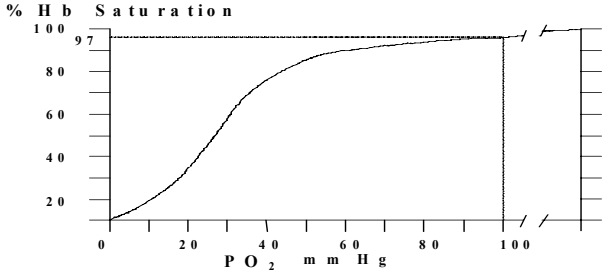

Fig. 2. Oxygen dissociation curve.

III. Clinical Evaluation

The purpose of this evaluation was to compare manual, state machine, PID, and adaptive modeling control algorithms and determine any associated system response parameters. Percentage of controller time close to the target was used a measure of the controller's accuracy. Manual adjustments were measured as a means of gauging the potential for the controller to reduce clinical staff workload. Since we had already demonstrated the utility of the state machine algorithm in previous work, we spent more clinical time on the PID and adaptive model algorithms.

IV. Results

A total of sixteen clinical evaluations were performed on seven low birth weight ventilated babies in the Special Care Nursery of British Columbia's Children's Hospital. Before entering a baby into an evaluation, informed consent was obtained from the parents. Table I describes the patients studied. Each infant was studied with various control algorithms and data from manual control was collected on all. We purposely chose babies that were relatively unstable and would challenge the controller. A clinical investigator was present during all periods of automatic control. Their task was to monitor the controller's performance while nursery staff managed the subject's care. The investigator did not apply therapy to the infant.

Table I. Subject characteristics.

Neonate	Gender	Age (days)	Gestation Age (weeks)	Corrected Age (weeks)	Birth Weight (gms)
A	M	13	29.00	30.86	1400
B	F	23	29.00	32.39	1500
C	M	8	31.00	32.14	1500
D	M	21	29.00	32.00	1450
E	M	13	26.57	28.43	950
F	M	14	27.00	29.00	885
G	M	9	25.00	26.29	905

The target SpO_2 was varied, and all automatic algorithms were studied at targets of 92%, 93% and 94%. Manual oxygen therapy followed standard hospital procedure and the staff did not make an attempt to hold the infant's SpO_2 to specific target. Their goal was to keep the baby within a range of 90%-96% SpO_2.

Figure 3 summarizes the percentages of study time spent by each control algorithm within various ranges of the target SpO_2. An artificial target of 93% was set for manual mode as a means of producing comparable data. It should be noted that the SpO_2 distribution for manual oxygen therapy is representative for the types of neonates we studied and not for all neonates under oxygen therapy. The total number of hours spent at each control algorithm is summarized in Table II. With respect to the automatic control algorithms, more clinical time was spent on PID control as a means of understanding and improving our ability to tune its gain factors. We collected 18.43 hours during manual oxygen therapy for comparison to the automatic control data. In addition to these data, we collected 116.62 hours of additional manual oxygen therapy data to build up our knowledge base. The distribution of manual mode time spent near target during the study (i.e. 18.43 hours) was comparable to the distribution for the extended set of manual mode data (i.e. 116.62 hours).

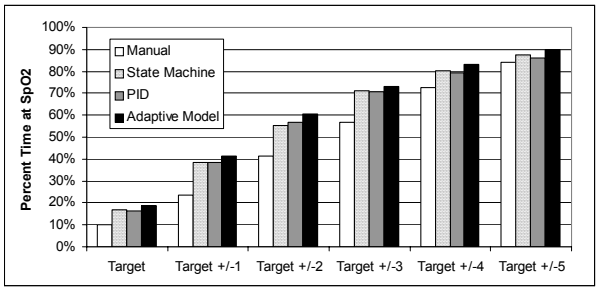

Fig. 3. Histogram of percent of test duration at various ranges of SpO_2 from the controller target.

Manual adjustments are inevitable in most control systems. For example, an automobile's cruise control allows the driver to quickly adjust the vehicle's speed based upon variables that the control algorithm does not have. For examples, slowing for an obstruction in the road or speeding up to pass another vehicle. During closed loop control, the oxygen therapy device also provides the user with a mechanism to manually adjust the FiO_2 levels. A reduction in these manual adjustments, compared to manual therapy, can be seen as a means of reducing clinical staff workload. Table II presents the number of manual adjustments per hour for each algorithm.

Table II. Summary of manual adjustments.

Algorithm	Total Hours	Total Manual Adjustments	Manual Adjustments per Hour
Manual (study)	18.43	69	3.74
State Machine	14.72	7	0.48
PID	42.20	19	0.45
Adaptive Model	21.42	5	0.23

V. Discussion

All three control algorithms increased the percentage of time spent closer to the target SpO_2 than manual oxygen therapy. A tuned PID algorithm had a performance equivalent to the state machine algorithm, both in terms of the SpO_2 distribution and the number of manual adjustments per hour. The adaptive model algorithm performed better than all the algorithms. It also had the added feature of requiring no manual tuning to support changes in patient physiology.

As the debate over appropriate SpO_2 levels continues, it may be possible that the fidelity of the oxygen therapy algorithm is not as important as the ability to keep the neonate within a prescribed range. As indicated by Figure 3,

as the bandwidth increases to target +/- 5% SpO_2, the algorithms converge towards equivalent performance. This implies that the primary utility of the controller may be its ability to reduce the workload of clinical staff. If this is the case, the adaptive control algorithm, with its ease of use (i.e. self tuning capability) and its lowest number of manual adjustments, has the most promise.

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