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Clinical implementation of automated O_2 titration in a tertiary care hospital

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Abstract

Background: When treating acute respiratory failure, both hypoxemia and hyperoxemia should be avoided. SpO_2 should be monitored closely and O_2 flows adjusted accordingly. Achieving this goal might be easier with automated O_2 titration compared to manual titration of fixed-flow O_2. We evaluated the feasibility of using an automated O_2 titration device in subjects treated for acute hypoxemic respiratory failure in a tertiary care hospital.

Methods: Healthcare workers received education and training about oxygen therapy and were familiarized with an automated O_2 titration device (FreeO_2, Oxynov, Quebec City, Canada). A coordinator was available from 8 am to 5 pm during week days to provide technical assistance. The ability of the device to maintain SpO_2 within the prescribed therapeutic window was recorded. Basic clinical information was recorded.

Results: Subjects were enrolled from November 2020 to August 2022. We trained 508 healthcare workers on use of automated O_2 titration which was finally used on 872 occasions in 763 subjects, distributed on the respiratory, COVID-19 and thoracic surgery wards and the emergency room. Clinical information could be retrieved for 609 (80%) subjects who were on the system for a median of 3 days (interquartile range: 2 to 6 days) representing 2567 subject-days of clinical experience with the device. In the 82 (14%) subjects for whom this information was available, the system maintained SpO_2 within the prescribed targets 89% of the time. Ninety-six subjects experienced clinical deterioration as defined by the need to be transferred to the intensive care unit and/or requirement of high nasal flow oxygen but none of these events were judged to be related to the O_2 device.

Conclusions: Automated O_2 titration could be successfully implemented in hospitalized subjects with hypoxemic respiratory failure from various causes. This experience should foster further improvement of the device and recommendations for an optimized utilization.

Word count: 300 words

Key words: respiratory failure, oxygen supplementation, automated oxygen titration, hypoxemia, hyperoxemia, oxygen saturation.

Introduction

Oxygen supplementation is ubiquitous in hospitalized subjects with hypoxemic respiratory failure. Traditionally, the main concern of clinicians was to alleviate hypoxemia with little concern for hyperoxemia, except in the neonatal population[1] and in chronic obstructive pulmonary disease (COPD) where the avoidance of hyperoxia to protect against worsening of respiratory acidosis was recommended[2]. However, the appreciation that hyperoxemia may also be harmful in other conditions such as sepsis, myocardial infarction, and following emergency surgery[3] has led to recommendations that SpO_2 should be maintained within therapeutic zones that vary according to the cause of respiratory failure. For example, the British Thoracic Society has proposed SpO_2 targets of 94 to 98% for most acutely ill subjects or 88 to 92% in subjects at risk of hypercapnic respiratory failure[4]. Although guidelines for oxygen therapy are not uniform[4-8], their implications are that SpO_2 should be monitored closely and O_2 flows adjusted repeatedly to maintain subjects within a relatively narrow therapeutic window. Achieving this goal with manual O_2 titration is labor-intensive, and often not feasible in the context of routine clinical care[9]. As such, it is common that subjects are found outside the desired range of SpO_2, both in the hypoxemic and hyperoxemic ranges[10-12].

Automated O_2 titration with devices that are based on closed-loop algorithms has been developed with the objective of maintaining SpO_2 by providing continuous adjustment of O_2 flows in the context of fluctuating oxygen requirements[13,14]. These devices have been shown to increase the proportion of time spent in the desired SpO_2 range in various clinical situations, including hospitalized subjects with acute COPD exacerbation[11,14], subjects in the emergency department[12], following surgery[15,16], and in COVID-19 related hypoxemic respiratory failure[17]. Automated O_2 titration has also been shown to be effective in situations where rapid adjustments of O_2 flows is required, such as during exercise[18-20]. It may also accelerate weaning from oxygen and hospital discharge[11,12,21], with potential reduction in hospitalization costs[22]. Automated O_2 titration has been implemented with high flow nasal cannula (HFNC) showing efficacy of the system to maintain SpO_2 within the desired target zone during walking exercise in patients with COPD and in the context of hypoxemic respiratory failure[23,24]. By reducing the requirement for direct contacts between hospital workers and subjects as the O_2 flows are automatically adjusted, the risk of

transmission of contagious disease is reduced[25]. This is an important consideration given the scarcity of hospital workers, overloaded health care systems, and high risk of hospital transmission of pathogens[25,26], among healthcare workers during the recent pandemic[27].

The cumulative experience with automated O_2 titration has been obtained in the research context, data also needs to be obtained in the clinical setting. Recognizing that automated O_2 titration has the potential of facilitating the implementation of clinical guidelines regarding the use of oxygen, we evaluated the feasibility of using this technology in the clinical care of subjects treated for acute hypoxemic respiratory failure in a tertiary care hospital.

Methods

In 2019, a multidisciplinary committee advised hospital administrators on the possibility of implementing automated O_2 titration within the context of clinical care. In 2020, 30 automated O_2 titration devices were acquired by the hospital to treat subjects in the emergency room or the hospital wards with various forms of hypoxemic respiratory failure, including COPD exacerbation, exacerbation of interstitial lung disease, viral (COVID-19) or bacterial pneumonia and heart failure. This was done in the context of a prospective observational technological evaluation that took place between September 2020 and August 2022 at the *Institut universitaire de cardiologie et de pneumologie de Québec*, a 330-bed tertiary-care, university-affiliated hospital with specialization in cardiology and respiratory medicine. When possible, clinical information, including etiology of respiratory failure, duration of O_2 therapy and length of hospital length of stay were noted by the coordinator of the project. Prospectively collecting clinical data on participants was exempted from ethics committee review by the institution because this was considered to be part of routine clinical care. The permission to use the clinical data anonymously for a scientific report was granted by the medical director of the hospital with waiver of consent from the institutional ethics review board considering that this evaluation was done in the context of clinical care. The manufacturer had no role in data collection, interpretation and presentation.

The automated O_2 titration device used in this technological evaluation (FreeO_2, Oxynov, Quebec City, Canada)[13] relies on continuous SpO_2 recording to feed a closed-loop algorithm which allows automatic O_2 flow titration to maintain SpO_2 within a target window prescribed by the clinician. The device is coupled with a finger sensor linked to an embedded pulse oximeter (OEM III Module, Nonin Medical). It has three operating modes, the closed-loop mode being the primary operating mode, whereby O_2 flow is changed based on measurement of SpO_2. In the closed-loop mode, O_2 flow is automatically titrated based on the difference between the real-time SpO_2 and the target value using a proprietary proportional integral algorithm with a O_2 flow command adjustment rate of once per second to achieve or maintain a pre-set SpO_2 level. O_2 flow is limited to 0.1 to 20.0 LPM. O_2 flow may increase or decrease in order to maintain a stable SpO_2 value. The constant-flow mode is comparable to a standard O_2 regulator with the device only providing fixed O_2 flow as set by the attending physician, between 0.1-20.0 LPM. In the acquisition mode, the device only monitors the oximeter readings (SpO_2, respiratory rate and heart rate) without any oxygen being provided. Data is visible on the front screen and captured in the device memory from which it can be retrieved as long as the corresponding subject has been appropriately identified in the system (name, date of birth) when initiating therapy. However, this was not mandatory to initiate treatment with O_2 titration device and this step was often overlooked by healthcare workers.

The implementation of automated O_2 titration in clinical care of the hospital followed a multistep process to acclimate hospital workers to its use. A multidisciplinary implementation committee composed of nurses, respiratory therapists, physicians, a physiotherapist and a patient representative oversaw the implementation of the devices and made recommendations about use (**Table 1**). A coordinator (PAB), helped by a senior nursing consultant (GPR) and one physician (FL), trained hospital workers (nurses, respiratory therapists, physicians) in various aspects of oxygen therapy and about the use of automated O_2 titration. Training sessions were planned to be done in-person but due to infection control measures in the COVID-19 pandemic, they were delivered remotely. The teaching material remained available for subsequent consultation if needed. The main topics covered were: *i)* update on oxygen therapy, including the importance of avoiding hypoxemia and hyperoxemia, *ii)* prescribing oxygen with a lower and upper SpO_2 boundaries in specific patient population and revision of the current guidelines and *iii)* practical use of automated O_2 titration, including monitoring of subjects with the device, accurate patient selection, accurate SpO_2 target,

and potential issues associated with improper use of the device. A key learning objective was the detection of clinical deterioration with automated O_2 titration. With fixed O_2 flow, clinical deteriorations are detected when SpO_2 worsens. With automated O_2 titration, SpO_2 remains stable during disease instability. This is due to the intrinsic ability of automated O_2 titration to maintain SpO_2 within the target zone as long as the maximum O_2 flow allowed by the device is not surpassed. With automated O_2 titration, clinical deteriorations are rather detected when requirements for O_2 flow increase to maintain the target SpO_2, which is a major change of practice for healthcare workers.

The coordinator oversaw the use of automated O_2 titration from 8 am to 5 pm during week days to address any concerns or technical questions with its use. He served as clinical expert to support healthcare workers selecting appropriate candidates for automatic O_2 titration and assist with the initiation and weaning of the device. He was also in contact with the biomedical engineering department of the hospital to help with any troubleshooting of the device. In addition, four advanced practice nurses were available to accompany the hospital workers in the early weeks of the project when familiarity with the system had to be developed.

A clinical protocol was developed by advanced practice nurses and respiratory therapists to address practical issues with the use of automated O_2 titration (**Table 2**). This document covered the following topics: *i)* contraindications to automated O_2 titration, *ii)* initiation of the device, *iii)* setting of the clinical parameters of the device according to the clinical situation, *iv)* how to mobilize subjects on the device, v) clinical surveillance for nurses and respiratory therapists of subjects on automated O_2 titration and *vi)* weaning from automated O_2 titration.

Subjects admitted to the emergency room, respiratory and thoracic surgery wards, or COVID-19 unit with a diagnosis of hypoxemic respiratory failure were potentially eligible to be treated with automated O_2 titration when a device was available. Patients with one or more of the following characteristics were not considered for automated O_2 titration: *i)* requirement for > 8 L/min of O_2 to obtain a SpO_2 of ≥ 92% on the respiratory ward or emergency room or > 6 L/min of O_2 to obtain a SpO_2 of ≥ 90% on the COVID-19 unit, *ii)* requirement for non-invasive ventilation, high-flow nasal cannula, imminent endotracheal intubation, or cardiac arrest; *iii)* impossibility of measuring SpO_2

(poor peripheral perfusion, Raynaud, scleroderma), *iv)* agitation and/or absence of collaboration. We did not collect information about patients who were not considered for automated O_2 titration.

The proposed SpO_2 targets were 88 to 90% for COPD and 90 to 92% for other causes of hypoxemia but the final decision belonged to the physician. These SpO_2 targets are lower than typically recommended[4-8]; they were selected based on our findings that the integral oximeter that was used with the automated O_2 titration device (OEM III Module, Nonin Medical) systematically underestimates SaO_2[28] and with the objective of avoiding hypoxemia and hyperoxemia. Weaning from automated O_2 titration was proposed when O_2 flow was ≤ 1 L/min. O_2 flow, SpO_2, and breathing frequency alarms were set at 8 L/min, 85%, and 40 breaths/min, respectively. The use of nasal cannula was recommended when O_2 flows were < 5L/min; oxygen masks (OxyMask or simple O_2 mask) were used when O_2 flows ≥ 5L/min or if more comfortable.

Healthcare workers had the opportunity to answer anonymously a short survey about their experience with automated O_2 titration. The survey was available for one day, covering the three working shifts. The following questions were asked: *i)* would you consider using an automated O_2 titration device for your subjects on oxygen, rarely, occasionally, often?, *ii)* did you receive sufficient technical support for the use of automated O_2 titration, yes or no? and *iii)* on a 0 to 10 scale, 0 being completely useless and 10 being the most useful, how do you rate the clinical utility of automated O_2 titration?.

We report data to support the feasibility of using an automated O_2 titration device in clinical practice including number of patients for each hospitalization site (respiratory ward, COVID-19 unit, emergency room, thoracic surgery), etiology of respiratory failure, duration on automated O_2 titration, length of hospital length of stay, SpO_2 targets, and SpO_2 data. Clinical deterioration defined as the need for high flow nasal oxygen and/or transfer to the intensive care unit was recorded. Whether this was associated to the use of automated O_2-titration or to progression of the underlying disease was documented from the medical chart or by discussing with the attending physician. We did not pre-specify the number of participants; this was determined by the duration of the project and by the availability of O_2 titration devices. Some subjects were treated twice during the same hospitalization; when this happened, we only report the first use.

Categorical variables were presented as absolute or relative frequencies and were analyzed using the Fisher's exact test. Continuous variables were expressed as mean ± standard deviation (SD) or as median with associated 25th and 75th interquartile range (IQR) according to the variable distribution. Between-group comparison for continuous variables was to perform a one-way ANOVA. The normality assumption was verified with the Shapiro-Wilk tests using residuals from the statistical model. The Brown and Forsythe's variation of Levene's test statistic was used to verify the homogeneity of variances. Length of hospital stay was log-transformed to fulfill the normality and variance assumptions. We used the Wilcoxon rank-sum test to compare groups when the normality and variance assumptions were rejected. Statistical significance was present with a two-tailed p value < 0.05. Analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC, U.S.A.).

Results

The automated O_2 titration system began to be used within the respiratory ward in November 2020, on the COVID-19 unit in January 2021, at the emergency room on April 2021, and finally on the thoracic surgery ward on March 2022, with the last patient enrolled on August 24th, 2022 (**Figure 1**). 508 healthcare workers were trained to the use of automated O_2 titration, including 399 nurses and respiratory therapists, 16 physiotherapists, 28 nurse assistants, 27 physicians (14 emergency physicians and 13 pulmonologists) and 38 medical residents.

The flow of patients is presented in **Figure 2**. O_2 therapy was administered with the automated O_2 titration device on 872 occasions in 763 subjects distributed on the respiratory, COVID-19 and thoracic surgery wards and in the emergency room (**Figure 3**). Of this number, we could retrieve clinical information on 609 subjects who were on the system for a median of 3 days (IQR 2 to 6 days), representing 2567 patient-days of clinical experience with the device. The characteristics of these subjects are presented in **table 3**. Mean age of subjects was 72 ± 12 years, median hospital length of stay was 9 days (IQR: 6 to 15 days). Automated O_2 titration was started at a median of 0 day (IQR: 0 to 1) after hospitalization, most subjects being previously treated with fixed-flow O_2 at 2 L/min (IQR: 1 to 3 L/min). 302/609 subjects (49.6%) were weaned from oxygen while being on automated O_2 titration, the remaining ones had a few hours of fixed-flow O_2 at low flows before O_2 therapy was stopped. Due to disease worsening or instability, 42 subjects (7.0%) had to be transferred to the intensive care unit and 81 subjects (13.3%) had to be treated with high nasal-flow oxygen, including 54 who received this therapy outside the intensive care unit. Thus, a total of 96 subjects (15.8%) reached the definition of clinical worsening. Under those circumstances, automated O_2 titration was stopped according to the clinical care protocol. Attending physicians attributed these events to deterioration of the underlying condition and not to the use of the automated O_2 titration device. With earlier versions of the software, the system was occasionally unstable and would stop automatically adjusting O_2 flows for unclear reasons. When this occurred, the system automatically reverted to the constant-flow mode, delivering a O_2 flow based on the analysis of the last 15 minutes of treatment. This functionality, which is also activated when the SpO_2 signal is interrupted or of poor quality, was created for safety purposes. These situations were immediately reported to the manufacturer and software updated version 1.2.6 which was found to be reliable and working as expected.

SpO_2 targets prescribed by clinicians were generally in agreement with those proposed by the implementation committee (**table 4**). Based on the analysis of 387 subjects for whom the information could be retrieved from the device memory, the SpO_2 target was 88% to 90% in 306 (79%) of the cases while SpO_2 target ≥ 93% was used in 8 (2.1%) of subjects. The ability of automated O_2 titration to maintain SpO_2 within the desired range could be assessed in 82 subjects for whom detailed SpO_2 data could be retrieved from the device memory, 38 from the respiratory ward, 9 from the COVID-19 unit and 35 from the emergency room. Baseline characteristics of these 82 subjects were similar to those of the 527 subjects for whom the oxygenation data was not available (**table 3**). As can be seen in **table 5**, subjects were maintained within the SpO_2 target zone for 89% of the time. Hypoxemia (SpO_2 < 85%) occurred in < 5% of recording time while hyperoxemia (SpO_2 ≥ 98%) was found < 1% of recording time.

Thirty-six of 508 healthcare workers (7.1%) who used the automated O_2 titration device filled the survey about its utilization. Twenty-two of 36 (61%) healthcare workers would often consider using automated O_2 titration for subjects on O_2 therapy, 10/36 (28%) would do so occasionally, while 4/36 (11%) reported that they would rarely use it. Twenty-eight of 36 respondents (78%) considered that the technical support was sufficient and felt comfortable with the use of the device. On a 0 to 10 scale, 2, 1, 5, 10, 5 and 13 health-care workers gave a utility score of 5, 6, 7, 8, 9 and 10, respectively with a mean utility rating score for automated O_2 titration of 8.5 ± 1.5.

Discussion

We report our clinical experience with the feasibility of using an automated O_2 titration device in subjects with acute respiratory failure requiring O_2 therapy as a part of their routine clinical care. The cumulative data during this evaluation extends previous clinical trials in showing that the ability of automated O_2 titration to maintain SpO_2 within the desired range in various diseases[10-12,14-17] may also apply to "real life" clinical situations. Clinical worsening, defined as the requirement for high flow nasal oxygen and/or transfer to the intensive care unit in 96 subjects (15.8%) was attributed to progression of the underlying disease. Although not a unanimous choice amongst 36 healthcare workers who responded to a short survey, the automated O_2 titration device was felt useful and a positive experience was reported by the majority of users. This evaluation of the use of automated O_2 titration in routine clinical care, provided several learning opportunities that helped to address some frequently overlooked practical issues related to *i)* oxygenation measurements with pulse oximetry and definition of optimal oxygenation with corresponding SpO_2 targets, *ii)* organizational factors including healthcare workers training and supervision with the use of automated O_2 titration, *iii)* optimal utilization of automated O_2 titration systems, *iv)* limitations in the accuracy of SpO_2 readings with currently available oximeters.

This technological evaluation provided an opportunity for nurses, physicians, respiratory therapists, and researchers from our institution to reflect and discuss various aspects of O_2 therapy. The use of an automated O_2 titration device, which forces clinicians to consider SpO_2 targets adapted to the clinical situation, may be helpful in implementing the recommendations that SpO_2 should be maintained in pre-specified therapeutic windows, avoiding both hypoxemia and hyperoxemia. Despite clear recommendations about the benefits of prescribing oxygen according to target ranges, clinical implementation of this approach is challenging and required numerous trainings, discussions and feedback from clinicians. For example, in a recent audit of O_2 therapy conducted in New Zealand, SpO_2 targets could be found in only 60% of hospitalized patients[29].

SpO_2 monitoring with the an automated O_2 titration device made us even more aware of the fluctuations in O_2 needs in subjects with acute respiratory failure, especially in subjects with COVID-19, something that is not typically addressed with only intermittent (and often infrequent)

SpO_2 measurements. Automated O_2 titration in response to SpO_2 fluctuations was more effective than manual O_2 titration to maintain subjects in the desirable SpO_2 range as previously reported in a variety of clinical situations such as critically injured trauma subjects[10], in subjects admitted to the emergency departement[12], following thoracic or abdominal surgery[15], acute COPD exacerbation[11,14], exercise in subjects with chronic lung diseases[19], and in the pediatric population[30]. Typically, SpO_2 is maintained in the therapeutic zone 80% of the time with automated O_2 titration compared to 40 to 55% of the time with manual O_2 titration[10-12,14-17]. Considering the importance of avoiding both hyperoxemia and hypoxemia[31], the goal of maintaining subjects within a safe SpO_2 target zone is an argument in favor of automated O_2 adjustment when caring for subjects with hypoxemic respiratory failure.

Our goal was to test the clinical implementation of an automated O_2 titration device and not to make recommendations about O_2 targets in specific conditions and our experience should interpreted in this context. The suggested SpO_2 targets from the implementation committee (88 to 90% in subjects with COPD, 90 to 92% in other situations) were lower than typically recommended, particularly in subjects other than COPD, where targets ranging between 90 to 98% have been recently proposed[4-8]. The SpO_2 targets that were used took into consideration a study from our center which provided evidence that SpO_2 readings from the built-in Nonin oximeter, systematically underestimate SaO_2 and are lower than those of other oximeters[28]. In this study, it was found that SpO_2 readings were on average, 3% to 4% lower with the Nonin oximeter than with the Philips, Nellcor or Masimo oximeters[28]. One advantage of the Nonin oximeter is that a SpO_2 target of 90% allowed to detect all the hypoxemic episodes while other tested pulse oximeters only detected 11 to 37% of these occurrences[28]. We were therefore confident that proposing SpO_2 targets of 88% in COPD and 90% in other diseases with the system that was used in this technological evaluation would protect against hypoxemia and hyperoxemia while avoiding the risk of worsening hypercapnia in COPD and ensuring safety of subjects[28]. Although no blood gas data is available in the present report, a recent study from our group support this practice by showing the a SpO_2 target of 90% with the Nonin oximeter is appropriate to protect against and hypoxemia and hyperoxemia[32]. Another consideration is that using higher targets could delay weaning of O_2 and therefore unduly prolong hospital stay, a situation that is more likely to occur when using an oximeter that systematically underestimates SpO_2. Some clinicians showed some reluctance with our proposal for SpO_2 targets early in the

technological evaluation, but as clinical experience was gained and with appropriate teaching, most of them became comfortable with their use as shown in table 3. The proposed SpO_2 targets were applied primarily in people with light skin pigmentation who constitute the vast majority of the population treated in our hospital, an important consideration given the possibility to overestimate SaO_2 with pulse oximetry in people with dark skin pigmentation[33].

In theory, automated O_2 titration, which allows for multiple adjustments of O_2 flows, should be safer than relying on the current practice where it is challenging for health-care workers to precisely titrate O_2 flows[9]. However, we acknowledge that confirmation of this theory would require a formal randomized clinical trial. In patients with hypercapnic respiratory failure, the avoidance of hyperoxemia, which was infrequently observed (table 4), should reduce the risk of worsening respiratory acidosis. Ninety-six subjects, representing 15.8% of the study population required high nasal-flow oxygen and/or transfer to the intensive care unit. According to attending physicians, this was due to deterioration of the underlying condition and not to the use of the automated O_2 titration device.

For automated O_2 titration to be used safely, the premise that SpO_2 is an accurate surrogate of SaO_2 should be fulfilled and, unfortunately, this is not always the case[28,34,35]. Indeed, oximetry readings should be viewed as approximating SaO_2 rather than considered as an accurate vital sign. Although imprecision of oximetry readings was reported years ago[34,35] this finding was largely unheeded by the medical community, with potential clinical consequences. For example, using an oximeter that systematically underestimates SaO_2 may lead to unduly high O_2 flows if the SpO_2 target is not adjusted accordingly[32]. In people with dark skin pigmentation, overestimation of SaO_2 by pulse oximetry may lead to the occurrence of undetected hypoxemia and the risk of undertreatment based on certain SpO_2 thresholds[33]. Low perfusion and motion artifact may also compromise reliable SpO_2 readings and thus any valid estimation of SpO_2[35]. These limitations are not specific to automated O_2 titration devices as they applied to any situations where O_2 therapy is governed by SpO_2 readings. What remains to be seen is to which extent imprecision of oximetry readings influences clinical outcomes but increased hospital mortality has been associated with the presence of undetected hypoxemia[36]. While we are awaiting for better oximeter accuracy, the understanding of current limitations of pulsed oximetry should help to provide safer medical care[37].

When this project was conceived in 2019, we did not foresee the use of an automated O_2 titration device in subjects hospitalized with severe COVID-19 pneumonia. It turned out that such a system was useful in this circumstance because of the ability to continuously adjust O_2 flows without direct contact between subjects, nurses and respiratory therapists. This offered added safety for the subjects and for hospital workers, likely reducing the risk of transmission of contagious disease[27]. Another advantage of automated O_2 adjustment was the reduction in the use of personal protective equipment which was a major issue early in the pandemic due to scarcity. Our experience with automated oxygen titration is consistent with a that of Danish investigators who reported a similarly positive experience in 20 hospitalized COVID-19 subjects with mild to moderate hypoxemic respiratory failure[17].

Implementing a new technology in clinical practice is challenging. Changing medical practice is a slow process and there are multiple barriers to the adoption rate of healthcare solutions[38,39]. The importance of education and continued support and feedback to the medical team cannot be overemphasized. We also observed some clinical situations during which the behavior of the system was difficult to understand by the clinical team. On some occasions, subjects with COPD required relatively high O_2-flows (4 to 6 L/min) to maintain target SpO_2. These situations were uncomfortable for clinicians who are generally trained to avoid high O_2 flows in COPD without appreciating that it is hyperoxemia and not high O_2 flows per se that are responsible for worsening hypercapnia. In this context, the use of automated O_2 titration may offer additional protection to subjects because as long as SpO_2 is maintained within a safe therapeutic window, hyperoxemia and worsening hypercapnia should not occur.

Some clinical situations were difficult to comprehend because of the time lag between oxygenation status (SpO_2) and incremental (or decremental) adjustments in O_2 flows. Once such situation is illustrated in **Figure 4**. A recovering subject resumed mild physical activities during which O_2 desaturation was observed. This provoked a dip in SpO_2 to which the automated O_2 titration device responded by increasing O_2 flow. Upon return to rest, SpO_2 remained higher than the target value for some time while O_2 flows progressively returned to lower values. For example, at 1000 sec, O_2 flow of 4 L/min could appear unexpected because the SpO_2 was above the target. In this situation,

instantaneous reading of the physiological parameters displayed on the automated O_2 titration device showing O_2 flows that were higher than expected from the SpO_2 value could have misleadingly led to the conclusion that the device was not operating as intended while, this was simply a reflection of a time-lag between the SpO_2 correction and the O_2 flow response. Inspecting SpO_2 and O_2 flow trend report from the device is crucial to understand the nature of the situation. Another example that requires some experience with the device is when the required O_2 flow is low (around or less than 1 L/min) and the patient is almost ready to be weaned from oxygen. Small fluctuations in SpO_2 related to physical activities could induce transient increase in O_2 flow which may prevent or slow O_2 discontinuation. This situation may generally be resolved by simply stopping oxygen and monitoring the patient to ensure that SpO_2 remains adequate.

There are limitations to the present report that should be considered in interpreting the findings and their generalizability. The most obvious is that data are available only for a fraction of patients. There was a shortage of resources to collect detailed information in a systematic fashion as we are accustomed to in clinical research. For example, detailed SpO_2 data could only be retrieved for 13% of subjects; due to the fact that many were not appropriately identified in the device making it impossible to match recorded oxygenation data with the corresponding subjects. Although the availability of detailed SpO_2 data in only a small portion of subjects raises questions about the external validity of the findings, we were reassured that the proportion of time spent within the SpO_2 targets was similar to that previously observed in other clinical circumstances[10-12,14-17]. Only a small number of nurses and respiratory therapists responded to the survey about the utilization of automated O_2 titration. Therefore, its interpretation should be done cautiously. For example, it is possible that only those who had a positive experience with the device took the time to answer the survey. Lastly, the decision to use or not the automated O_2 titration system was made by the clinical team and we do not have data to estimate the proportion of hospitalized patients requiring oxygen therapy treated with the device.

Conclusion

We found that automated O_2 titration could be implemented safely in the context of routine clinical care in subjects with hypoxemic respiratory failure of various etiology. Based on this clinical experience, and on pilot data suggesting the possibility to reduce hospital length of stay with

automated O_2 titration[11], we encourage the conduct of randomized clinical trials testing the impact of automated O_2 titration on hospital stay compared to the standard care of manual O_2 flow in subjects with acute hypoxemia.

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Legends for figures

Figure 1. Chronology of the implementation of the automated O_2 titration device.

Figure 2. Flow of patients.

Figure 3. Distribution of subjects on the automated O_2 titration device.

Figure 4. Relationship between SpO_2 and O_2 flow in one subject who was treated with the automated O_2 titration device while transitioning from walking in the corridor to bed rest. Target SpO_2 was set at 90%. During walking, a sudden fall in SpO_2 down to 80% provoked a rapid rise in O_2 flow aiming to return SpO_2 in the target zone. An overshoot in SpO_2 up to 95% was noted. Returning to bed resulted in reduced O_2 needs as seen by a progressive decline in O_2 flow down to 0 L/min over a 10-min period while SpO_2 remained at the target value of 90%.

Quick look

Current knowledge

It is now recommended that SpO_2 be closely monitored to avoid hypoxemia and hyperoxia when treating subjects with acute respiratory failure. Maintaining SpO_2 within a relatively narrow therapeutic window may be challenging with manual O_2 titration, the standard of care in oxygen therapy. Automated O_2 titration systems are currently being developed to reach this objective but their use is mostly limited to research settings.

What this paper contributes to our knowledge

This technological evaluation indicated that automated O_2 titration may be implemented safely in the clinical care of subjects treated for hypoxemic respiratory failure in a tertiary care hospital. We also found that that the ability of automated O_2 titration to maintain SpO_2 within the desired range in various diseases may also apply to “real life” clinical situations.

Table 1. Composition and role of members of the multidisciplinary team

Respiratory physicians	Patient safety O_2 prescription rules
Nurses – Respiratory therapists	Elaborating nurse practice rules Uniformizing practices regarding O_2 therapy Initiating O_2 therapy Surveillance and patient follow-up O_2 weaning
Physiotherapists	Patient mobilization Ensuring appropriate oxygenation during mobilization
Patient representative	Patient comfort and safety
Project coordinator	Teaching of hospital workers Overseeing the use of automated O_2 titration in the hospital Addressing any questions/concerns about the device

Table 2. Clinical care protocol for the installation of automated O_2 titration

Rule out contraindications	• requirement for more than 8 L/min of O_2 to maintain $SpO_2 \geq 92\%$ or more than 6 L/min of O_2 to maintain $SpO_2 \geq 90\%$ on the COVID-19 unit • non-invasive ventilation • imminent intubation or cardiac arrest • high-flow nasal oxygen • impossibility to measure SpO_2 • CO poisoning • Agitation/Confusion/Delirium or non collaborative patient
How to initiate automated O_2 titration	• proper connection of the device to wall O_2 • verification of O_2 prescription with SpO_2 targets • choosing interface (nasal prongs or mask) • ensure appropriate SpO_2 signal • ensure patient' comfort
Setting the clinical parameters of the device	• set oxygenation mode • set target SpO_2 according to prescription • set maximum O_2 flow (10 L/min or according to clinical situation) • set maximum O_2 flow alarm (8 L/min) • set minimum SpO_2 alarm (85%) • set respiratory rates alarm (according to clinical situation)
Mobilizing patient within the clinical unit	• changing the O_2 source from the wall to O_2 cylinders
Clinical surveillance for nurses	• parameters to be monitored: respiratory rate, SpO_2 and O_2 flows, trends in O_2 flows and SpO_2 • verification of SpO_2 probe and O_2 interface • verification of alarms • frequency: q 1hr at initiation and then q 4 hr in the emergency room or in the COVID-19 • unit; BID + PRN on the regular ward • contact treating physician when sustained increase in O_2 flow $\geq$ 3 L/min from baseline or in case of clinical deterioration
Clinical surveillance for respiratory therapists	• parameters to be monitored: respiratory rate, SpO_2 and O_2 flows, trends in O_2 flows and SpO_2 • verification of SpO_2 probe and O_2 interface • verification of alarms • frequency: at initiation, when administering nebulized medication, during routine visit
Weaning of O_2	• initiate weaning when O_2 flow $\leq$ 1 L/min • place the automated O_2 titration device in the surveillance mode • ensure SpO_2 remains $\geq$ lower SpO_2 target

Table 3. Subjects' characteristics

	All subjects (n = 609)	Subjects with oxygenation data (n = 82)	Subjects without oxygenation data (n = 527)	P value
Age, years	72.4 ± 12.1	74.0 ± 11.4	72.1 ± 12.2	0.20
Sex, M/F	303/306	41/41	262/265	1.00
Admission diagnoses				
Pneumonia (including COVID-19)	355 (58.3%)	45 (54.9%)	310 (58.8%)	
COPD/asthma exacerbation	131 (21.5%)	20 (24.4%)	111 (21.1%)	
Pulmonary vascular diseases	19 (3.1%)	2 (2.4%)	17 (3.2%)	0.74
Other respiratory diseases	48 (7.9%)	5 (6.1%)	43 (8.2%)	
Cardiovascular diseases	56 (9.2%)	10 (12.2%)	46 (8.7%)	
Delay between hospital admission and initiation of automated O_2 titration, hours	0 [0, 1]	0 [0, 1]	0 [0, 1]	0.16
O_2 flow, L/min	2 [1, 3]	2 [1, 3]	2 [1, 3]	0.52
Duration of hospitalization, days	9 [6, 15]	10 [6, 16]	9 [5, 15]	0.29
Clinical deterioration*, n (%)	96 (15.8%)	16 (19.5%)	80 (15.2%)	0.33

Data are mean ± SD or median [25th and 75th interquartile range].
*Clinical deterioration: requirement for high nasal flow oxygen and/or transfer to the intensive care unit.

Table 4. Prescribed SpO_2 targets in 387 subjects on the respiratory ward, COVID-19 unit and emergency room

	Respiratory ward n = 178	COVID-19 unit n = 59	Emergency room n = 150
SpO_2 88 to 90 %	154 (86.5%)	42 (71.2%)	110 (73.3%)
SpO_2 91 to 92 %	23 (12.9%)	16 (27.1%)	34 (22.7%)
$SpO_2 \geq 93\%$	1 (0.6%)	1 (1.7%)	6 (4.0%)

Abbreviation: SpO_2; O_2 pulsed saturation. Data represents the number of subjects (%).

Table 5. SpO_2 data in 82 admissions on the respiratory ward, COVID-19 unit and emergency room

	Respiratory ward (n = 38)	COVID-19 unit (n = 9)	Emergency room (n = 35)
Recording time (hours)	27.5 [10.1, 78.8]	29.1 [20.9, 49.2]	5.4 [3.4, 10.3]
% recording time with SpO_2 signal (%)	89.3 ± 8.7	95.9 ± 2.4	92.3 ± 9.9
Mean O_2 flow (L/min)	2.4 ± 1.7	2.0 ± 0.6	2.3 ± 2.2
Mean SpO_2 (%)	89.2 ± 1.2	90.0 ± 0.9	89.8 ± 1.8
% Time in the SpO_2 target zone	88.7 ± 1.0	89.5 ± 0.9	89.4 ± 1.7
% Time with SpO_2 below 85%	4.0 ± 3.3	1.2 ± 0.8	3.2 ± 5.1
% Time with SpO_2 ≥ 98%	0.5 ± 1.2	0.1 ± 0.1	1.2 ± 2.6
% Time with SpO_2 below 3 to 5% of SpO_2 target	4.7 ± 3.2	3.2 ± 1.8	5.5 ± 6.7
% Time with SpO_2 above 3 to 5% of SpO_2 target	11.5 ± 8.3	9.3 ± 6.2	7.9 ± 8.1

Data are median [25th and 75th interquartile range] or mean ± SD.
Abbreviation: SpO_2; O_2 pulsed saturation.