Oxygen Conservation Methods With Automated Titration

Stéphane Bourassa, Pierre-Alexandre Bouchard, Marc Dauphin, and François Lellouche

BACKGROUND: Oxygen titration is recommended to avoid hyperoxemia and hypoxemia. Automated titration, as well as the S_{pO_2} target, may have an impact on oxygen utilization, with potential logistical effects in emergency and military transportation. We sought to assess the oxygen flow required for different S_{pO_2} targets in spontaneously breathing subjects, and to evaluate individualized automated oxygen titration to maintain stable oxygenation in subjects with COPD and healthy subjects with induced hypoxemia. METHODS: In the first part of the study, oxygen flow was evaluated in hospitalized subjects for different S_{pO_2} targets from 90% to 98%. Oxygen requirements to reach these targets were determined using a device that automatically adjusts oxygen flow every second on the basis of the S_{pO_2} target. In the second part of the study, the same automated oxygen titration method was used to correct hypoxemia in subjects with COPD and in healthy subjects with induced hypoxemia while the subjects wore a gas mask. Oxygen flow, S_{pO_2}, and heart rate were continuously recorded. RESULTS: Thirty-six spontaneously breathing hospitalized subjects were included in the first part of the study. Oxygen flow was reduced more than 6-fold when the S_{pO_2} target was decreased from 98% to 90%. The second part of the study included 15 healthy and 9 subjects with stable COPD. In healthy subjects, heterogeneous oxygen flows were required to correct induced hypoxemia (0.2–2.5 L/min). In subjects with COPD, oxygen flow varied from 0 L/min (in 9 of 18 tested conditions) to 2.9 L/min. CONCLUSIONS: Significant reductions in the amount of oxygen delivered could be obtained with optimized S_{pO_2} targets. Oxygen delivery through a gas mask to correct hypoxemia is feasible, and automated oxygen titration may help individualize oxygen administration and reduce oxygen utilization. (ClinicalTrials.gov registration: NCT02782936, NCT02809807.) *Key words: gas exchange; hypoxemia; gas mask; protective respiratory devices; chemical; biological; radiological; nuclear and explosives; automated oxygen titration; $FreeO_2$.* [Respir Care 2020;65(10):1433–1442. © 2020 Daedalus Enterprises]

Introduction

Modern continuous oxygen therapy on the battlefield to treat injuries caused by chlorine gas during the First World War was described by Haldane over a century ago.[1,2] The amount of oxygen delivered was already a major concern.[3,4] Oxygen is frequently used to correct hypoxemia, defined in the latest guidelines as a $S_{pO_2} < 90\%$ for the general population and $< 88\%$ for COPD patients,[5,6] in military and non-military settings.[5-19] In 2015, Johannigman et al[12] reported that 90% of military subjects experienced at least one desaturation event with an $S_{pO_2} < 90\%$ and that more than half of the subjects had S_{pO_2} values $< 85\%$ during aeromedical evacuations. Numerous studies have highlighted the

Mr Bourassa, Mr Bouchard, and Dr Lellouche are affiliated with the Centre de Recherche de l'Institut Universitaire de Cardiologie et de Pneumologie de Québec, Université Laval, Québec City, Québec, Canada. Dr Dauphin is a Retired Officer of the Royal Canadian Medical Service. Dr Dauphin is the Former Commanding Officer of NATO Role 3 Afghanistan in 2009, NATO Multi-National Kandahar Hospital. Mr Bourassa is a PhD Candidate in Experimental Medicine, Montréal University, Faculty of Medicine, Montréal, Canada. Mr Bourassa is a Retired Officer of the Canadian Armed Forces Intelligence Services.

Dr Lellouche is co-inventor of the $FreeO_2$ system and co-founder of Oxynov, a company that develops automated respiratory support systems; no support was received from this company for the study. The other authors have disclosed no conflicts of interest.

Correspondence: François Lellouche MD PhD, Centre de Recherche de l'Institut Universitaire de Cardiologie et de Pneumologie de Québec, 2725 Chemin Sainte-Foy, Québec City, Québec G1V 4G5, Canada. E-mail: francois.lellouche@criucpq.ulaval.ca.

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requirement for accurate oxygen administration to avoid both hypoxemia and hyperoxemia. In the latest guidelines, hyperoxemia is defined as an $S_{pO_2} > 94\%$ for the general

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population and > 92% for patients with COPD.[5-9,11-17,19] An S_{pO_2} target of 88–92% reduced mortality in patients with respiratory distress in comparison with current practices of an S_{pO_2} frequently > 92% and oxygen flows ranging from 8 to 15 L/min.[8,9,10,15,19] In most cases, the frequent liberal use of oxygen leads to detrimental consequences,[6,7,9,11,14,17,19-22] particularly in patients with trauma or respiratory distress and during myocardial infarction.[5,9,21-23]

Safety as well as logistical issues are relevant to oxygen administration in emergency transportation and in military medical facilities.[9,14,15] As an example, oxygen containers and oxygen-generation equipment were estimated to be between 15% and 30% of the logistics footprint of a deployed combat medical asset.[13,14] In Operation Iraqi Freedom alone, it is estimated that 90 tons of compressed oxygen were required each month.[14]

Closed loops to titrate F_{IO_2} in mechanically ventilated military subjects have been evaluated, and reports suggest that oxygen delivery may be reduced.[13,14] A device that automatically adjusts oxygen flow based on a selected S_{pO_2} target (FreeO$_2$, Oxynov, Canada) has been developed for civilian use and may also be useful for the military.[24-30] The first objective of this device is to avoid hypoxemia and hyperoxemia.[24-28,30]

In this study, we evaluated different strategies to reduce oxygen flow by lowering S_{pO_2} targets, as well as the utilization of automated oxygen titration rather than continuous oxygen flows.

QUICK LOOK

Current knowledge

Oxygen is a vital support for many patients, both in hospitals and outside hospitals. During emergency transportation and for military use, there are health and logistical issues related to the management of oxygen resources. Although conservative administration of oxygen is recommended due to its toxicity, there are no data evaluating the potential for reducing the quantity of oxygen delivered with these new recommendations.

What this paper contributes to our knowledge

We used an automated oxygen-titration device to accurately quantify the gain in oxygen savings with different strategies. By decreasing the S_{pO_2} target from 98% to 90% in hospitalized subjects receiving oxygen, the oxygen flow was reduced > 6-fold. By individualizing oxygen flows with automated titration in subjects with desaturation when a gas mask was worn, further significant reductions in the amounts of oxygen delivered were achieved in comparison with usual protocols to correct hypoxemia with continuous oxygen flow.

Methods

This study evaluated 2 methods to reduce oxygen delivery: lowering the S_{pO_2} target, and automated oxygen titration rather than fixed continuous oxygen flows (Fig. 1). The study was conducted in two parts and involved human subjects (individuals with COPD and healthy participants); both parts were approved by the Ethics Review Board of the Quebec Heart and Lung University Institute Research Center. All subjects signed an informed consent form prior to their inclusion in the study. In each phase, a device (FreeO$_2$, Oxynov, Quebec, Canada) that automatically titrates oxygen flow from 0–20 L/min with steps of 0.1 L/min was used to achieve the set S_{pO_2} targets.[27] This device has been described in several studies.[24-28,30,31]

Part 1: Evaluation of Oxygen Utilization Based on S_{pO_2} Targets

This phase was conducted at the Quebec Heart and Lung University Institute and included hospitalized subjects receiving oxygen therapy via nasal cannula. Several categories of subjects were included: patients with COPD exacerbation, patients with pneumonia, and patients with various conditions requiring oxygen supplementation. All subjects were clinically stable. Oxygen flow was evaluated at steady state for each subject for different S_{pO_2} targets set on the FreeO$_2$ device. S_{pO_2} targets were set at 90%, 92%, 94%, 96%, 98%, then 96%, 94%, 92%, and 90%. Steady state was defined as a stable S_{pO_2} with values within ± 1% of the set S_{pO_2} target for 2 min. Data on O_2 flow, S_{pO_2}, and heart rate were reported by the FreeO$_2$ device every second and were recorded to be used for computations. Oxygen flow at steady state (in 2-min durations) was averaged for each S_{pO_2} step.[4,29,30]

Part 2: Individual Oxygen Needs With Automatic Titration of Oxygen Flows

We evaluated individual oxygen requirements with and without gas masks, which were used to induce desaturation as previously shown, both in healthy subjects with induced hypoxemia and in subjects with COPD. In the masked

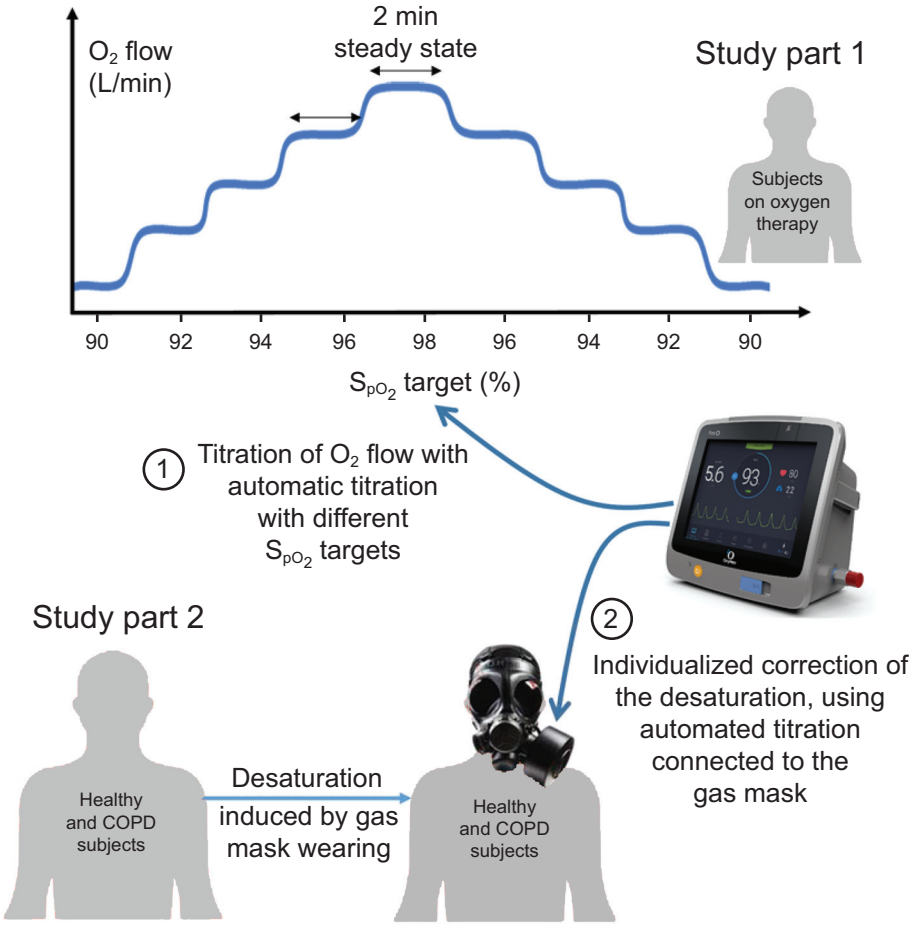

Fig. 1. Summary of the methodology used to estimate the reduction in the amount of oxygen delivered with automated oxygen titration. Study part 1 ($n = 36$ hospitalized subjects receiving oxygen therapy): O_2 flow was determined at steady state for different S_{pO_2} targets with automated oxygen titration. The S_{pO_2} targets set on the automated oxygen titration device were increased from 90% to 98% and then decreased from 98% to 90%. The mean oxygen flow was computed within 2 min at steady state defined by a S_{pO_2} value at target ± 1%. A graph of typical variations in the oxygen flows with the various levels of S_{pO_2} set is shown. Study part 2 ($n = 15$ healthy subjects and 9 subjects with COPD): Individualized oxygen flows were delivered with automated oxygen titration in healthy subjects with induced hypoxemia and in subjects with COPD wearing gas masks (leading to hypoxemia). At baseline, the S_{pO_2} was > 90%. With gas masks, all subjects experienced moderate desaturation, and oxygen therapy was administered with an automated oxygen titration device set to maintain the baseline S_{pO_2}.

conditions, all subjects wore the C4 gas mask (Airboss, Bromont, Canada). The second part of the study is a combination of supplementary material coming from 2 previous studies that investigated the physiological impact of gas masks in healthy subjects and in subjects with COPD.[29,30]

Healthy subjects were included if no significant disease was diagnosed. Three 10-min randomized conditions were tested: induced hypoxemia with and without a mask, and corrected hypoxemia with a mask (using automated oxygen titration with the S_{pO_2} target set at 96%). A 10-min washout period was observed after each condition. Hypoxemia was induced using a mixture of air and nitrogen, which resulted in a breathed F_{IO_2} of 14%, a model previously used.[27] The mixture generated moderate desaturations in a range estimated between 87% and 95%.

Subjects with COPD were walk-in patients, had a FEV_1 in the 30–80% range, and did not require long-term oxygen therapy. We evaluated three 10-min randomized testing conditions at rest: without a gas mask; with a gas mask mounted with cartridge filter A (3.5 cm H_2O, at 1 L/s); with a gas mask mounted with cartridge filter B (2.2 cm H_2O, at 1 L/s).

Data Collected

For tested conditions in both parts of the study, the O_2 flow, S_{pO_2} and heart rate were continuously monitored with the oximeter embedded in the $FreeO_2$ device (OEM III oximetry module from Nonin), which provided data every second. Spirometry and basic demographic data were

Table 1. Demographic Data

	n	Age, y	Male Gender	FEV_1, % of Predicted	FEV_1, L	FVC, L	FEV_1/FVC	Body Mass Index, kg/m^2	Baseline Flow, L/min
Part 1									
All	36	68 ± 13	21 (58)	44 ± 19	1.0 ± 0.5	2.0 ± 0.7	40 ± 28	30 ± 12	2.8 ± 1.5
COPD	16	74 ± 8	9 (56)	41 ± 17	0.9 ± 0.4	2.0 ± 0.7	47 ± 14	29 ± 9	2.4 ± 1.1
Pneumonia	7	67 ± 18	5 (71)	40 ± 15	1.1 ± 0.4	2.4 ± 0.5	31 ± 20	24 ± 5	3.2 ± 1.7
Other	13	63 ± 14	7 (54)	53 ± 24	1.3 ± 0.6	1.7 ± 0.9	35 ± 41	33 ± 17	3.1 ± 1.5
Part 2									
Healthy subjects*	15	38 ± 6	13 (92)	111 ± 14	4.4 ± 0.8	5.7 ± 0.9	76 ± 5	26 ± 4	0
COPD*	9	69 ± 4	7 (87.5)	47 ± 14	1.3 ± 0.6	3.3 ± 1.6	44 ± 7	31 ± 8	0

Values are presented as mean ± SD or *n* (%).
* Breathing room air.

collected from each subject after enrollment to establish a baseline. We compared the oxygen flow with automated titration to the flow recommended in several protocols using normal manual oxygen titration. Our hypothesis of a flow between 3 L/min and 10 L/min is based on the literature for prehospital management and may be conservative in comparison with other protocols and current practice.[7,11,17,19]

The outcome criteria for Part 1 were savings in oxygen delivery with different S_{pO_2} targets (ie, 90%, 92%, 94%, 96%, and 98%); the outcome criteria for Part 2 included savings in oxygen delivery in subjects wearing a gas mask with an automated oxygen titration in comparison with different constant oxygen flows (ie, 2.5, 5, 10, and 15 L/min).

Statistical Analysis

For each part of the study, biostatistics tests were conducted to compare the oxygen flow for the different S_{pO_2} targets and the O_2 titrated flow; the one used at various standard usual O_2 flows of 2.5–15 L/min was based on published data and recommendations.[7,11,17,19]

Data were expressed using mean ± SD or median (interquartile range) to summarize subject characteristics. Continuous measurements obtained at different target levels were analyzed with a mixed model. A linear mixed model was fitted to compare 5 different S_{pO_2} targets (90%, 92%, 94%, 96%, and 98%) measured on the same subject using a repeated-measure factor and an autoregressive covariance matrix because correlation decreases as percentages between observations increase. Because data are correlated, a transformation (Cholesky factorization) was performed on the error distribution from the statistical model to verify the normality assumption with the Shapiro-Wilk tests. The Brown and Forsythe variation of the Levene statistical test was used to verify the homogeneity of variances. A posteriori comparison was performed with a Tukey comparison. Oxygen flow with gas mask data were analyzed with a Student *t* test to compare with a reference value (ie, 2.5, 5, 10, and 15 L/min). The results were considered significant with P values $< .05$. All 6 analyses were conducted using the R 3.2 (R Foundation for Statistical Computing, Vienna, Austria) and SAS 9.4 (SAS Institute, Cary, North Carolina).

Results

Populations

The characteristics of the studied populations are summarized in Table 1. In the first part of the study, 36 hospitalized subjects were included: 16 with COPD, 7 with pneumonia, and 13 with miscellaneous main diagnosis (7 with pulmonary fibrosis, 4 with obesity hypoventilation syndrome, 1 with cystic fibrosis, and 1 with acute coronary syndrome on oxygen therapy). The mean age of the subjects was 68 y, and the baseline oxygen flow was 2.8 L/min.

In the second part of the study, 15 healthy subjects (mean age 38 y) and 9 outpatients with COPD (mean age 69 y; none received oxygen supplementation at baseline) were enrolled. One healthy subject was excluded due to vasovagal shock.

Oxygen Flow Delivered for Various S_{pO_2} Targets

In the first part of the study, oxygen requirements increased > 6-fold based on prescribed S_{pO_2} targets ranging from 90% to 98% (Table 2, Figure 2). The impact of the S_{pO_2} targets on O_2 flow was the most marked in subjects with COPD (Table 2).

Individual Oxygen Flow Delivered With Automated Oxygen Titration

In the second part of the study, we evaluated the variability of oxygen administration through the gas mask. The oxygen flow needed to correct induced hypoxemia varied widely among healthy subjects (Figure 3) and among those with stable COPD (Table 3 and Figure 4).[7]

Table 2. Oxygen Flow Linked to Different S_{pO_2} Targets (Study Part 1)

	n	S_{pO_2} Targets					Ratio 98%/90%	Ratio 94%/90%
		90%	92%	94%	96%	98%		
All	36	0.8 ± 1.0	1.6 ± 1.0	2.8 ± 2.0	4.0 ± 1.9	4.8 ± 1.7	6.2	3.5
COPD	16	0.5 ± 0.6	1.4 ± 1.1	2.4 ± 1.8	4.0 ± 2.2	5.2 ± 1.9	10.0	4.7
Pneumonia	7	1.4 ± 1.4	1.7 ± 1.0	3.7 ± 3.1	4.4 ± 2.1	5.5*	3.9	2.6
Other	13	0.9 ± 1.1	1.1 ± 1.3	2.7 ± 1.3	4.0 ± 1.6	4.5 ± 2.2	5.0	3.0

Values are presented as mean ± SD. Mean oxygen flows used at steady state for the various S_{pO_2} targets and populations are displayed. The ratio of oxygen delivery savings with S_{pO_2} at 90% in comparison to 98% and 94% are indicated. For the whole population, a reduction of the mean S_{pO_2} from 98% to 90% would reduce oxygen use by a factor of 6.2.
* Extrapolated value based on a conservative linear relationship.

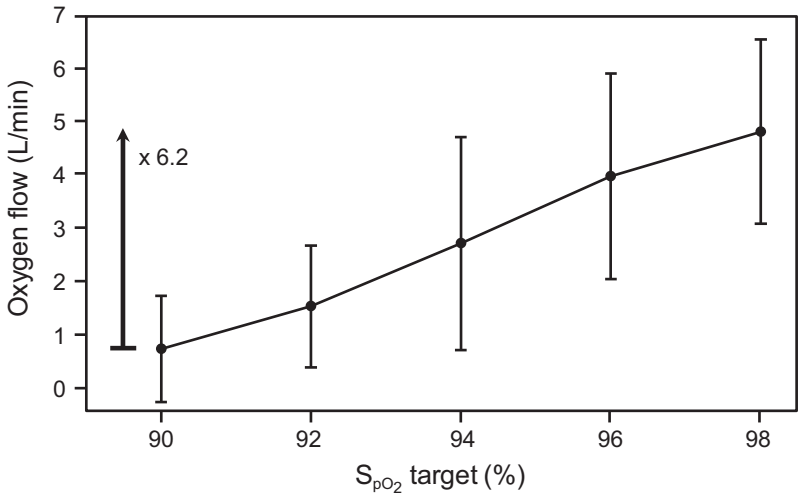

Fig. 2. Oxygen flows administered in relation to S_{pO_2} prescribed targets ($n = 36$ subjects) in part 1 of the study. In all included subjects, for each S_{pO_2} target (90–98%), the oxygen flow provided with automated oxygen titration after 2 min of steady state were collected. Values are presented as mean ± SD. All comparisons were statistically significant when analyzing increasing flow/S_{pO_2} or when analyzing decreasing flow/S_{pO_2}.

We induced moderate hypoxemia in healthy subjects. Mean steady state S_{pO_2} values (ie, the last 2 min of the recordings) during tested conditions were as follows: 88 ± 1% (hypoxemia without masks); 89 ± 0% (hypoxemia with masks), and 95 ± 1% (corrected hypoxemia with masks) (Figure 5). In healthy subjects, the highest O_2 flow necessary for the correction of induced hypoxemia was approximately 2.5 L/min (Figure 3).

Only 4 of the 9 subjects with COPD required oxygen supplementation while wearing the gas mask (Figure 4). Compared to the oxygen supplementation usually recommended in protocols to correct hypoxemia (with constant oxygen flows of 2.5–15 L/min), automatic oxygen titration allowed a significant reduction in oxygen flow (Table 3).

Discussion

In this study, we showed 2 methods that could lead to significant reductions in the amount of oxygen delivered: (1) the utilization of a lower S_{pO_2} target from 98% to 90% allowed a reduction in oxygen delivery by a factor of 6; (2) the utilization of automated oxygen titration to individualize oxygen administration led to significant oxygen savings by a factor from 6 to 35 in comparison with the protocols of constant oxygen administration. These strategies, used separately or in combination, may have a significant impact on the logistical burden related to oxygen stocks and on oxygen costs.

Impact of the S_{pO_2} Target on Oxygen

Depending on the population studied, the reduction of the S_{pO_2} target from 98% to 90% allowed a reduction of the oxygen flow by a factor of 4 to 10. The highest S_{pO_2} level we tested in the study was 98%, which is not recommended in the general population but is frequently encountered in patients managed during transport and in the health care system.[6,19] In contrast, the lowest tested S_{pO_2} level (ie, 90%) is recommended for patients with COPD and for populations at risk of hypercapnia.[5,18] With the exception of

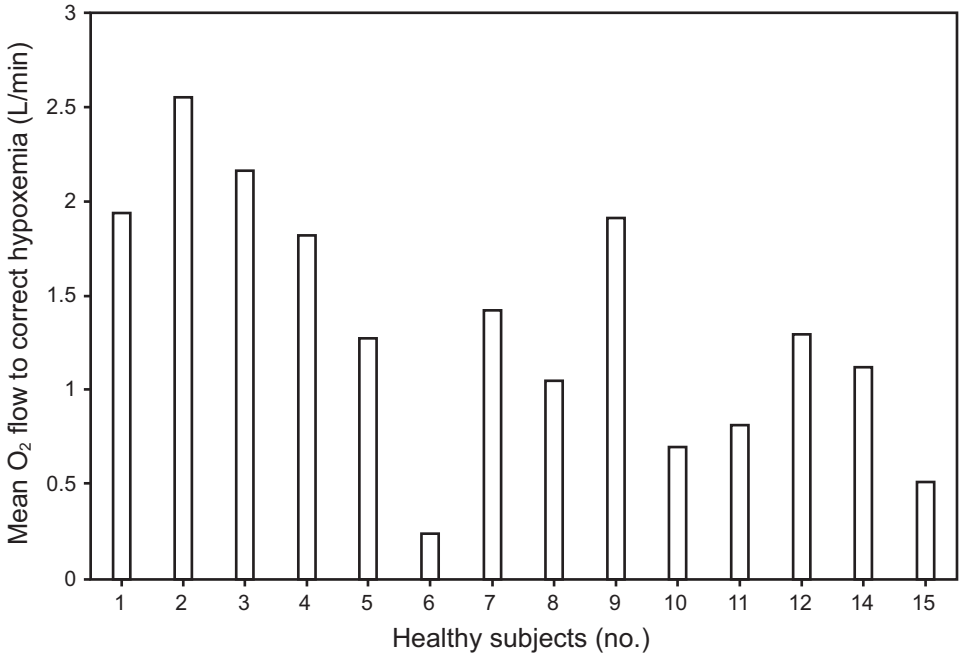

Fig. 3. Mean individualized oxygen flow delivered in a 10-min duration to correct induced hypoxemia (ie, healthy subjects wearing a gas mask connected to an automated oxygen titration device set to maintain S_{pO_2} at 96%) in part 2 of the study. For a similar target S_{pO_2}, the oxygen needs varied widely by a factor of 10 between the subject with the highest oxygen needs (subject 2) and the subjects with the lowest oxygen needs (subject 6).

brain trauma patients, this level and even lower S_{pO_2} targets could probably be adequate for several populations, especially for short-distance transportations.[32] Indeed, "permissive hypoxemia" strategies have been discussed in specific situations.[20] Very low S_{pO_2} are frequently encountered at altitude, and S_{pO_2} targets between 88% and 95% are recommended in mechanically ventilated patients with ARDS.[12,33] Although not recommended for all patients due to the lack of data, it was previously reported that moderate hypoxemia is safe for short-term exposure, even in the case of critically ill patients with septic shock.[34] There are mechanisms to compensate for acute hypoxemia and avoid cell hypoxia, such as increased cardiac output, vasodilatation, reduced cellular metabolism, and long-term mechanisms such as increased hemoglobin concentration.[20,21,35] In studies of healthy subjects breathing 7% oxygen, leading to a P_{aO_2} of 34 mm Hg (around 65% S_{pO_2}), minor electroencephalogram abnormalities (ie, slowing without seizures) were detectable in 2 of 7 subjects.[9,11,19,36] However, even if moderate hypoxemia (around 85% S_{pO_2}) might be well tolerated, there is no currently clear evidence to recommend it.

With a pulse oximetry saturation target of 90%, the volume of oxygen provided to the patient could be reduced. This amount could be further reduced when the pulse oximetry saturation target is lowered to approximately 86%.[6] Mild hypoxemia does not induce long-term damage when a patient's arterial oxyhemoglobin saturation is approximately 86%. The effects of the hypoxemia on cognition are well known and are related to acute and severe hypoxemia.[37] However, with moderate desaturation values close to 86%, as measured with S_{pO_2}, no major deleterious effects were present, even in subjects diagnosed with COPD.[38,39]

Impact of Automated Oxygen Titration

Automated oxygen titration allows for the individualized adjustment of oxygen flow, which is useful due to large variations in the patient requirements. In this study, the oxygen flow was reduced by a factor of 12–23 in comparison to constant flows of 5–10 L/min, which are frequently used in patients managed for hypoxemia during transport. Instead of fixed, and usually high, oxygen flows, which are used in many emergency transport protocols, automated titration optimizes oxygen administration and avoids needlessly high flows. Even within protocols and studies, compliance with the reduction of oxygen flow to attain S_{pO_2} targets of 88–92% was low.[5,7,18,40]

We previously reported that, in subjects with COPD, S_{pO_2} targets of 88–92% were reached only in 10% of the cases treated in emergency transportation for acute respiratory failure.[31] This is in line with several studies conducted in different countries. Many users do not believe in oxygen toxicity, and the changes are difficult to implement in clinical practice.[5,8,18] In clinical evaluations with automated oxygen titration, S_{pO_2} targets set as recommended were attained 80–95% of the time.[25-27,31]

Table 3. Ratio of Oxygen Savings With Titrated O_2 Compared to Constant O_2 Flows

Subject	Titrated O_2 Flow, L/min*	Constant O_2 Flow, L/min			
1A	0.3	2.5	5.0	10	15
2A	0.4	2.5	5.0	10	15
3A	0	2.5	5.0	10	15
4A	1.7	2.5	5.0	10	15
5A	2.9	2.5	5.0	10	15
6A	0.2	2.5	5.0	10	15
7A	0	2.5	5.0	10	15
8A	0	2.5	5.0	10	15
9A	0	2.5	5.0	10	15
1B	0	2.5	5.0	10	15
2B	0.4	2.5	5.0	10	15
3B	0	2.5	5.0	10	15
4B	1.5	2.5	5.0	10	15
5B	0	2.5	5.0	10	15
6B	0.2	2.5	5.0	10	15
7B	0.2	2.5	5.0	10	15
8B	0	2.5	5.0	10	15
9B	0	2.5	5.0	10	15
Mean ± SD	0.4 ± 0.8**	2.5 ± 0.0**	5.0 ± 0.0**	10.0 ± 0.0**	15.0 ± 0.0**
Ratio of oxygen savings with titrated O_2 compared to constant O_2 flows		5.9	11.8	23.5	35.3

Subjects wore a gas mask with one of two different cartridge filters (A or B) with individualized O_2 flow to maintain baseline S_{pO_2} with automated oxygen titration or different constant oxygen flows of 2.5, 5.0, 10, or 15 L/min used in protocols to manage hypoxemia or respiratory distress. The ratio of oxygen savings is the ratio of oxygen flow delivered at different constant flows to the oxygen flows with titrated O_2. For example, this ratio at a constant O_2 flow of 2.5 L/min is 5.9 (ie, 2.5/0.4), ie, with automated titration set for a patient with COPD and a target S_{pO_2} of 90%, the oxygen use would be reduced by a factor of 5.9 compared to a protocol with a constant oxygen flow of 2.5 L/min.

* With $FreeO_2$ and individualized S_{pO_2} targets.

** $P < .001$ for comparisons with titrated oxygen flow.

In several publications, automated oxygen titration reduced oxygen requirements by 44% in mechanically ventilated subjects and by 2-fold in spontaneously breathing subjects.[13,25] In our study, automated oxygen titration reduced oxygen requirements by a factor of 6–35 when compared with a constant oxygen flow of 2.5–15 L/min.

Impact on Trauma and Medical Evacuation

It is well accepted that hypoxemia with desaturation < 90% is a factor associated with poor outcomes in patients with brain trauma and hypotension.[32] In this situation, especially when shock is present, it may not be recommended to target S_{pO_2} levels < 90% to reduce oxygen utilization as the treatment of hypoxemia should remain the first objective. However, high S_{pO_2} levels (ie, > 94%) may not be desirable in trauma with shock.[41] The systematic delivery of oxygen with an S_{pO_2} target of 95% or above relies on very little data.[42] In an animal study of blast injury with hemorrhagic shock and saline resuscitation, one group of pigs breathed air while the other group received oxygen to maintain $S_{pO_2} > 95\%$.[42] Survival was significantly increased in the group managed with oxygen; in the control group, however, the desaturation was very low ($S_{pO_2} < 70\%$).[42] That study confirmed that very severe desaturation is bad when associated with shock, but this does not provide insight into the optimum S_{pO_2} target in such situations.[43] In a recent systematic review, authors did not find sufficient evidence to determine the optimal oxygenation target in trauma patients. However, they concluded that conservative use of oxygen was associated with similar or better outcomes in critically ill subjects.[43]

Cost and Logistical Impacts Prehospital and in Military Operations

Since the first medical use of oxygen, logistical issues have been raised, and users initially had to produce their own gas.[3,4] Currently, utilization of oxygen in hospitals has been facilitated by the unrestricted availability of medical oxygen in most developed countries. There were some examples of oxygen shortages, such as the unfortunate story of an interrupted oxygen supply leading to > 100 deaths in an Indian hospital.[44] Outside hospitals, logistics in transport and on the battlefield remain daily challenges. In many hostile environments where military conflicts may arise, it may be demanding to supply caregivers with oxygen, hence the more liberal use of oxygen concentrators. Although it is impractible to have combat medics carry oxygen cylinders, most armed forces command authorities ensure that their evacuation vehicles are equipped with O_2 administration equipment. In recent conflicts, however, evacuation has at times been prolonged, sometimes up to 25 h and up to several days.[45,46] In the case of prolonged evacuations, maximum oxygen savings may be vital to complete medical tasks that require an oxygen supply throughout.

Where military conflicts arise, it may be complicated to supply medical theater facilities and caregivers with an adequate supply of oxygen, hence the more liberal use of oxygen concentrators, even at level I medical theater facilities. But because war trauma is generally more severe than civilian trauma, with injury severity scores almost always > 15–20 and often in the > 50 range, and tends to occur in groups of individuals, most militaries make herculean efforts to supply oxygen.

Impact of Oxygen Use in Chemical, Biological, Radiological, Nuclear and Explosives Medical Evacuation

The literature has remained vague regarding the use of oxygen in casualties exposed to weapons of mass

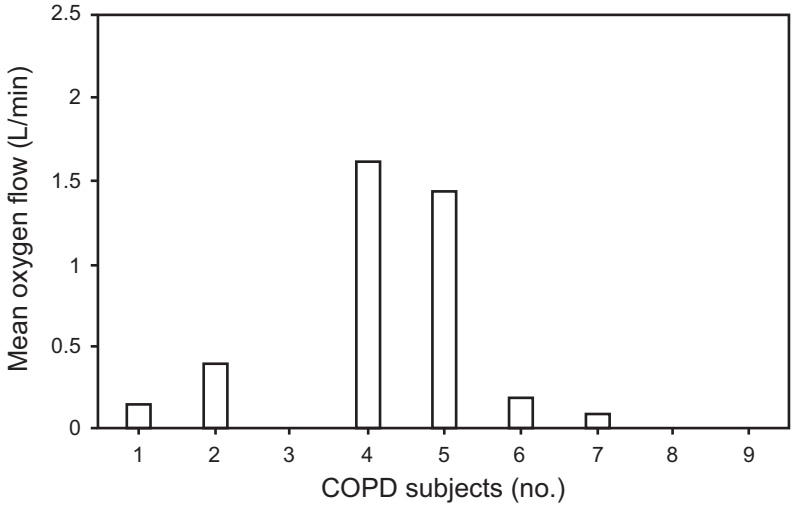

Fig. 4. Mean individualized oxygen flow for all COPD subjects wearing a gas mask (study part 2). Oxygen was administered through the mask with an automated titration device to maintain the initial S_{pO_2} value when subjects were breathing ambient air without a gas mask. Different oxygen flows were required to correct desaturation when a gas mask was worn.

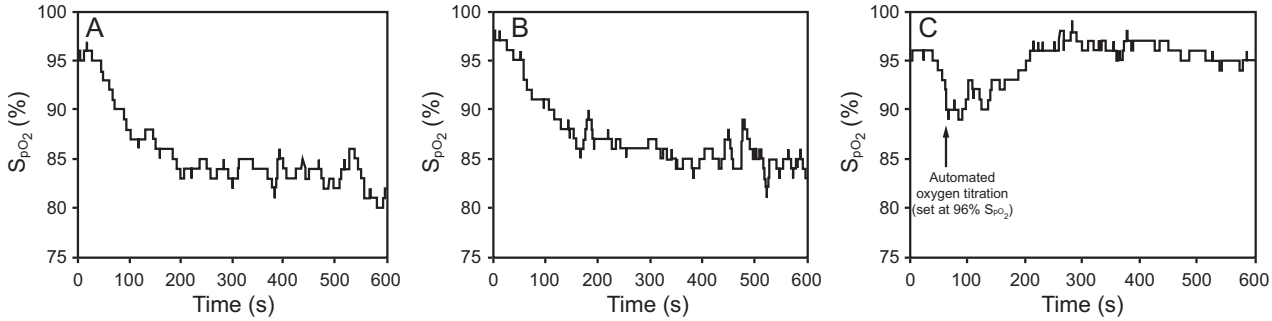

Fig. 5. Representation of the S_{pO_2} (%) in all the tested conditions in 14 healthy subjects. Induced hypoxemia (A) without a gas mask and (B) with a gas mask; (C) corrected hypoxemia with automated oxygen titration (with the S_{pO_2} target set at 96%) through a gas mask. The entire 600-s duration was recorded for each tested condition (10 min; data shown from subject 3).

destruction. It is primarily the National Association of Emergency Medical Technicians that recommends the use of high oxygen flows without providing any ranges of values according to the type of exposure, nor any specification for an S_{pO_2} target. To our knowledge, there is only one ongoing study, a systematic review of chemical exposure in subjects with ARDS during evacuations, that is evaluating these types of details during oxygen delivery (https://www.crd.york.ac.uk/prospero/display_record.php?recordid=104473; ClinicalTrials.gov registeration: CRD42019104473, *accessed May 8, 2019*). The second part of our study presents additional data for controlling S_{pO_2}, correcting hypoxemia, and administering oxygen safely in both healthy and COPD subjects wearing a gas mask with an automated oxygen titration system attached. The results of part 2 of this study pave the way for further medical research in the field of chemical, biological, radiological, nuclear, and explosives defense, particularly with the use of automated systems and oxygen administration through gas masks.

Study Limitations

The data were obtained in experimental conditions in a research laboratory (for induced hypoxemia) and in a hospital setting as opposed to data military operations, which could not have been obtained. However, our data indicate that the results of a reduction of the oxygen requirements along with a lowering of the S_{pO_2} targets are generalizable.

Estimates of oxygen savings with automated titration have been made under conditions that may be different from military operations, but in our view they are nevertheless relevant to military operations. The comparison of different S_{pO_2} targets indicated oxygen savings of a factor of 4–10 in hospitalized subjects under oxygen therapy when comparing 90% and 98% S_{pO_2} targets. In addition, automated individualized titration of oxygen was compared with constant flows

arbitrarily selected from 2.5 to 15 L/min, with savings ranging from a factor of 6 for the former to 35 for the latter. This comparison is artificial, but the values of constant oxygen flow are to be compared with the protocols used in each center. In emergency transport, the oxygen flows used are often close to 10 L/min, and some military guidelines even recommend flows approaching 15 L/min.[10] Nevertheless, in view of recent recommendations, the trend should be toward a more restrictive use of oxygen.

The description of the relationship between oxygen flow and oxygenation parameters is not new, nor is it surprising. Campbell described this relationship almost 60 years ago.[22] However, to our knowledge, there is no study that has accurately evaluated the possible reduction in the amount of oxygen delivered with different S_{pO_2} targets at steady state. The utilization of automated oxygen titration allowed this evaluation simply by varying the selected S_{pO_2} target and recording the mean oxygen flow required for various specific targets.

Conclusions

Our results indicate that different strategies may significantly reduce oxygen use. The reduction of the S_{pO_2} targets has a major impact on oxygen savings, and the needs may easily be reduced by a factor of 3–10. The individualization of oxygen delivery with automated titration rather than a constant oxygen flow delivery may also reduce the global needs. These findings may have a significant impact in specific situations. Oxygen usage is a major logistical issue; this is particularly true for emergency transport as well as in a military setting.

We also successfully explored an innovative approach to providing oxygen therapy to chemical, biological, radiological, nuclear, and explosives casualties, which we hope will help rekindle interest in further research in clinical practice and advance scientific knowledge in this field. These innovative solutions in administering oxygen have the potential to optimize the practice of this pivotal life-support measure.

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