

# Liberal Versus Conservative Oxygen Therapy's Effectiveness And Safety In Critically Ill People; Systematic Review

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## Abstract

**Background:** Adult patients experiencing acute illness are frequently given large doses of supplemental oxygen, yet the validity of the supporting data is questionable. We conducted a thorough analysis comparing the safety and effectiveness of liberal and conservative oxygen treatment for critically ill adults.

**Method:** Without regard to language, we searched the Cochrane, MEDLINE, and Embase databases from 2011 to 2016 for randomized controlled trials that contrasted the use of liberal and conservation oxygen therapy in critically ill individuals for this systematic review. Database searches were complemented by checking the reference lists of pertinent papers and reviews. PRISMA guidelines were adhered to.

**Results and conclusion:** This systematic review includes 5 randomized controlled trials that were carried out in Italy, Sweden, France, Australia, New Zealand, and the United Kingdom. Research focused on individuals suffering from traumatic brain damage, cardiac arrest, myocardial infarction, and intensive care unit admission. There is insufficient evidence to justify the regular use of oxygen in individuals who have myocardial infarction and are not suffering from severe hypoxia or cardiogenic shock at the time of presentation. In the pre-hospital context, titrating oxygen administration to SpO<sub>2</sub> after cardiac arrest resuscitation was not practical. After arriving at the hospital, titrating oxygen can be an option. Patients with head trauma can have better results if they get normobaric oxygen treatment during the first six hours following the incident.

**Keywords:** Liberal oxygen therapy, conservative oxygen therapy, effectiveness, safety, critically ill adult

## Introduction

In acute care, oxygen was initially mentioned as a therapy in 1885 (1). Supplemental oxygen is routinely given to critically ill patients in modern clinical practice—roughly 34% of patients in ambulances, 25% of people in emergency departments (2), and 15% of patients admitted to hospitals in the UK. Due to attempts to avoid or correct hypoxaemia, 50–84% of patients in these settings are exposed to excess oxygen and

hyperoxaemia(3). Furthermore, regardless of the existence or absence of hypoxaemia, a large number of medical professionals view supplementary oxygen as a safe and perhaps helpful treatment (4).

The potential negative effects of excessive oxygen supplementation, such as absorption atelectasis, inflammatory cytokine production, acute lung injury, central nervous system toxicity, and reduced cardiac output, are becoming more and more of a concern, even though adequate oxygen delivery is necessary to treat hypoxaemia(5,6).

There is a lack of solid data to support recommendations (7,8) on the use of extra oxygen for different acute diseases in adults. Furthermore, despite the completion of several randomised controlled studies contrasting liberal and conservative oxygen therapy for a range of acute illnesses, the trial results have not been combined. Two systematic reviews (9,10) serve as examples: they both concentrated only on patients with critical illness, failed to find any pertinent randomized controlled trials, and had significant heterogeneity and bias risk in their meta-analyses of observational data. Therefore, the main goal of our research was to thoroughly examine randomized controlled studies that looked at the safety and effectiveness of liberal vs conservative oxygen therapy for individuals who were critically ill.

## Method

Without regard to language, we searched the Cochrane, MEDLINE, and Embase databases from 2011 to 2016 for randomized controlled trials that contrasted the use of liberal and conservation oxygen therapy in critically ill individuals for this systematic review. In addition to database searches, relevant papers and reviews' reference lists were examined. Research that reported an interesting outcome and compared liberal and conservative oxygenation techniques in critically ill individuals were included in the analysis. Any ailment that required a non-elective hospital hospitalization and the possibility of being exposed to extra oxygen was considered acute illness. We used admittance to an intensive care unit as our definition of serious illness.

Titles and abstracts of chosen papers were screened by four writers, each working independently. Disputes about inclusion were settled by consensus. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (11) is followed in the reporting of this study. Each author used a pre-made data-form on a Google sheet to extract data in team work to avoid information missing or duplication. Mortality and morbidity were the relevant outcomes.

## Result and discussion

We included 5 randomized controlled trials in this systematic review study, studies were conducted in Sweden, France, Australia, New Zealand, Iran and UK. Studies targeted patients with myocardial infarction, patients in intensive care unit and those with cardiac arrest and traumatic brain injury. According to Panwar et al. study, no noticeable variances occurred between the groups for any metrics linked to new organ failure, ICU mortality, or 90-day mortality. The percentage of time with SpO<sub>2</sub> less than 88% was 1% compared to 0.3% in the conservative vs. liberal arm, whereas the percentage of time with SpO<sub>2</sub> higher than 98% was 4% compared to 22%. The adjusted hazard ratio for 90-day mortality in the conservative arm was 0.77 overall and 0.49 in the predefined subgroup of patients whose baseline PaO<sub>2</sub>/FiO<sub>2</sub> was less than 300.

Supplemental oxygen is widely used in standard practice, according to a number of observational studies conducted in various critical care settings in recent years(12). The oxygenation levels attained in the study's liberal arm were comparable to those previously documented by other observational studies in conventional practice. On the other hand, the liberal arm's proportion of time spent in hyperoxia was less than previously documented (13). The only research that has compared a conservative oxygenation aim to standard practice is a single-center prospective before-and-after feasibility study (14).

A cautious oxygenation technique was linked to a decreased frequency of new organ dysfunction in the before-and-after trial (14). On the other hand, none of the indicators of new organ dysfunction showed any significant between-group differences in the Panwar et al. investigation. While there was no difference in the length of vasopressor therapy or days without vasopressor use across the groups in the Panwar et al. research, the liberal oxygenation arm required a lower vasopressor dosage. The vaso-constrictor impact of greater oxygenation levels, which has been previously described for several vascular beds (15), might be one reason for this observation.

Numerous observational studies showed that in some subgroups of critically ill patients, arterial hyperoxia was associated with increased mortality(10).In vitro, short-term exposure to high levels of normobarichyperoxia reduces the production of cytokines by human leukocytes(16) and causes structural alterations in alveolar macrophages, leading to a notable decrease in the macrophages' ability to fight microbes and a notable reduction in the amount of inflammatory cytokines they produce in response to stimulation(17,18). In a pneumonia animal model, mice subjected to normobarichyperoxia showed markedly higher rates of mortality and infection spread in the lung and spleen as compared to infected mice kept in room air(19).

Pulmonary toxicity induced byHyperoxiaresult in histopathologic alterations comparable to those reported in ARDS and ventilator-induced lung damage (20).

An assessment of the consequences of normobarichyperoxia in individuals with severe TBI was conducted by Taher et al. According to the results of their study, oxygen treatment with the mechanical ventilator in the first 6 hours after tracheal intubation in severe TBI patients can enhance the final GOS; this could also improve the long term prognosis of these patients.

The observed normobarichyperoxia may be a reflection of the main trauma-related therapeutic intervention (21). Numerous studies have revealed a significant death rate among patients with severe TBI; Raj et al. reported a mortality rate of around 39%, whereas Rockswold et al. investigation found a rate of 42% (21,22). However, as was observed in earlier published research (23,24), Raj et al. discovered that the addition of hyperoxia resulted in a considerable relative risk decrease for death (21).

It has been shown that normobarichyperoxia is helpful in maintaining cerebral perfusion pressure, and controlling intracranial pressure. Retaining cerebral oxygenation levels between 20 and 25 mmHg has been associated with lower death rates and better therapeutic outcomes. In the first 24 to 48 hours following an accident, the danger of inadequate brain oxygen is at its highest. Up until patients are admitted to the ICU for the installation of intrusive neurocritical care monitoring systems, the emergency department's use of oxygen with a high FIO<sub>2</sub> can be effective in treating TBIs. In order to avoid low brain oxygen levels, the proportion of inspired oxygen levels must be titrated (25,26).

In a multicenter feasibility trial, Young et al.(27) compared titrated oxygen treatment to conventional oxygen therapy for patients receiving cardiopulmonary resuscitation following cardiac arrest. Regarding the ICU phase of treatment, their results are in line with those of another research in a general ICU population which found that aiming for a SpO<sub>2</sub> of 90 to 92% was safe and did not appear to increase the incidence of hypoxaemia episodes(14).Thirteen Despite being in the titrated treatment arm and having three individuals with confirmed SpO<sub>2</sub> <88% in the ICU, Young et al.(27)small sample size meant that there was no statistically significant increased risk of hypoxaemia. Recent evidence indicates that controlling carbon dioxide levels may have an impact on how well people who have had cardiac arrest recover(28).

A research by Ranchord et al. found no compelling evidence to support the regular oxygen treatment in individuals who have myocardial infarction that is not accompanied by cardiogenic shock or significant hypoxia at the time of presentation. Multicenter randomized controlled studies with enough power to ascertain whether the two treatments have a clinically meaningful impact on mortality are highly recommended. Ranchord et al. agree with the recent oxygen guidelines recommendation that supplemental oxygen should not be routinely administered to patients with acute chest pain of suspected cardiac origin. Instead, it should be limited to patients in whom hypoxia is present, with oxygen saturation monitored and used to guide its administration. This recommendation is contingent upon the outcome of such studies (29).

**Table 1: characteristics and main findings of the included studies**

Citation	Country	Study setting	Sample size	Study main findings
Taher et al.(30)	Iran	Traumatic brain injury	68	The ultimate GOS, Barthel index, and mRS scores of patients with severe traumatic brain injury can be improved by oxygen treatment administered by mechanical ventilator during the first six hours of damage, according to the study's findings. Additionally, it could raise quality of life, rehabilitation, and long-term results.
Khoshnood et al.(31)	Sweden	Myocardial infarction	160	Despite being a common element of treatment, oxygen therapy may not be helpful or perhaps dangerous for patients with Myocardial infarction.
Panwar et al.(32)	France Australia new Zealand	Critical care unit	104	No discernible variations were between the groups for any metrics related to new organ dysfunction, ICU mortality, or 90-day mortality. In the conservative vs liberal arm, the proportion of time with SpO <sub>2</sub> less than 88% was 1% against 0.3%, while the percentage of time with SpO <sub>2</sub> more than 98% was 4% compared 22%. In the conservative arm, the adjusted hazard ratio for 90-day death was 0.49 in the predetermined subgroup of patients whose baseline PaO <sub>2</sub> /FiO <sub>2</sub> was less than 300, and 0.77 overall.
Ranchord et al. (33)	UK New Zealand	Myocardial infarction	148	The high-concentration and titrated oxygen groups had 1.5% and 2.9% fatalities, respectively; a meta-analysis combining these data with those from the two earlier investigations revealed an odds ratio of 2.2 for high-concentration oxygen mortality relative to room air or titrated oxygen. When comparing high-concentration to titrated oxygen, there was no discernible change in troponin T, infarct mass, or infarct mass percentage.
Young et	New	Cardiac	17	Titrated oxygen treatment group SpO <sub>2</sub>

al. (27)	Zealand	arrest		levels were lower than standard care group during the pre-hospital interval. Seven out of eight patients in the titrated oxygen group and three out of nine patients in the conventional care group had low measured oxygen saturation. After being admitted to the hospital, the groups' oxygen exposure was well separated, and the number of hypoxic incidents did not significantly rise. The Data Safety Monitoring Board and Management Committee decided that safe administration of titrated oxygen treatment in the pre-hospital period was not practicable based on gathered data, which led to the trial's termination.
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### Conclusion

There is insufficient evidence to justify the regular use of oxygen in individuals who have myocardial infarction and are not suffering from severe hypoxia or cardiogenic shock at the time of presentation. In the pre-hospital context, titrating oxygen administration to SpO<sub>2</sub> after cardiac arrest resuscitation was not practical. After arriving at the hospital, titrating oxygen can be an option. Patients with head trauma can have better results if they get normobaric oxygen treatment during the first six hours following the incident.

### Abbreviation

GOS, Glasgow outcome scale

TBI, traumatic brain injury

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