Apneic oxygenation during intubation in the emergency department and during retrieval: A systematic review and meta-analysis

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ABSTRACT

Background: Hypoxemia increases the risk of intubation markedly. Such concerns are multiplied in the emergency department (ED) and during retrieval where patients may be unstable, preparation or preoxygenation time limited and the environment uncontrolled. Apneic oxygenation is a promising means of preventing hypoxemia in this setting.

Aim: To test the hypothesis that apnoeic oxygenation reduces the incidence of hypoxemia during endotracheal intubation in the ED and during retrieval.

Methods: We undertook a systematic review of six databases for all relevant studies published up to November 2016. Included studies evaluated apneic oxygenation during intubation in the ED and during retrieval. There were no exemptions based on study design. All studies were assessed for level of evidence and risk of bias. The Review Manager 5.3 software was used to perform meta-analysis of the pooled data.

Results: Six trials and a total 1822 cases were included for analysis. The study found a significant reduction in the incidence of desaturation (RR = 0.76, p = 0.002) and critical desaturation (RR = 0.51, p = 0.01) when apneic oxygenation was implemented. There was also a significant improvement in first pass intubation success rate (RR = 1.09, p = 0.004).

Conclusion: Apneic oxygenation may reduce patient hypoxemia during intubation performed in the ED and during retrieval. It also improves intubation first-pass success rate in this setting.

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1. Introduction

Endotracheal intubation is a life-saving therapy implemented in both the pre-hospital and hospital settings. Though intubation is often considered a routine intervention, it is far from risk-free. Intubation may be particularly troublesome when performed away from the operating room, such as in prehospital or non-critical care based setting, where the support staff may be less experienced, the facilities inadequate and the patient status less stable [1-4].

Apneic oxygenation aims to maintain oxygenation in the absence of patient respiratory effort [2]. The technique was first described in 1959 and uses nasal cannulae to supply high-flow oxygen to the nasopharynx [1,5]. Given a patent airway and minimal cardio-pulmonary shunting, the oxygen may then diffuse into the alveoli and sustain blood oxygenation [5,6].

Apneic oxygenation is of particular interest when considering endotracheal intubation. The enforced apnea during the procedure makes hypoxemia a significant risk [2,7]. Pre-oxygenation - the administration of 100% oxygen for a period prior to intubation – is widely employed to buy time before oxygen desaturation occurs, the so-called safe-apnea time [2]. Despite this, hypoxemia remains a concern and particularly so in the emergency department and during patient retrieval, where patients may be unstable, preparation or pre-oxygenation time limited and the environment uncontrolled [3,5,8-10].

Multiple studies have examined the utility of apneic oxygenation during intubation across an array of clinical settings. Differing protocols and patient groups make comparing these trials error-prone. In order to generate a clinically meaningful analysis for emergency and retrieval specialists, only trials carried out in these settings were included in this meta-analysis. Primarily, the aim of this systematic review and meta-analysis was to assess the effect of apneic oxygenation on hypoxemia (lowest SpO2 and incidence of both desaturation and critical desaturation) during intubation undertaken in the ED and during retrieval. The secondary aim was to investigate the impact of apneic oxygenation on first pass success rate of intubation in these settings.

2. Methods

2.1. Search strategy

Two independent reviewers (RH, LW) systematically searched five databases (SCOPUS, Web of Science, CINAHL, Medline and PubMed)
for articles up to and including the 19th November 2016. Search terms applied were (1) (endotracheal intubation) AND (apneic oxygenation) and (2) (endotracheal intubation) AND (apneic oxygenation). A manual check of reference lists to detect additional studies followed this.

2.2. Inclusion criteria

Articles were included if they assessed the performance of apneic oxygenation during intubation with that of a control group in the pre-hospital or emergency department setting. Two reviewers (RH, LW) independently assessed the papers against these criteria. There were no restrictions on study design.

2.3. Data extraction

Indication for intubation, apneic oxygenation intervention and patient outcomes were extracted. The collected data was then assessed for heterogeneity.

2.4. Outcome measures

The pooled data was analysed for desaturation, incidence of critical desaturation and first-pass successful intubation.

2.5. Definition(s)

Apneic oxygenation: administration of oxygen via nasal cannulae at flow rates of 5–60 L per minute during intubation. Low flow apneic oxygenation: administration of oxygen via nasal cannulae at flow rates of 15 L per minute or less during intubation. High flow apneic oxygenation: administration of oxygen via nasal cannulae at flow rates of 50–60 L per minute during intubation. Desaturation: reduction in oxygen saturations (SpO2) to <93–95% during intubation. Critical desaturation: reduction in oxygen saturations (SpO2) to <80% during intubation.

2.6. Statistical analyses

The combined data was examined using the RevMan 5.3 software (The Nordic Cochrane Centre, Copenhagen, Denmark). Dichotomous outcomes were assessed for relative risk (RR) with 95% confidence interval (CI). The Mantel-Haenszel (M-H) fixed effects model was used. Heterogeneity was assessed by use of $I^2$ and chi squared statistics. Heterogeneity was deemed significant if $I^2 > 50\%$. A p value of <0.05 indicated statistical significance when calculating RR, WMD or $I^2$.

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**Table 1**

<table>
<thead>
<tr>
<th>Study</th>
<th>Study type</th>
<th>Number of patients</th>
<th>Patient group</th>
<th>Nasal prong oxygen intervention (no of pts)</th>
<th>Primary outcome(s)</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sakles et al.[3]</td>
<td>Prospective comparative</td>
<td>635</td>
<td>ED patients</td>
<td>0 L/min (255) 5–15 L/min (380)</td>
<td>1) Desaturation 2) Lowest SpO2 3) First pass success 4) Desaturation 5) Incidence of critical desaturation (SpO2 &lt; 80%)</td>
<td>2</td>
</tr>
<tr>
<td>Sakles et al.[10]</td>
<td>Prospective comparative</td>
<td>127</td>
<td>ED intracranial haemorrhage patients</td>
<td>0 L/min (55) 5–15 L/min (72)</td>
<td>1) Desaturation 2) First pass success 3) Incidence of critical desaturation (SpO2 &lt; 80%)</td>
<td>2</td>
</tr>
<tr>
<td>Wimalasena et al.[7]</td>
<td>Retrospective observational</td>
<td>728</td>
<td>Helicopter emergency medical service</td>
<td>0 L/min (310) 15 L/min (418)</td>
<td>1) Desaturation 2) First pass success 3) Incidence of critical desaturation (SpO2 &lt; 80%)</td>
<td>3</td>
</tr>
<tr>
<td>Caputo et al.[11]</td>
<td>Randomized controlled trial</td>
<td>100</td>
<td>ED patients</td>
<td>0 L/min (50) Intervention rate not specified (50)</td>
<td>1) Desaturation 2) First pass success 3) Incidence of critical desaturation (SpO2 &lt; 80%)</td>
<td>1</td>
</tr>
<tr>
<td>Dyett et al.[12]</td>
<td>Prospective comparative</td>
<td>139</td>
<td>ED patients- subgroups of respiratory failure and non-respiratory failure</td>
<td>0 L/min (92) 15 L/min (47)</td>
<td>1) Desaturation 2) First pass success 3) Incidence of critical desaturation (SpO2 &lt; 80%)</td>
<td>2</td>
</tr>
<tr>
<td>Riyapan et al.[13]</td>
<td>Retrospective comparative</td>
<td>93</td>
<td>Retrieval respiratory failure</td>
<td>0 L/min (39) 15 L/min (14)</td>
<td>1) First pass success 2) Incidence of critical desaturation (SpO2 &lt; 80%)</td>
<td>3</td>
</tr>
</tbody>
</table>

* Level of evidence evaluated with the Centre for Evidence Based Medicine (CEBM): levels of evidence introduction document [14].
3. Results

The initial systematic literature review identified 2011 citations (Fig. 1). This total was filtered by duplicate exclusion and abstract review, yielding 30 trials. Specific inclusion criteria eliminated a further 24 papers during full-text review, leaving 6 articles and a total 1822 cases for analysis [3,7,10-13]. There was one high quality level one randomized controlled trial [11], three low quality level 2 prospective comparative trials [3,10,12], one level 3 retrospective comparative trial [13] and one level 3 retrospective observational trial [7] (Table 1, Fig. 2). The six papers measured three outcomes in total (Table 1).

All but one [13] of the included studies examined the incidence of desaturation when apneic oxygenation was and was not utilized [3,7,10-12]. This outcome showed a significant relative risk reduction (RR = 0.76, 95% CI = 0.60 to 0.90, p = 0.002) with significant heterogeneity (I² = 80%, p = 0.0005) (Fig. 3).

A group of three studies investigated the incidence of critical desaturation during intubation [10,11,13]. Regarding this outcome, there was a significant reduction in relative risk ratio (RR = 0.51, 95% CI = 0.30 to 0.87, p = 0.01) without significant heterogeneity (I² = 43%, p = 0.17) (Fig. 4).

Three studies evaluated the first-pass success rate of intubation [3,10,13]. In this reason there was a significant increase in successful first pass intubation (RR = 1.09, 95% CI = 1.03 to 1.16, p = 0.004) with no heterogeneity (I² = 0%, p = 0.87) (Fig. 5).

4. Discussion

This is the first systematic review and meta-analysis to investigate the use of apneic oxygenation during intubation in emergency department and retrieval patients. The review was tailored to the emergency and retrieval cohort to offer results of clinical relevance to emergency and retrieval specialists. A total of 6 studies were included in this analysis, offering a pool of 1822 patients. Five papers used low flow oxygen at 15 L/min and the sixth did not offer flow rate information [11].

The primary outcome of this systematic review and meta-analysis was the relationship between blood oxygen levels during intubation and the use of apneic oxygenation. Firstly, across the five studies that measured the incidence of desaturation (SpO2 < 93–95%) during intubation, there was a significant improvement in hypoxemia of 3.04% [3,7,10-12]. This result is striking when one considers the sigmoid relationship between blood oxygen levels and haemoglobin saturation. However, the result came with significant heterogeneity between the studies. This was primarily due to the result delivered by Caputo et al. (2016), which showed a significantly increased rate of hypoxemia. Unfortunately, these were interim results from a published abstract, making comparison of the methodology and analysis with other studies difficult. The other measure of hypoxemia in this analysis, the rate of critical desaturation, was studied by three trials [10,11,13]. According to these findings, the risk of critical desaturation was halved (RR = 0.51, p = 0.01) in these trials when apneic oxygenation was employed [3,7,10,11].

It may be hypothesized that the additional clutter of high flow nasal cannulae would complicate the process of intubation. Three studies evaluated the first-pass intubation success rate in patients with and without apneic oxygenation [3,10,13]. The meta-analysis revealed a significant increase in first pass success rate (RR = 1.09, p = 0.004) with no heterogeneity. This result potentially reflects the prolonged safe apnea time offered by apneic oxygenation and the additional time allowed to locate the epiglottis and laryngeal vestibule. Knowledge of this supplementary time may also help to reassure and steady a practitioner faced with an emergent intubation.

5. Limitations

This study is limited by a relatively small patient pool (n = 1822) that was spread across patient outcomes that were inconsistently assessed. The included studies included a single randomized controlled trial (abstract only) and were predominantly level 2 prospective cohort studies, limiting their internal validity. The necessary brevity of Caputo et al.’s [11] abstract and its subsequent lack of details regarding study design make it difficult to analyse. This is poignant given it was the sole outlier in the analysis of incidence of desaturation.

![Fig. 3. Incidence of desaturation with (n = 967) and without (n = 762) apneic oxygenation during intubation.](image)

![Fig. 4. Incidence of critical desaturation (Sp02 < 80%) with (n = 151) and without (n = 169) apneic oxygenation during intubation.](image)
Study protocols differed in their methods of pre-oxygenation, with some employing positive pressure ventilation. Accordingly, baseline alveolar recruitment will have varied.

The lack of analysis of all-cause 30-day mortality in the included studies is an important oversight, but an understandable one given patient flow from the emergency department and retrieval.

6. Conclusions

This study found a significant improvement in blood oxygenation during intubation in the emergency department and during retrieval when apneic oxygenation is used. Employing the technique may reduce the incidences of both desaturation and critical desaturation. The meta-analysis also found a significant improvement in successful first-pass intubation when using apneic oxygenation. Despite these promising results, apneic oxygenation in the ED and retrieval scenarios is in need of further investigation. Future high quality randomized controlled trials using standardized outcomes will help to bolster the results of this study.

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Ethics

No ethics approval required.

References