Intubation using apnoeic oxygenation to prevent desaturation: A systematic review and meta-analysis

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Abstract

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Purpose: To determine whether or not apnoeic oxygenation reduces the incidence of hypoxaemia during endotracheal intubation.

Materials and methods: A systematic search of six databases for all relevant studies until November 2016 was performed. All study designs using apnoeic oxygenation during intubation were eligible for inclusion. All studies were assessed for level of evidence and risk of bias. A meta-analysis was performed on all data using Revman 5.3.

Results: Seventeen studies including 2422 patients were retrieved. Overall there was a significant reduction in the incidence of desaturation (RR = 0.65; p < 0.00001), critical desaturation (RR = 0.61; p = 0.002) and safe apnoea time (WMD = 1.73 min; p < 0.00001). There was no significant difference in mortality (RR = 0.77; p = 0.08).

Conclusions: In patients whom are being intubated for any indication other than respiratory failure, apnoeic oxygenation at any flow rate 15 L or greater is likely to reduce their incidence of desaturation (~90%) and critical desaturation (~80%). However, further high quality RCTs are required given the high degree of heterogeneity in many of the outcomes and subgroup analyses.

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Intubation
Desaturation

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1. Introduction

Endotracheal intubation, a life-saving intervention, is a commonly used procedure in the operating theatre (OT), emergency department (ED), and the intensive care unit (ICU) [1]. Whilst endotracheal intubation is seen as a regular intervention, in certain circumstances the procedure can potentially be high-risk, especially if performed outside of an OT [1,2].

Hypoxaemia is often seen to be one of the most significant complications that can arise during endotracheal intubation [1,3], and has been strongly associated with cardiac arrest and death in critically ill patients [3]. Hypoxaemia can be ameliorated by providing pre-oxygenation prior to or during endotracheal intubation. This has been established to result in a prolonged ‘safe apnoea time’ – a term used to describe a period of time before a patient undergoes critical arterial desaturation [1]. However, this has been shown to be significantly less effective when applied to a critically ill population [4].

Apnoeic oxygenation, a technique first devised in 1959 [5], aims to prevent hypoxaemia from occurring during endotracheal intubation. The technique involves providing a constant stream of oxygen via nasal cannulae during intubation or any period of apnoea. If a patent upper airway is present, and there is an absence of pulmonary shunting, this prolonged oxygenation is theorised to facilitate mass diffusion of gas from the pharynx to the alveoli, thereby providing an increased volume of oxygen to diffuse into the arterial circulation and delay hypoxaemia [6,7].

Current literature provides numerous studies regarding the use of apnoeic oxygenation during intubation, including several level one randomised controlled trials (RCTs). Despite this, there are currently no systematic reviews or meta-analyses on the topic. We hypothesise that apnoeic oxygenation will reduce the incidence of desaturation during intubation. The primary aim of this systematic review and meta-analysis was to investigate whether or not apnoeic oxygenation is shown to reduce the incidence of hypoxaemia (incidence of desaturation, lowest SpO2 and critical desaturation) during endotracheal intubation. The secondary aims included determining the effect of apnoeic oxygenation during intubation on safe apnoea times, adverse outcomes during intubation and longer term outcomes such as duration of ventilation and mortality.

2. Methods

2.1. Search strategy

Five databases (CINAHL, SCOPUS, PubMed, Medline and Web of Science) were systematically searched up to and including 19th November 2016. Search terms were determined using the key words included in several of the large studies on this topic. Two independent reviewers (RH, LW) searched the databases using the terms (1) (apnoeic oxygenation) AND (endotracheal intubation); (2) (apnoeic oxygenation) AND (endotracheal intubation). A manual reference check of recent papers was then performed to identify any additional studies. There were no language restrictions.

2.2. Inclusion criteria

For a study to be included, the study was required to compare apnoeic oxygenation during intubation to a control group included. Two reviewers (RH, LW) assessed each study for inclusion in this systematic review. All study designs were eligible for inclusion.

2.3. Data extraction

Data from studies that met the inclusion criteria were extracted. This included the indication for intubation, apnoeic oxygenation intervention and clinical outcome results. The data collected by each reviewer was then assessed for homogeneity.

2.4. Outcome measures

Data extracted from each included paper was grouped into outcomes for analysis. This included both short and medium-to-long-term outcome measures. The short term outcomes included measures of desaturation during intubation, lowest measured SpO2 during intubation, critical desaturation during intubation, time to desaturation and resaturation, first pass intubation success, intra-procedural arrhythmias and cardiac arrest. The medium-to-long-term outcomes included duration of ventilation, length of ICU stay and mortality.

2.5. Definition(s)

Low Flow Apnoeic Oxygenation: oxygen delivered via nasal cannulae at flow rates of 15 L/min or less during the period of intubation.

High Flow Apnoeic Oxygenation: oxygen delivered via nasal cannulae at flow rates of 50 to 60 L/min during the period of intubation.

Desaturation: a decrease in oxygen saturation (SpO2) during intubation to <93–95%.

Critical Desaturation: a decrease in oxygen saturation (SpO2) during intubation to <80%.

Safe Apnoea Time: duration of apnoea without desaturation.

Mortality: death during ICU admission or within 28 days of intubation.

2.6. Sensitivity analysis

Where possible data was subdivided into indication for intubation; respiratory failure and other indications. Within these two indications, where possible, data was grouped into low flow and high flow apnoeic oxygenation.
2.7. Statistical analyses

The combined data were analysed using RevMan 5.3 software (The Nordic Cochrane Centre, Copenhagen, Denmark). The relative risk (RR) with 95% confidence interval (CI) for dichotomous outcomes, and the weighted mean difference (WMD) with 95% CI for continuous outcomes. Heterogeneity was assessed using the chi squared and I² statistic, with an I² > 50% indicating significant heterogeneity. p value of <0.05 provided evidence of statistically significant RR, WMD or I².

3. Results

3.1. Literature search results

The systematic literature search yielded 2011 citations, 15 additional citations were identified on manual reference check. Of these 2011 citations, 1033 duplicates were removed, leaving 978 available citations. Sixty-eight article abstracts were retrieved for review based on their title mentioning apnoeic oxygenation and intubation. Of the 68 abstracts reviewed, 30 mentioned apnoeic oxygenation during intubation. The full texts of these 30 articles were reviewed. Of these 30 articles, 17 met the inclusion criteria, i.e. intubations were performed with both a control group (no apnoeic oxygenation) and an intervention group (apnoeic oxygenation during intubation) (Fig. 1). These 17 studies included 2422 patients (Table 1). Each study was then screened for risk of bias (Fig. 2) without heterogeneity (I² = 0% (p = 0.55) (Table S1).

3.2. Primary outcomes

3.2.1. Desaturation

Eight studies measured incidence of desaturation (n = 1895) [2-4, 7-10]. Overall there was a significant reduction with apnoeic oxygenation (RR = 0.65, 95%CI = 0.55 to 0.77, p < 0.00001). There was however significant heterogeneity (I² = 64%, p = 0.007). On subgroup analysis of patients intubated for reasons other than respiratory failure with low flow oxygen (n = 1795), the risk reduction and heterogeneity remained significant (Table S1). Apnoeic oxygenation consistently (I² = 0%) had no effect (p = 0.61) on respiratory failure patients (Table S1).

3.2.2. Lowest SpO2

Eight studies investigated lowest SpO2 (n = 645), demonstrating a significantly higher lowest SpO2 (WMD = 3.28, 95%CI = 2.89 to 3.67, p < 0.00001) [4,7,11-16]. There was significant heterogeneity within the group (I² = 83%, p < 0.00001; Fig. 3). On subgroup analysis of respiratory failure patients the benefit of apnoeic oxygenation remained significant (p < 0.00001), as did the heterogeneity (I² = 88%). The same trend was shown in the subgroup analysis of patients intubated for other indications with a significant improvement (p < 0.00001) and an I² of 78% (Fig. 3; Table S1).

3.2.3. Critical desaturation

Eight studies measured incidence of critical desaturation (n = 728) [8,10-12,14-17]. Overall there was a significant reduction in the incidence of SpO2 < 80% (RR = 0.61, 95%CI = 0.44 to 0.84, p = 0.002; Fig. 4) without heterogeneity (I² = 0%, p = 0.14). When divided into indication for intubation the effect became non-significant for the respiratory failure (p = 0.13) group, but remained significant for other indication (p = 0.003) group (Fig. 4; Table S1).

3.3. Secondary outcomes

3.3.1. Safe apnoea time

Three studies (n = 94) investigated safe apnoea time in patients intubated for reasons other than respiratory failure using low flow oxygen [7,9,18]. With apnoeic oxygenation there was a significant increase in safe apnoea time of 1.73 min (95%CI = 1.50 to 1.97, p < 0.00001) without statistically significant heterogeneity (I² = 63%, p = 0.07).

3.3.2. PaO2 at 3–4.5 min

Two studies measured the PaO2 at 3–4.5 min post apnoea for indications other than respiratory failure (n = 74) [19,20]. Overall there was a significant difference (WMD = 95.67, 95%CI = 55.14 to 136.20, p < 0.00001) with no significant heterogeneity (I² = 0%, p = 0.55) (Table S1).

3.3.3. Resaturation time

Two studies investigated resaturation time (n = 758) [3,7], showing a significant reduction with apnoeic oxygenation (WMD = −66.55, 95%CI = −95.10 to −38.10, p < 0.00001) with no heterogeneity (I² = 0%, p = 0.33). Both studies were intubation for indications other than respiratory failure (Table S1).

3.3.4. First pass success

Seven studies (n = 1901) [3,4,8,11,14,16,17] showed statistically significant improvement in first pass success without heterogeneity (RR = 1.06, 95%CI = 1.02 to 1.10, p = 0.006) without heterogeneity (I² = 0%, p = 0.81). On subgroup analysis the improved first pass intubation rate remained for the patients intubated for reasons other than respiratory failure (p = 0.005; Table S1). The respiratory failure group showed no effect (p = 0.95; Table S1).

Fig. 1. Literature search and screening process.
<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>Studies of non-respiratory failure patients</td>
<td>RCT</td>
<td>34</td>
<td>Elective gastric surgery patients</td>
<td>0 L/min (17)</td>
<td>1) Safe apnoea time</td>
<td>1</td>
</tr>
<tr>
<td>Baraka et al. (2007) [9]</td>
<td>RCT</td>
<td>41</td>
<td>Elective healthy surgical patients</td>
<td>0 L/min (14)</td>
<td>1) Partial pressure of arterial oxygen at 4.5 min of apnoea</td>
<td>1</td>
</tr>
<tr>
<td>Christodoulou et al. (2013) [19]</td>
<td>RCT</td>
<td></td>
<td></td>
<td>0 L/min (11)</td>
<td>1) Partial pressure of arterial oxygen at 3 min of apnoea</td>
<td>2</td>
</tr>
<tr>
<td>Lee (1998) [20]</td>
<td>RCT</td>
<td>46</td>
<td>Elective healthy surgical patients</td>
<td>0 L/min (23)</td>
<td>1) Safe apnoea time</td>
<td>1</td>
</tr>
<tr>
<td>Ramachandran et al. (2009) [7]</td>
<td>RCT</td>
<td>30</td>
<td>Elective obese surgical patients</td>
<td>0 L/min (15)</td>
<td>2) Desaturation</td>
<td>2</td>
</tr>
<tr>
<td>Sakles et al. (2016a) [4]</td>
<td>Prospective comparative</td>
<td>635</td>
<td>ED patients</td>
<td>0 L/min (255)</td>
<td>4) Resaturation time</td>
<td>2</td>
</tr>
<tr>
<td>Sakles et al. (2016b) [8]</td>
<td>Prospective comparative</td>
<td>127</td>
<td>ED intracranial haemorrhage patients</td>
<td>0 L/min (55)</td>
<td>5) Short term mortality</td>
<td>1</td>
</tr>
<tr>
<td>Semler et al. (2016) [14]</td>
<td>RCT</td>
<td>150</td>
<td>ICU patients</td>
<td>0 L/min (73)</td>
<td>6) Length of ICU stay</td>
<td>1</td>
</tr>
<tr>
<td>Taha et al. (2005) [18]</td>
<td>RCT</td>
<td>30</td>
<td>Elective healthy surgical patients</td>
<td>0 L/min (15)</td>
<td>7) Short term mortality</td>
<td>1</td>
</tr>
<tr>
<td>Wimalasena et al. (2015) [3]</td>
<td>Retrospective observational</td>
<td>728</td>
<td>Helicopter emergency medical service</td>
<td>0 L/min (310)</td>
<td>8) Length of ICU stay</td>
<td>1</td>
</tr>
<tr>
<td>Studies of respiratory failure patients</td>
<td>Prospective cohort</td>
<td>52</td>
<td>ICU-respiratory failure</td>
<td>0 L/min (39)</td>
<td>9) Length of ICU stay</td>
<td>1</td>
</tr>
<tr>
<td>Besnier et al. (2016) [10]</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)</td>
<td>10) Length of ICU stay</td>
<td>1</td>
</tr>
<tr>
<td>Dyett et al. (2015) [2]</td>
<td>Prospective comparative</td>
<td>47</td>
<td>ICU-respiratory failure</td>
<td>0 L/min (24)</td>
<td>11) Length of ICU stay</td>
<td>1</td>
</tr>
<tr>
<td>Jaber et al. (2016) [11]</td>
<td>RCT</td>
<td></td>
<td></td>
<td>0 L/min (24)</td>
<td>12) Length of ICU stay</td>
<td>1</td>
</tr>
<tr>
<td>Miguel-Montanes et al. (2015) [12]</td>
<td>Prospective cohort 'quasi-experimental'</td>
<td>101</td>
<td>ICU-respiratory failure</td>
<td>0 L/min (50)</td>
<td>13) Length of ICU stay</td>
<td>1</td>
</tr>
<tr>
<td>Riyapan et al. (2016) [17]</td>
<td>Retrospective comparative</td>
<td>93</td>
<td>Retrieval respiratory failure</td>
<td>0 L/min (39)</td>
<td>14) Length of ICU stay</td>
<td>1</td>
</tr>
<tr>
<td>Simon et al. (2016) [15]</td>
<td>RCT</td>
<td>40</td>
<td>ICU-respiratory failure</td>
<td>0 L/min (24)</td>
<td>15) Length of ICU stay</td>
<td>1</td>
</tr>
<tr>
<td>Vourc’h et al. (2015) [16]</td>
<td>RCT</td>
<td>118</td>
<td>ICU-hypoxaemic respiratory failure</td>
<td>0 L/min (57)</td>
<td>16) Length of ICU stay</td>
<td>1</td>
</tr>
</tbody>
</table>

* Level of Evidence assessed using the Centre for Evidence Based Medicine (CEBM): Levels of evidence introduction document.
3.3.5. SpO2 at 5 and 30 minutes post intubation

From two studies of respiratory failure patients (n = 148), there was no significant difference in SpO2 with apnoeic oxygenation measured at 5 min (n = 148, WMD = 0.00, 95%CI = −0.08 to 0.08, p = 0.99) [11, 12] and 30 min (n = 148, WMD = 0.00, 95%CI = −0.07 to 0.07, p = 0.99) [11,12] post intubation (Table S1).

3.3.6. Arrhythmia and cardiac arrest during intubation

In the four studies investigating arrhythmia during intubation (n = 210) [7,11,12,18], no difference was demonstrated (RR = 0.58, 95%CI = 0.08 to 4.29, p = 0.60, I2 = 0%). Three studies (n = 180) showed no difference in the incidence of cardiac arrest during intubation (RR = 0.33, 95%CI = 0.01 to 7.84, p = 0.49) [7,11,12]. There was no heterogeneity in either outcome (I2 = 0% in both).

3.3.7. Duration of ventilation, ICU stay and mortality

Duration of ventilation was measured by two studies (n = 268) [14, 16], showing no significant difference (WMD = −1.97, 95%CI = −5.89 to 1.95, p = 0.32) with significant heterogeneity (I2 = 98%, p < 0.00001). Two studies (n = 199) investigated length of ICU stay showing a significant reduction (WMD = −2.88, 95%CI = −3.25 to −2.51, p < 0.00001) with significant heterogeneity (I2 = 96%, p < 0.00001) [11,14]. Finally, four studies (n = 419) assessed mortality [11,12,14,16], showing a non-significant reduction with apnoeic oxygenation (RR = 0.77, 95%CI = 0.59 to 1.03, p = 0.08) with no significant heterogeneity (I2 = 0%, p = 0.83). On subgroup analysis for respiratory failure, there was no effect on mortality (RR = 0.85, 95%CI = 0.56 to 1.27, p = 0.42, I2 = 0%).

4. Discussion

This is the most comprehensive review to date, combining seventeen studies and 2422 patients. These studies took place in a variety of settings including the intensive care unit, emergency department, operating theatres and out-of-hospital retrieval. Indications for intubation were subdivided into respiratory failure or other. To satisfying inclusion criteria, studies had to compare either apnoeic oxygenation to a control group during intubation. They could utilise low-flow (≤15 L/min) or high-flow (50–60 L/min) apnoeic oxygenation. Our systematic review reveals increasing interest in this field, with many recent publications adding knowledge to this pertinent area.

Overall our literature review revealed that of the seventeen included studies, eleven studied the effects of low-flow nasal cannulae oxygen with the remaining six examining high-flow technologies. Broadly the studies who’s patient cohort were in primary respiratory failure examined the use of high-flow nasal oxygen, whilst those studying other indications for intubation studied lower flow rates (Table 1). This may reflect discussions in the literature that in those patients with primary respiratory failure, passive ventilation is less likely to be effective given the potential for severe pulmonary circulatory shunting to be present [4]. This theory might render higher flow rates with some end-expiratory pressure more effective.

This review supports the notion that the use of apnoeic oxygenation reduces the risk of desaturation during intubation (RR = 0.65). This effect was observed in those patients who were intubated for ‘other’ indications, and there was no significant benefit in those with respiratory failure. Heterogeneity was largely limited to the effect size, rather than the absence of any effect. The variable definitions of ‘desaturation’ between groups are likely to have contributed to this; European groups tended to define an SpO2 of <92–93% as desaturation, whilst American groups were more likely to use 90% as their limit.

In all patient subgroups the use of apnoeic oxygenation significantly increased the lowest recorded SpO2 during intubation (Fig. 3). There was a greater effect seen for respiratory failure patients (WMD +3.72%) than for other indications (WMD +2.97%), however this variation is within confidence interval. This may suggest that whilst apnoeic oxygenation doesn’t prevent desaturation in respiratory failure patients (SpO2 below 90%), it can limit to what extent desaturation occurs. This effect was maintained in both high- and low-flow cannulae subgroups. Again there was significant heterogeneity, largely confined to the magnitude of the effect size, with every study contributing a positive mean difference to some extent.

The use of apnoeic oxygenation also reduced the incidence of critical desaturation events (RR 0.61). This is perhaps the outcome that has most clinically relevance in the included studies; morbidity and mortality has been associated with even brief episodes of desaturation in those who are clinically unwell and have little reserve [1,4,21]. Whilst the incidence of these events did not reach significance in the respiratory failure subgroup, there remains a clear trend toward benefit. Given the low incidence of these events, we felt this simply reflects the subgroup alone being underpowered to detect these relatively uncommon events. Each
subgroup contained ~140 patients receiving apnoeic oxygenation (Fig. 4). This understanding would concur with observation that only one large study included found a significant effect, whilst all others found a non-significant trend in favour of apnoeic oxygenation.

Safe apnoea time, PaO2 after 3–4.5 min and resaturation times were all only measured by studies utilising low-flow oxygen in those with other indications for intubation. Apnoeic oxygenation was associated with significantly prolonged safe apnoea time, higher PaO2 and shorter resaturation times. There was no difference in SpO2 at 5 and 30 min post-intubation, a measure utilised by some studies of respiratory failure patients. All patients had a SpO2 of 100% at these times, suggesting this was not a very discriminative outcome measure.

Few studies reported medium-to-long-term outcome measures. There was no significant difference in duration of ventilation, ICU length of stay or mortality. All of these outcomes were only measured by a small proportion of studies included in our review, with 200–400 patients included. There was however a trend toward reduced mortality overall (RR = 0.77, p = 0.08). This was significantly influenced by the one study in non-respiratory failure patients that measured mortality, which found a relative reduction of 15% [14].

4.1. Limitations

There is the paucity of data available on apnoeic oxygenation during intubation. Despite seventeen studies being found on this topic, they include highly variable patient groups, in an array of clinical settings. Currently, there are not enough studies to allow for appropriate, clinically meaningful subgroup analyses to be performed. In addition to flow

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Apnoeic Oxygenation</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Fixed, 95% CI</th>
<th>Heterogeneity: df = 3 (P &lt; 0.0001); P = 88%</th>
<th>Test for overall effect: Z = 12.03 (P &lt; 0.0001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.9.1 Respiratory Failure</td>
<td>Jaber et al. 2016</td>
<td>98.75</td>
<td>1.25</td>
<td>23</td>
<td>95.75</td>
<td>1.75</td>
<td>24</td>
<td>20.3%</td>
<td>3.00 [2.13, 3.87]</td>
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</tr>
<tr>
<td></td>
<td>Miguel-Montanes et al. 2015</td>
<td>100</td>
<td>1.25</td>
<td>51</td>
<td>94.37</td>
<td>50</td>
<td>12.7%</td>
<td>6.00 [4.91, 7.09]</td>
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</tr>
<tr>
<td></td>
<td>Simion et al. 2016</td>
<td>89</td>
<td>18</td>
<td>20</td>
<td>86</td>
<td>11</td>
<td>20</td>
<td>0.2%</td>
<td>3.00 [2.65, 12.26]</td>
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<tr>
<td></td>
<td>Vourch et al. 2015</td>
<td>91.5</td>
<td>4</td>
<td>62</td>
<td>89.5</td>
<td>3.5</td>
<td>57</td>
<td>8.4%</td>
<td>2.00 [0.05, 3.95]</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>156</td>
<td>41.7%</td>
<td>3.72 [3.11, 4.32]</td>
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</tbody>
</table>

Heterogeneity: Chi² = 25.80, df = 3 (P < 0.0001); P = 88%
Test for overall effect: Z = 12.03 (P < 0.0001)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Apnoeic Oxygenation</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Fixed, 95% CI</th>
<th>Heterogeneity: df = 3 (P &lt; 0.0001); P = 78%</th>
<th>Test for overall effect: Z = 11.39 (P &lt; 0.0001)</th>
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<tr>
<td>1.9.2 Other</td>
<td>Ramachandran et al. 2009</td>
<td>94.3</td>
<td>4.4</td>
<td>15</td>
<td>87.7</td>
<td>9.3</td>
<td>15</td>
<td>0.8%</td>
<td>6.60 [3.19, 11.81]</td>
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<td>0.7</td>
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<td>14.1%</td>
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<td>Sakles et al. 2016</td>
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<td>2.7</td>
<td>73</td>
<td>22.0%</td>
<td>2.00 [1.17, 2.83]</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Semler et al. 2016</td>
<td>93</td>
<td>2.5</td>
<td>77</td>
<td>90</td>
<td>2.67</td>
<td>70</td>
<td>21.7%</td>
<td>3.00 [2.16, 3.84]</td>
<td></td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>175</td>
<td>58.3%</td>
<td>2.97 [2.46, 3.48]</td>
<td></td>
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</tbody>
</table>

Heterogeneity: Chi² = 13.35, df = 3 (P < 0.004); P = 78%
Test for overall effect: Z = 11.39 (P < 0.0001)

| Study or Subgroup | Apnoeic Oxygenation | Events | Total | Control | Events | Total | Weight | Risk Ratio | M.H. Fixed, 95% CI | Risk Ratio | M.H. Fixed, 95% CI | | |
|-------------------|---------------------|--------|-------|---------|--------|-------|--------|------------|-----------------|-------------|-----------------| | |
| 1.16.1 Respiratory Failure | Besnier et al. 2016 | 3 | 13 | 6 | 39 | 3.8% | 1.50 [0.44, 5.16] | | | |
| | Jaber et al. 2016 | 1 | 23 | 5 | 24 | 6.1% | 0.21 [0.03, 1.65] | | | |
| | Miguel-Montanes et al. 2015 | 1 | 51 | 7 | 50 | 8.8% | 0.14 [0.02, 1.10] | | | |
| | Rilayyan et al. 2016 | 5 | 29 | 14 | 64 | 10.9% | 0.79 [0.31, 1.98] | | | |
| | Simon et al. 2016 | 5 | 20 | 5 | 20 | 8.3% | 1.00 [0.34, 2.93] | | | |
| | Vourch et al. 2015 | 15 | 82 | 15 | 58 | 19.7% | 0.90 [0.49, 1.88] | | | |
| Subtotal (95% CI) | 198 | 253 | 55.6% | 0.73 [0.49, 1.10] | | | | | | | | |
| Total events | 30 | 52 | | | | | | | | | | |

Heterogeneity: Chi² = 5.97, df = 5 (P = 0.31); P = 16%
Test for overall effect: Z = 1.50 (P = 0.13)

| Study or Subgroup | Apnoeic Oxygenation | Events | Total | Control | Events | Total | Weight | Risk Ratio | M.H. Fixed, 95% CI | Risk Ratio | M.H. Fixed, 95% CI | | |
|-------------------|---------------------|--------|-------|---------|--------|-------|--------|------------|-----------------|-------------|-----------------| | |
| 1.16.2 Other | Sakles et al. ICH 2016 | 5 | 72 | 15 | 55 | 21.3% | 0.25 [0.10, 0.66] | | | |
| | Semler 2016 | 12 | 77 | 18 | 73 | 23.1% | 0.63 [0.33, 1.22] | | | |
| Subtotal (95% CI) | 149 | 128 | 44.4% | 0.45 [0.27, 0.77] | | | | | | | | |
| Total events | 17 | 33 | | | | | | | | | | |

Heterogeneity: Chi² = 2.41, df = 1 (P = 0.12); P = 58%
Test for overall effect: Z = 2.95 (P = 0.003)

| Study or Subgroup | Apnoeic Oxygenation | Events | Total | Control | Events | Total | Weight | Risk Ratio | M.H. Fixed, 95% CI | Risk Ratio | M.H. Fixed, 95% CI | | |
|-------------------|---------------------|--------|-------|---------|--------|-------|--------|------------|-----------------|-------------|-----------------| | |
| Total (95% CI) | 347 | 381 | 100.0% | 0.61 [0.44, 0.84] | | | | | | | | |
| Total events | 47 | 85 | | | | | | | | | | |

Heterogeneity: Chi² = 10.98, df = 7 (P = 0.14); P = 36%
Test for overall effect: Z = 3.05 (P = 0.002)
Test for subgroup differences: Chi² = 2.05, df = 1 (P = 0.15), P = 51.2%

Fig. 3. Lowest SpO2 during intubation with and without apnoeic oxygenation. Subgrouped into patients intubated for respiratory failure and patients intubated for other reasons.

Fig. 4. Critical desaturation (SpO2 < 80%) during intubation with and without apnoeic oxygenation. Subgrouped into patients intubated for respiratory failure and patients intubated for other reasons.
rate of apnoeic oxygenation and indication for intubation, there are a number of other subgroup analyses which would provide clinical benefit for example, setting of intubation (in-hospital versus out-of-hospital) or use in hypoxic intubation. Furthermore, there is a lack of level one RCTs, which limits the level of evidence that can be attached to our recommendations.

The present study showed a small (6%) but significant increase in first attempt success rate with apnoeic oxygenation. Given that four of the six were low quality cohort studies, this could represent an allocation bias affecting the broader results of this meta-analysis. This reinforces the need for further level one RCTs to be performed.

A large number of outcomes, even at the subgroup analysis level that showed significant heterogeneity. There are several reasons for this. As previously mentioned, the patient population and intubation settings were highly variable between studies and there is potential for significant allocation bias in the low quality studies. There was also a wide variation in the pre-oxygenation protocols. For example, some studies used positive pressure ventilation in the control groups which would likely have provided greater alveolar recruitment at baseline than the intervention group would have received from nasal cannulae pre-oxygenation [10,14]. This would subsequently mask the benefit provided by apnoeic oxygenation. Other studies included patients with inadequate pre-oxygenation whereby patients were hypoxic prior to intubation, and there were significant differences in pre-oxygenation levels between groups [17].

5. Conclusion

In patients whom are being intubated for any indication other than respiratory failure, apnoeic oxygenation at any flow rate 15 L or greater is likely to reduce their incidence of desaturation (<90%). Respiratory failure patients are likely to desaturation below this level despite the interventions examined here. However, the use of apnoeic oxygenation during intubation is associated with increasing the lowest recorded SpO2 by (WMD + 3.49%) for all patients, and is likely to reduce the incidence of critical desaturation events (RR 0.58). These effects are likely preserved in patients with respiratory failure if high-flow nasal cannulae are utilised. However, further high quality RCTs are required given the high degree of heterogeneity in many of the outcomes and subgroup analyses.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jcrc.2017.04.043.

Statement of contribution

All authors contributed significantly and equally to the production and proofing of this systematic review and meta-analysis.

Conflict 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