Meta-analysis of the effects of helmet-assisted non-invasive ventilation in the treatment of acute respiratory failure

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Abstract. – OBJECTIVE: To study the efficacy of helmet-assisted non-invasive ventilation and conventional ventilation in the treatment of acute respiratory failure (ARF).

MATERIALS AND METHODS: Cochrane Library, PubMed, Embase and CNKI databases were searched for randomized controlled trials and case-control trials of helmet-assisted noninvasive ventilation in the treatment of ARF. The outcome measures included respiratory rate, intubation rate, complication rate, mortality rate and arterial blood gas analysis of the commonly used indicators (Pa-CO₂/ PaO₂/ pH). The results of the included studies’ odds ratio (OR) and its 95% confidential interval (CI) were analyzed using Stata software.

RESULTS: The results of the analysis showed that the in-hospital mortality, intubation rate and complication rate were all significantly decreased with the p-value less than 0.05, which was statistically significant.

CONCLUSIONS: Helmet-assisted noninvasive ventilation can significantly reduce hospital mortality, intubation rate and complication rate, improving the survival rate and prognosis of patients with ARF.

Key Words: Noninvasive ventilation, Helmet-assisted, Acute respiratory failure (ARF), Meta-analysis.

Materials and Methods

Introduction

Noninvasive ventilation has provided a technology of gas exchange that reduces intubation and mortality. It is now widely used in the treatment of acute respiratory failure (ARF) in patients who have chronic obstructive pulmonary disease (COPD), acute cardiogenic pulmonary edema or thoracic trauma.¹,² It is, however, easy to cause complications due to complex conditions and high technical requirements, and the failure rate reaches 20-30%.³ Application of auxiliary facial mask to a great extent reduced the discomfort and complications caused by mechanical ventilation. Although the obvious advantages of auxiliary facial mask, in cases of patients with serious or complicated condition, long-term auxiliary facial mask may inevitably cause complications, such as skin injury, rhinalgia and anabrosis over the bridge of the nose.⁴,⁵ Also, differences exist in the effects of traditional or auxiliary facial mask ventilation on the intubation rate, mortality or arterial blood gases. Some researches confirmed auxiliary facial mask improves the oxygenation index of patients,⁶,⁷ while others showed there is no difference between traditional and auxiliary facial mask ventilation.⁸,⁹ Researcheseten even indicated auxiliary facial mask increases the re-inhalation of CO₂. In this work, therefore, a meta-analysis was used to detect the efficacy of non-invasive ventilation on ARF patients with emphases on the changes of mortality, intubation rate, respiratory rate, and arterial blood gases.

Two authors were arranged to search database including Cochrane Library, PubMed, Embase, and CNKI for related literature published from the creation of these databases to December 2018. Keywords used for searching were: “helmet” AND “mechanical ventilation” OR “noninvasive ventilation” OR “facial mask”. Experiment objects were limited to patients with ARF caused by various factors. The used language was not limited. References in the included literature were reviewed to remove the repeatedly published literature (Figure 1).

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Inclusion and Exclusion Criteria

Two authors were arranged to screen out simultaneously the relevant studies that used conventional ventilation or facial mask auxiliary treatment. Specific inclusion criteria were as follows: (1) The main purpose of the paper was to compare the outcomes of the two methods, including randomized controlled trials (RCT) and case-control trials; (2) the subjects were all adults with ARF; (3) outcome indicators include at least one of the followings: complications, intubation rate, mortality or arterial blood gases. The exclusion criteria: (1) trials of postoperative facial mask application; (2) conference, letters, case report or review of literature; (3) trials without a control group.

Data Extraction and Quality Assessment

Data extraction involved the extraction of general information and outcome indicators in papers. Binary data contained numbers of occurrence and samples in each group. Extraction of continuous data covered the mean, SD and sample size. Tools from Cochrane collaboration network were selected for quality assessment of methodologies containing RCT. Risks from research design had been assessed according to the following seven entries: random sequence generation, allocation concealment, blinding of participants and appraisers, blinding of outcome evaluation, integrity of result data, selective reporting and other factors. Under each of these entries, it was given “high-risk”, “low-risk” or “unclear” to the information provided. In terms of case-control trails, the Newcastle-Ottawa Scale (NOS) was adopted with the key evaluation points on selectivity, comparability, and exposure factors. A maximum of 9 points would be awarded for each literature. These above assessments were done independently by two authors that, when in disagreement, had to discuss first and then be arbitrated by a third party.

Statistical Analysis

Meta-analysis was developed for each of the included papers. Binary data were subjected to the combination of odds ratio (OR) and 95% confidence interval (CI) using Mantel-Haenszel method. Effect size from continuous data should be integrated using inverse variance and expressed as standard mean deviation (SMD) with 95% CI. In addition, for studies showing superior inter-study homogeneity, the fixed effect model was used, otherwise the random effect model was applied. Results of heterogeneity detection were determined with the values of I²: 25-50% represents a low heterogeneity; 50-75% means moderate; and 75% shows a high heterogeneity.

Results

Literature Search Results

Processes of literature screening have been reported in Figure 1. Preliminary literature was retrieved to 354 related articles, and 25 duplicated articles were excluded. According to the title and abstract of the literature, 298 articles were deleted according to inclusion and exclusion criteria, including 275 non-RCT or case-control trials, 23 reviews and 23 correspondence articles. A total of 33 articles needed to be obtained. 18 articles were excluded through full-text reading. Finally, 15 articles were included in the meta-analysis, and the basic information of the literature was included (Table I).

![Figure 1. Flow diagram of literature search.](image-url)
### Table I. Characteristics of included studies.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Country</th>
<th>Experiment design</th>
<th>Patients</th>
<th>Treatment group</th>
<th>Control group</th>
<th>Observed outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>S Patel et al14</td>
<td>2016</td>
<td>America</td>
<td>RCT</td>
<td>ARF caused by ARDS</td>
<td>44</td>
<td>39</td>
<td>Respiratory rate, intubation rate, period of NIV, complications, days without ventilator, hospitalization and mortality, pressure support level, ICU admission</td>
</tr>
<tr>
<td>Özlem et al16</td>
<td>2015</td>
<td>Turkey</td>
<td>RCT</td>
<td>Hypercapnia ARF</td>
<td>25</td>
<td>23</td>
<td>Respiratory rate, complications, period of NIV, mortality, ICU admission</td>
</tr>
<tr>
<td>Pisani et al13</td>
<td>2015</td>
<td>Italy</td>
<td>RCT</td>
<td>Hypercapnia ARF</td>
<td>39</td>
<td>41</td>
<td>Respiratory rate, complications, intubation rate, pressure support level, hemodynamic changes</td>
</tr>
<tr>
<td>Brambilla et al15</td>
<td>2014</td>
<td>Italy</td>
<td>RCT</td>
<td>Hypoxemia ARF</td>
<td>40</td>
<td>41</td>
<td>Intubation rate, hospitalization and mortality, complications</td>
</tr>
<tr>
<td>Antonaglia et al18</td>
<td>2011</td>
<td>Brazil</td>
<td>RCT</td>
<td>Hypercapnia ARF</td>
<td>20</td>
<td>20</td>
<td>Respiratory rate, ICU admission, ventilator assistance</td>
</tr>
<tr>
<td>Principi et al7</td>
<td>2004</td>
<td>Italy</td>
<td>Case-control</td>
<td>Hypoxemia ARF</td>
<td>17</td>
<td>17</td>
<td>Intubation rate, complications, period of NIV</td>
</tr>
<tr>
<td>Antonelli et al6</td>
<td>2004</td>
<td>Italy</td>
<td>Case-control</td>
<td>Hypercapnia ARF</td>
<td>33</td>
<td>33</td>
<td>Respiratory rate, Intubation rate, complications, days without ventilator, hospitalization and mortality, pressure support level, ICU admission</td>
</tr>
<tr>
<td>Rocco et al19</td>
<td>2004</td>
<td>Italy</td>
<td>Case-control</td>
<td>Hypoxemia ARF</td>
<td>19</td>
<td>19</td>
<td>Respiratory rate, intubation rate, period of NIV, complications, days without ventilator, hospitalization and mortality, ICU admission</td>
</tr>
<tr>
<td>Tonnelier et al20</td>
<td>2003</td>
<td>France</td>
<td>Case-control</td>
<td>Hypoxemia ARF</td>
<td>11</td>
<td>11</td>
<td>Respiratory rate, complications, in-hospital mortality</td>
</tr>
<tr>
<td>Antonelli et al21</td>
<td>2002</td>
<td>Italy</td>
<td>Case-control</td>
<td>Hypoxemia ARF</td>
<td>33</td>
<td>66</td>
<td>Respiratory rate, intubation rate, period of NIV, complications, hospitalization and mortality, pressure support level, ICU admission</td>
</tr>
<tr>
<td>Yang et al22</td>
<td>2013</td>
<td>China</td>
<td>RCT</td>
<td>COPD/asthma/left heart failure combined with ARF</td>
<td>43</td>
<td>43</td>
<td>Intubation rate, complications, hospitalization and mortality, ICU admission</td>
</tr>
<tr>
<td>Wu et al23</td>
<td>2011</td>
<td>China</td>
<td>RCT</td>
<td>Hypercapnia ARF</td>
<td>25</td>
<td>25</td>
<td>Complications, arterial blood gas analysis, ICU admission</td>
</tr>
<tr>
<td>Xing et al24</td>
<td>2011</td>
<td>China</td>
<td>RCT</td>
<td>Hypercapnia ARF</td>
<td>20</td>
<td>20</td>
<td>Complications, arterial blood gas analysis, ventilator assistance</td>
</tr>
<tr>
<td>Xuan et al25</td>
<td>2010</td>
<td>China</td>
<td>RCT</td>
<td>Hypercapnia ARF</td>
<td>21</td>
<td>21</td>
<td>Respiratory rate, arterial blood gas analysis, complications</td>
</tr>
</tbody>
</table>
Results of Quality Assessment

As shown in Table II on the quality assessment to case-control studies, the obtained score greater than 4 points was supposed to be a high-quality paper. All the literature clearly reported the outcome indicators in the case and control groups. Figure 2 and 3 showed the results of RCT test evaluation, of which most indicated a low risk, but the “double blinding of participants and personnel” notably suggested a high risk that was inevitable in actual clinical treatment.

Heterogeneity and Publication Bias Test

Both of the two groups were subjected to the combined analysis of complications, mortality, intubation rates, respiratory rates, oxygen pressure, PaCO₂, PaO₂, and pH in the blood. Besides, heterogeneity, publication bias (Begg and Egger) and significance tests were carried out (Table III). The publication bias tests showed there was no bias existing among these included studies.

Meta-Analysis Results

In binary data, 8 studies involving 535 patients reported in-hospital mortalities. The Forest of combined analysis have been shown in Figure 4A where OR=0.50 (95% CI: 0.33-0.78), p=0.002. The in-hospital mortality of mask group was 15.4% (39/254) while the in-hospital mortality of non-mask group was 29.2% (82/281). 11 studies containing 685 patients reported intubation rates as shown in Figure 4B where OR=0.39 (95% CI: 0.27-0.56), p=0.000. The intubation rate in mask group was 14.9% (49/328) while the intubation rate in non-mask group was 38.4% (137/357). 10 studies including 637 patients gave the occurrence rate of complications. Their Forest of combined analysis were shown in Figure 4C where OR=0.57 (95% CI: 0.39-0.84) and p=0.04. Occurrence rate of complications in mask group was 16.8% (51/304) and the occurrence rate of complications in non-mask group 31.5% (105/333). As for continuous data, two groups of contrastive analysis in terms of respiratory rate, PaCO₂, PaO₂, and pH, were reported (Figure 5). Considering the high heterogeneity, random effect model was selected for combined analysis which then showed in the results that both the respiratory rate and PaCO₂ of the facial mask auxiliary ARF group were lower than that of the control group: SMD=-0.28 (95% CI: -0.77-0.21), p=0.262; SMD=-0.29 (95% CI: -1.04-0.47), p=0.457; the PaO₂ and pH were inversely higher than that of the control group: SMD=0.28 (95% CI: -0.11-0.67), p=0.153; SMD=0.24 (95% CI: -0.32-0.79), p=0.399.

There was no difference between subgroups and the combined analyses. Subgroup analysis showed that in those included RCT trails, patients who underwent auxiliary laryngeal mask ventilation have significantly reduced the occurrence rate of complications and mortality (p<0.001) (Figure 4A-B), but higher intubation rates than those in case-control trails. From subgroup analyses of respiratory rate, PaCO₂, PaO₂ and pH, the results of RCT and case-control trails were basically consistent (Figure 5), that is, auxiliary laryngeal mask may not have greatly improved the respiratory rate, PaCO₂, PaO₂ or pH of patients with ARF.

Discussion

As shown in the comparison between auxiliary laryngeal mask and conventional ventilation, mask auxiliary noninvasive ventilation greatly reduced the mortality, intubation rate, and occurrence of complications, but showed little effects on the PaCO₂, PaO₂ or pH. Noninvasive respirator supports respiration without endotracheal stoma or tracheostoma. Wearing auxiliary facial mask, patients have full access to the respirator by the nose, mouth and face, avoiding damage in airway or of swallowing ability. Appropriate respiratory support with auxiliary facial mask may reduce the mortality of ARF patients. However, it should be noted that persistent mask wearing probably makes the patient uncomfortable, lowers the therapeutic effects or even increases the occurrence of complications. This meta-analysis involving RCT and case-control trails indicated that noninvasive ventilation with auxiliary facial mask lowered in-hospital mortality, i.e. the mask itself may enhance the survival rate of patients with ARF. This is a specific advantage that any other ventilatory support cannot provide. In the first place, ventilation with auxiliary facial mask impacts little on patients' diet or verbal communication; secondly, patients are highly tolerant to facial mask auxiliary ventilation, elevating the success rate of noninvasive treatment. Furthermore, respiratory support with auxiliary facial mask accommodates to more critical illnesses and even variation coming from different appearances. In short, auxiliary facial mask improved the comfort through the ventilatory support and was well tolerated by patients, let alone the reduced occurrence of pneumonia, in-hospital mortality and other factors. It was suggested to generally accept the application of auxiliary mask.
Table II. NOS score of case-control studies.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Is the case definition adequate?</th>
<th>Representative of the cases</th>
<th>Selection of controls</th>
<th>Definition of controls</th>
<th>Control for important factors</th>
<th>Control for additional factors</th>
<th>Ascertainment of exposure</th>
<th>Same method of ascertainment cases and controls</th>
<th>Non response rate</th>
<th>Overall stars</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principi et al</td>
<td>2004</td>
<td>✶ ✶ ✶</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>8</td>
</tr>
<tr>
<td>Antonelli et al</td>
<td>2004</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>5</td>
</tr>
<tr>
<td>Rocco et al</td>
<td>2004</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>✶</td>
<td>✶ ✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>5</td>
</tr>
<tr>
<td>Tonnelier et al</td>
<td>2003</td>
<td>✶ ✶</td>
<td>✶ ✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>6</td>
</tr>
<tr>
<td>Antonelli et al</td>
<td>2002</td>
<td>✶ ✶</td>
<td>✶</td>
<td>✶ ✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>✶</td>
<td>6</td>
</tr>
</tbody>
</table>

Figure 2. Summary of each risk item of RCT.
What worthy of attention is ventilatory support with auxiliary facial mask reduces the in-hospital complications and mortality. Several studies have attempted to demonstrate the efficacy of mask auxiliary noninvasive ventilation in patients with ARF, but the prognosis is limited probably due to different breathing patterns of ARF patients caused by acid-base imbalance: mouth breathing is more common in patients with hypoxemia, leading to a better effect of mask auxiliary. This, however, does not mean that auxiliary mask noninvasive ventilation will not impact the mortality of ARF patients. Two small-sample studies have found that, for ARF patients with hypercapnia, ventilatory support with auxiliary facial mask improves survival rate, but it was still not hard evidence. Further researches are needed.

Conclusions

This meta-analysis indicated auxiliary mask noninvasive ventilation made the prognosis of ARF patients better and reduced the rate of intubation and complications. Auxiliary mask could enhance the gas exchange efficiency. Nevertheless, it was worth noting that the advantages of facial mask application have not been scientifically evidenced so more RCT or case-control trails are strongly needed to support the reliability.

Sources of Funding

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Conflict of Interests

The authors declare that they have no conflict of interests.

Table III. Heterogeneity and publication bias test.

<table>
<thead>
<tr>
<th>Index</th>
<th>Analysis model</th>
<th>Heterogeneity</th>
<th>Begg</th>
<th>Egger</th>
<th>X²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I² (%)</td>
<td>p</td>
<td>z</td>
<td>p</td>
</tr>
<tr>
<td>Complications</td>
<td>Fixed</td>
<td>47.7</td>
<td>0.045</td>
<td>0.09</td>
<td>0.929</td>
</tr>
<tr>
<td>Mortality</td>
<td>Fixed</td>
<td>0%</td>
<td>0.935</td>
<td>-1.24</td>
<td>0.216</td>
</tr>
<tr>
<td>Intubation rate</td>
<td>Fixed</td>
<td>19.3</td>
<td>0.259</td>
<td>0.08</td>
<td>0.938</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>Random</td>
<td>80.2</td>
<td>0</td>
<td>0.45</td>
<td>0.652</td>
</tr>
<tr>
<td>PaCO2</td>
<td>Random</td>
<td>92.1</td>
<td>0</td>
<td>-1.04</td>
<td>0.297</td>
</tr>
<tr>
<td>PaO2</td>
<td>Random</td>
<td>75.1</td>
<td>0</td>
<td>-0.27</td>
<td>0.788</td>
</tr>
<tr>
<td>pH</td>
<td>Random</td>
<td>86.3</td>
<td>0</td>
<td>1.88</td>
<td>0.061</td>
</tr>
</tbody>
</table>

Notes: *p<0.05, **p<0.01, ***p<0.001.
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References


5) Yamaguti WP, Moderno EV, Yamashita SY, Gomes TG, Madia AL, Kondo CS, de Salles IC, de Brito CM. Treatment-related risk factors for development of skin breakdown in subjects with acute respiratory failure undergoing noninvasive ventilation or CPAP. Respir Care 2014; 59: 1530-1536.


Figure 5. Forests of continuous data. A, Forest gram of respiratory rate ratio. B, Forest gram of PaCO2 ratio. C, Forest gram of PaO2 ratio. D, Forest gram of pH ratio.


