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The Efficacy of High-flow Oxygen Versus Conventional Oxygen for Asthma Control: A Meta-analysis of Randomized Controlled Studies

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Abstract

Introduction: The efficacy of high-flow oxygen versus conventional oxygen therapy for asthma control remains controversial. We conduct a systematic review and meta-analysis to explore the influence of high-flow oxygen versus conventional oxygen therapy on asthma control.

Methods: We have searched PubMed, EMbase, Web of science, EBSCO, and Cochrane library databases through May 2021 for randomized controlled trials (RCTs) assessing the efficacy of high-flow oxygen versus conventional oxygen therapy for asthma control. This meta-analysis is performed using the random-effect model.

Results: Four RCTs are included in the meta-analysis. Overall, compared with conventional oxygen therapy for asthma, high-flow oxygen is associated with significantly lower dyspnea score (SMD=-0.63; 95% CI=-1.08 to -0.17; P=0.008), but reveals no remarkable influence on PaCO2 (SMD=0.28; 95% CI=-0.22 to 0.77; P=0.28), PaO2 (SMD=0.44; 95% CI=-1.34 to 2.22; P=0.63), intubation (OR=1.09; 95% CI=0.15 to 8.21; P=0.93) or hospital length of stay (SMD=-0.07; 95% CI=-0.41 to 0.27; P=0.67).

Conclusions: High-flow oxygen may benefit to reduce dyspnea score than conventional oxygen therapy for asthma.

Introduction

Asthma, a chronic inflammatory airway disease has the features of airway hyperresponsiveness and reversible airflow obstruction [1-5]. It has become one of the most common airway diseases in both children and adults [6]. It is estimated that the incidence of childhood asthma is 10% to 13%, which its incidence of adults is lower at 4% [7-9]. The exacerbation of asthma results in an acute obstruction of expiratory airflow due to airway inflammation, bronchospasm, and hypersecretion, which needs the increased work of breathing [10, 11]. If emergent and effective treatment is conducted for asthma exacerbation, the respiratory muscles may fatigue, accompanied by hypercapnia, severe hypoxemia, and consequently respiratory failure [12].

The Global Initiative for Asthma (GINA) guideline recommends early administration of supplemental oxygen and medications such as nebulized bronchodilators and systemic corticosteroid for the management of acute severe asthma [6]. The administration approaches of oxygen mainly include nasal cannula and nonrebreather mask which are promising for chronic obstructive pulmonary disease (COPD), but shows limited success for acute severe asthma [13]. High-flow oxygen therapy is the oxygen-delivering method of inspired fraction (FiO2) up to 1.0 via a purposely made high-flow nasal cannula across a range of flows from 2 to 60 L/min. It also provides positive airway pressure and decreases rebreathing from anatomic dead space, which help reduce respiratory effort [14, 15]. Many studies reported the effectiveness of high-flow oxygen therapy all-cause hypoxemic respiratory failure and cardiogenic pulmonary edema [16, 17].

Current evidence is insufficient for routine clinical use of high-flow oxygen therapy for asthmatic patients. Recently, several studies have investigated the efficacy of high-flow oxygen versus conventional oxygen therapy for these patients, but the results are conflicting [12, 18, 19]. This systematic review and meta-analysis of RCTs aims to assess the efficacy of high-flow oxygen versus conventional oxygen therapy in asthmatic patients.

Materials And Methods

This systematic review and meta-analysis are performed based on the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement and Cochrane Handbook for Systematic Reviews of Interventions [20-22]. No ethical approval and patient consent are required because all analyses are based on previous published studies.

Literature search and selection criteria

We have systematically searched several databases including PubMed, EMbase, Web of science, EBSCO, and the Cochrane library from inception to May 2021 with the following keywords: “high-flow oxygen” AND “asthma”. The reference lists of retrieved studies and relevant reviews are also hand-searched and the process above is performed repeatedly in order to include additional eligible studies.

The inclusion criteria are presented as follows: (1) study design is RCT, (2) patients are diagnosed with asthma, and (3) intervention treatments are high-flow oxygen versus conventional oxygen therapy.

Data extraction and outcome measures

Some baseline information is extracted from the original studies, and they include first author, number of patients, age, female, medial history of asthma and detail methods in two groups. Data are extracted independently by two investigators, and discrepancies are resolved by consensus. We have contacted the corresponding author to obtain the data when necessary.

The primary outcome is dyspnea score. Secondary outcomes include PaCO2, PaO2, intubation, and hospital length of stay.

Quality assessment in individual studies

The methodological quality of each RCT is assessed by the Jadad Scale which consists of three evaluation elements: randomization (0-2 points), blinding (0-2 points), dropouts and withdrawals (0-1 points) [23]. One point would be allocated to each element if they have been conducted and mentioned appropriately in the original article. The score of Jadad Scale varies from 0 to 5 points. An article with Jadad score≤2 is considered to be of low quality. The study is thought to be of high quality if Jadad score≥3 [22, 24].

Statistical analysis

We assess standard mean difference (SMD) with 95% confidence intervals (CIs) for continuous outcomes (dyspnea score, PaCO2, PaO2 and hospital length of stay) and odd ratio (OR) with 95% CI for dichotomous outcome (intubation). Heterogeneity is evaluated using the I^2 statistic, and $I^2 > 50\%$ indicates significant heterogeneity [25]. The random-effects model is used for all meta-analysis. We search for potential sources of heterogeneity for significant heterogeneity. Sensitivity analysis is performed to detect the influence of a single study on the overall estimate via omitting one study in turn or performing the subgroup analysis. Owing to the limited number (<10) of included studies, publication bias is not assessed. Results are considered as statistically significant for $P < 0.05$. All statistical analyses are performed using Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

Results

Literature search, study characteristics and quality assessment

Figure 1 shows the detail flowchart of the search and selection results. 152 potentially relevant articles are identified initially. Finally, four RCTs are included in the meta-analysis [12, 18, 19, 26].

The baseline characteristics of four included RCTs are shown in Table 1. These studies are published between 2018 and 2021, and the total sample size is 175. High-flow oxygen ranges from 2 to 60 L/min. one RCT involves children with asthma [26], while the other three RCTs involve adult patients [12, 18, 19].

Two studies report dyspnea score [12, 19], two studies report dyspnea score PaCO2, PaO2 and intubation [12, 18], and three studies report dyspnea score hospital length of stay [12, 18, 26]. Jadad scores of the four included studies vary from 3 to 4, and all four studies have high-quality based on the quality assessment.

Primary outcome: dyspnea score

The random-effect model is used for the analysis of primary outcome. The results find that compared to conventional oxygen therapy for asthma, high-flow oxygen is associated with significantly lower dyspnea score (SMD=-0.63; 95% CI=-1.08 to -0.17; P=0.008), with no heterogeneity among the studies (I^2=0%, heterogeneity P=0.87, Figure 2).

Sensitivity analysis

There is no heterogeneity for dyspnea score, and thus we do not perform sensitivity analysis by omitting one study in each turn to detect the source of heterogeneity.

Secondary outcomes

In comparison with conventional oxygen therapy for asthma, high-flow oxygen shows no obvious impact on PaCO2 (SMD=0.28; 95% CI=-0.22 to 0.77; P=0.28; Figure 3), PaO2 (SMD=0.44; 95% CI=-1.34 to 2.22; P=0.63; Figure 4), intubation (OR=1.09; 95% CI=0.15 to 8.21; P=0.93; Figure 5) or hospital length of stay (SMD=-0.07; 95% CI=-0.41 to 0.27; P=0.67; Figure 6).

Table 1 Characteristics of included studies

NO.	Author	High flow group					Control group					Jadad score
		Number	Age (years)	Female (n)	Duration of asthma (year)	Methods	Number	Age (years)	Female (n)	Duration of asthma (year)	Methods	
1	Ruangsomboon 2021	19	63.7±16.9	16	-	35 L/min, adjusted from 30 to 60 L/min according to the participant's level of comfort	18	63.2±21.8	15	-	standard oxygen nasal cannula	3
2	Geng 2020	16	43.3 ± 10.6	10	6.38 ± 1.28	initial gas flow of 30–40 L/min, to maintain pulse oxygen saturation at 92%–96%	20	37.5 ± 8.4	12	5.95 ± 1.36	standard oxygen nasal cannula	4
3	Raeisi 2019	20	50.75±10.7	15	5.3±2.7	flow range 15–35 L/min	20	44.4±11.6	13	6.4±3.4	standard oxygen nasal cannula	4
4	Ballestero 2018	30	3.0 (1.7-6.0), median (range)	15	-	flow range 2-25 L/min	32	3.0 (2.0-6.0)	14	-	standard oxygen nasal cannula	3

Discussion

Several studies demonstrated the benefit of high-flow oxygen therapy in decreasing the arterial partial pressure of carbon dioxide ($PaCO_2$) in patients with hypercapnic respiratory failure secondary to COPD [27–29]. In patients with severe asthma, high-flow oxygen therapy also showed favorable benefit to decrease respiratory rate and increase their expiratory time which thereby help decrease dynamic hyperinflation. In addition, heated and humidified air could increase the comfort and reduce bronchoconstriction induced by cold air [12].

Our meta-analysis included four RCTs and 175 patients, and the results revealed that high-flow oxygen therapy was associated with significantly lower dyspnea score than conventional oxygen therapy for asthma, but $PaCO_2$, PaO_2, intubation and hospital length of stay were found to be similar between two groups. In pediatric patients with acute severe asthma, high-flow oxygen therapy was approved to improve clinical severity compared with both conventional oxygen therapy [26, 30]. Its benefits to decrease $PaCO_2$ and an increase in the pH level were also confirmed in children and adolescents [31].

In Fig. 3, only adults patients were included for the meta-analysis of $PaCO_2$ after pooling the results of two RCTs [12, 18]. These suggested that high-flow oxygen therapy may provide better efficacy to decrease $PaCO_2$ and improve clinical severity in pediatric patients than that in adult patients. Regarding the sensitivity analysis, although there is no significant heterogeneity, several factors may produce some bias. Firstly, children and adult patients are both included in this meta-analysis, which may affect the evaluation of efficacy such as the decrease in $PaCO_2$. Secondly, the flow range and detail methods of high-flow oxygen therapy were various among the four RCTs. Thirdly, the severity of asthma were different, which may affect the efficacy evaluation of high-flow oxygen therapy.

Several limitations exist in this meta-analysis. Firstly, our analysis is based on only four RCTs, and more RCTs with large sample size should be conducted to explore this issue. Next, although there is no significant heterogeneity, different flow range and severity of asthma may lead to some bias. Finally, it is not feasible to perform the analysis of some outcomes such as modified Borg scale and respiratory rate.

Conclusion

High-flow oxygen therapy may benefit to decrease dyspnea score than conventional oxygen therapy in asthmatic patients.

Abbreviations

randomized controlled trials: RCTs

mean differences: MDs

confidence intervals: CIs

risk ratios: RRs

Declarations

Ethical Approval and Consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of supporting data

Not applicable.

Competing interests

The authors declare no conflict of interest.

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Not applicable.

Authors' contributions

Juan Li conducted the design, Jialing Jiang conducted the study planning, data analysis and data interpretation, Kaijin Wang wrote and revised the article. All authors read and approved the final manuscript.

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Figures

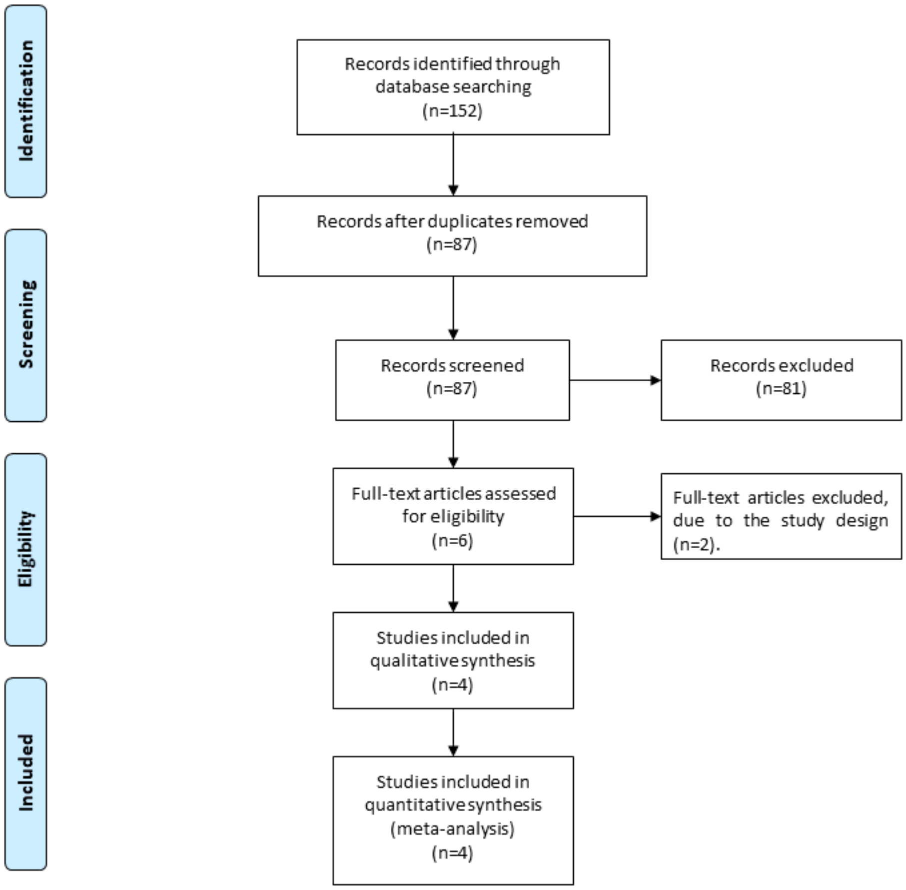

Figure 1

Flow diagram of study searching and selection process.

	High flow group			Control group				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Raeisi 2019	6.45	0.51	20	6.89	0.9	20	52.3%	-0.59 [-1.22, 0.04]
Ruangsomboon 2021	1.4	2.5	19	3.1	2.5	18	47.7%	-0.67 [-1.33, -0.00]
Total (95% CI)			**39**			**38**	**100.0%**	**-0.63 [-1.08, -0.17]**

Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%
Test for overall effect: Z = 2.67 (P = 0.008)

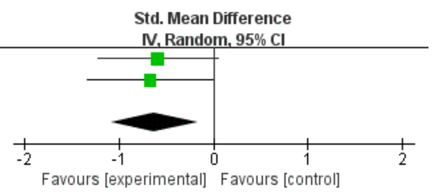

Figure 2

Forest plot for the meta-analysis of dyspnea score.

	High flow group			Control group				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Geng 2020	40.22	4.37	16	39.87	4.35	20	57.5%	0.08 [-0.58, 0.74]
Ruangsomboon 2021	37.9	8.7	18	33.3	7.4	11	42.5%	0.54 [-0.22, 1.31]
Total (95% CI)			**34**			**31**	**100.0%**	**0.28 [-0.22, 0.77]**

Heterogeneity: Tau² = 0.00; Chi² = 0.81, df = 1 (P = 0.37); I² = 0%
Test for overall effect: Z = 1.08 (P = 0.28)

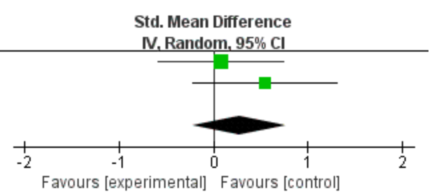

Figure 3

Forest plot for the meta-analysis of PaCO2.

	High flow group			Control group				Std. Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**
Geng 2020	94.73	4.43	16	86.98	6.42	20	50.2%	1.35 [0.61, 2.08]
Ruangsomboon 2021	119.2	37	18	139.4	48.9	11	49.8%	-0.47 [-1.23, 0.29]
Total (95% CI)			**34**			**31**	**100.0%**	**0.44 [-1.34, 2.22]**

Heterogeneity: Tau² = 1.50; Chi² = 11.31, df = 1 (P = 0.0008); I² = 91%
Test for overall effect: Z = 0.49 (P = 0.63)

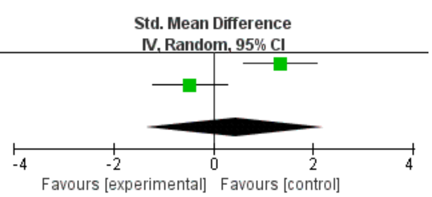

Figure 4

Forest plot for the meta-analysis of PaO2.

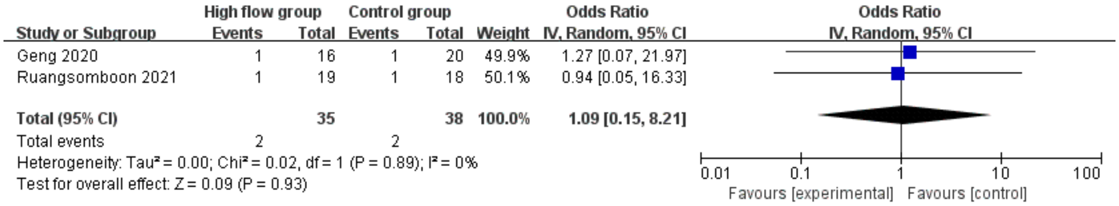

Figure 5

Forest plot for the meta-analysis of intubation.

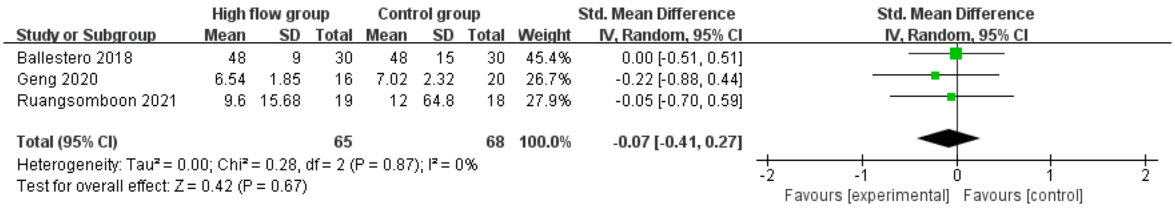

Figure 6

Forest plot for the meta-analysis of hospital length of stay.