

• 论著 •

经鼻高流量氧疗预防术后呼吸衰竭疗效的Meta分析

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【摘要】目的评价经鼻高流量氧疗(HFNC)预防术后呼吸衰竭(呼衰)的有效性和安全性。**方法**以经鼻高流量氧疗、鼻导管高流量氧疗、高流量鼻导管氧疗、经鼻高流量加温加湿吸氧、术后呼衰患者为中文检索词,以high flow nasal cannulae、high flow nasal cannulae oxygen therapy、nasal high flow、adult、postoperative respiratory failure为英文检索词,计算机检索美国国立医学图书馆数据库(PubMed)、Cochrane图书馆、荷兰医学文摘Embase、科学网(Web of Science)、中国知网数据库(CNKI)、维普数据库、万方数据库、中国生物医学文献数据库(CMB)等已发表的HFNC预防术后呼衰疗效的随机对照临床试验(RCT),检索时间为各数据库建库至2017年6月。仔细阅读文献,按照严格的纳入和排除标准纳入符合标准的研究。由2名作者独立提取资料,并进行质量评价,提取呼吸支持升级率、住院病死率、住院时间等资料。使用RevMan 5.3软件进行Meta分析;采用漏斗图分析发表偏倚。**结果**Meta分析最后纳入6篇RCT共935例拔管后存在中高危呼衰风险的成年患者,试验组467例,对照组468例。与对照组比较,试验组患者呼吸支持升级率降低[优势比(OR)=0.55,95%可信区间(95%CI)=0.39~0.76,P=0.0003];试验组和对照组在改善患者住院病死率(OR=0.77,95%CI=0.17~3.48,P=0.73)和缩短住院时间[均数差(MD)=-0.48,95%CI=-1.37~0.41,P=0.29]方面比较差异均无统计学意义,但优势更倾向于试验组。漏斗图显示纳入文献分布基本对称,提示发表偏倚较小。**结论**与COT相比,HFNC可以降低术后呼衰患者呼吸支持升级率,虽然COT、HFNC对术后患者住院病死率、住院时间的影响差异无统计学意义,但优势倾向于HFNC。

【关键词】经鼻高流量氧疗; 术后呼吸衰竭; 成人; Meta分析

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The efficacy of high flow nasal cannula oxygen therapy in preventing postoperative respiratory failure: a Meta-analysis Liu Xin, Zhou Fachun, Liu Zhu, Wang Xiyu

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【Abstract】Objective To evaluate the efficacy and safety of high flow nasal cannula (HFNC) oxygen therapy in preventing postoperative respiratory failure. **Methods** HFNC, nasal catheter high flow oxygen therapy, high flow nasal catheter oxygen therapy, high-flow nasal humidifiers and oxygen inhalers, and patients with postoperative respiratory failure were used as Chinese terms, and high flow nasal cannulae, high flow nasal cannulae oxygen therapy, nasal high flow, adult, postoperative respiratory failure were used as English terms to retrieve, a computer was used to retrieve already published all available randomized controlled trials (RCTs) about using HFNC therapy to prevent patients from the occurrence of postoperative respiratory failure; the search was carried out from PubMed in literature database of American National Library, the Cochrane Library, Holland Medical Abstract Embase, Web of Science, China National Knowledge Infrastructure (CNKI), VIP database, Wanfang Database, China Biomedicine Database (CBM), and the articles were collected from the creation of various above databases to June 2017. The collected RCTs should be carefully read, and the inclusion or exclusion of an article should strictly follow the respective criteria. Two authors independently extracted data, conducted quality assessments, extract the elevation of respiratory support rate, hospital mortality and hospital length of stay, etc. Revman 5.3 software was used to carry out Meta analysis; funnel plots were applied to analyze the publication bias. **Results** Finally, after Meta analyses, 6 RCTs were included, involving 935 adult patients with existence of moderate to high risks of respiratory failure after the tube drawn out post-operatively, and there were 467 patients in the experimental group and 468 in control group. Compared with the control group, the escalation of respiratory support rate was reduced in the experimental group [odds ratio (OR) = 0.55, 95% confidence interval (95%CI) = 0.39 ~ 0.76, P = 0.0003]; There were no statistical significant differences in improving hospital mortality (OR = 0.77, 95%CI = 0.17 ~ 3.48, P = 0.73) and shortening hospital length of stay [mean difference (MD) = -0.48, 95%CI = -1.37 ~ 0.41, P = 0.29] in the comparisons between the two groups, but experimental group tended to be the one with more advantage. The funnel plot analysis suggested that the publication bias was relatively low, because the distribution of the included articles was basically symmetrical. **Conclusion** Compared with COT, HFNC could reduce the escalation of respiratory support rate in patients with postoperative respiratory failure, although there were no statistical significant differences in hospital mortality and hospital length of stay between HFNC and COT, the advantage tends toward the HFNC.

【Key words】 High flow nasal cannulae oxygen; Postoperative respiratory failure; Adult; Meta-analysis

Fund program: Chongqing Municipal Medical and Health Research Project (2013-1-007)

外科重症加强治疗病房(ICU)患者术后常并发低氧血症^[1],低氧血症是与患者不良结局相关的最主要因素之一,发生在手术后10%~50%的患者中^[2-3]。氧疗是治疗低氧血症的重要手段,但传统氧疗对有些患者不适用^[4]。无创正压通气(NPPV)是治疗术后呼吸衰竭(呼衰)的有效措施,但NPPV易导致患者面部皮肤损伤、鼻黏膜溃疡等不良事件,患者耐受性差。而经鼻高流量氧疗(HFNC)作为一种新型无创通气手段,既能提供一定的气道持续正压,增加功能残气量,改善氧合,减少呼吸作功^[5-6],又能输送总流量最高达60 L/min的温热加湿空气和氧气混合气体。研究显示,良好的气道湿化能降低呼吸机所致肺损伤^[7]。近年来,HFNC在患儿中已广泛应用^[8-10],但在成年患者中的应用经验较有限^[11]。本研究通过Meta分析评价HFNC预防成人术后呼衰的有效性与安全性,为其临床应用提供一定的循证支持。

1 资料与方法

1.1 文献纳入标准:① 内容为比较HFNC与常规氧疗(COT,通过鼻导管或面罩输送低流量氧气)预防成人术后呼衰的临床研究;② 研究的类型为临床随机对照试验(RCT);③ 研究对象为成人;④ 干预措施为试验组拔管后给予HFNC,对照组给予COT。

1.2 文献排除标准:无对照的临床试验;历史性对照临床试验;前后交叉临床试验。

1.3 疗效判定指标:呼吸支持升级率、住院病死率、住院时间。

1.4 文献检索策略:通过计算机检索国内外已发表的比较HFNC与COT预防成人术后呼衰的RCT。检索数据库包括美国国立医学图书馆数据库(PubMed)、Cochrane图书馆、荷兰医学文摘Embase、科学网(Web of Science)、中国知网数据库、维普数据库、万方数据库、中国生物医学文献数据库(CMB)等,检索时间为各数据库建库至2017年

6月。检索语种为中文及英文。以经鼻高流量氧疗、鼻导管高流量氧疗、高流量鼻导管氧疗、经鼻高流量加温加湿吸氧、术后呼衰患者为中文检索词;以high flow nasal cannulae、high flow nasal cannulae oxygen therapy、nasal high flow、adult、postoperative respiratory failure为英文检索词。

1.5 文献质量的评价方法:由2名作者浏览检索到的所有文献标题及摘要后,排除明显不相关的研究。阅读相关文献全文,按事先设定的纳入和排除标准筛选文献。如存在争议,则由第3名作者帮助评估,协商后达成一致。经阅读全文后提取试验时机、受试者、受试者纳入和排除标准、干预措施及结局等研究数据。然后由2名研究人员使用Cochrane偏倚风险表评估纳入研究的偏倚风险:是否为RCT,是否随机化隐藏,试验干预及结局评估是否采用盲法,不完全结局数据的处理,有无选择性报道,是否有提前终止试验的风险,试验组与对照组研究基线是否均衡,是否有来自赞助机构的偏倚。

1.6 统计学处理:采用RevMan 5.3软件进行Meta分析,结局为二分类变量,采用优势比(OR)以及95%可信区间(95%CI)表示,连续变量资料则采用均数差(MD)及95%CI表示。各纳入研究间的异质性均采用 I^2 检验,若 $I^2 > 50\%$ 提示存在高度异质性,采用随机效应模型; $I^2 \leq 50\%$ 提示研究间无明显异质性,采用固定效应模型。 $P < 0.05$ 为差异有统计学意义。采用漏斗图分析纳入研究的发表偏倚。

2 结果

2.1 检索结果:共检索出321篇文献,排除重复及不符合纳入标准的文献共298篇;进一步阅读全文,排除17篇不符合纳入标准的文献,最终纳入6篇^[2,12-16]外文文献进行Meta分析。

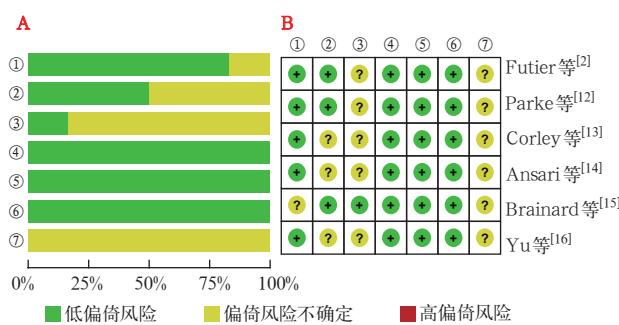
2.2 纳入研究的基本资料(表1):6篇文献共纳入成年术后患者935例,其中试验组467例,对照组468例。6篇文献均为RCT,均以全文发表,均为术后拔管后存在呼衰风险的成年患者。

表1 HFNC对预防术后呼衰患者疗效的Meta分析纳入研究的基本特征

纳入研究	发表时间	研究设计	例数(例)		性别(男性/女性,例/例)		干预措施		结局指标
			试验组	对照组	试验组	对照组	试验组	对照组	
Futier等 ^[2]	2016年	RCT	108	112	61/47	64/48	HFNC	COT	①②③
Parke等 ^[12]	2013年	RCT	169	171	129/40	129/42	HFNC	COT	①②③
Corley等 ^[13]	2015年	RCT	81	74	58/23	56/18	HFNC	COT	①
Ansari等 ^[14]	2016年	RCT	28	31	14/14	14/17	HFNC	COT	③
Brainard等 ^[15]	2017年	RCT	25	26	15/10	14/12	HFNC	COT	①③
Yu等 ^[16]	2017年	RCT	56	54	30/26	28/26	HFNC	COT	①②③

注:①为呼吸支持升级率;②为住院病死率;③为住院时间

2.3 纳入研究的偏倚风险(图1):综合7个项目的评估,纳入的所有研究均为低偏倚风险。所有研究随机序列的产生和分配隐藏均恰当。5篇使用计算机产生随机序列,1篇使用密封信封随机分配。考虑到干预措施的特点,难以实现对试验者及受试者的双盲。对于结局的评估,6篇文献均使用了盲法,且都有独立监督委员会保证数据的公正性。6篇文献均报告了预先设计的结局测量。6篇文献均无早期终止试验的情况,故均为低风险。



注:A为各偏倚风险构成比;B为各纳入研究的偏倚风险;①为随机分配方案的产生(选择性偏倚);②为分配隐藏(选择性偏倚);③为对患者和医生实施盲法(实施偏倚);④为对结果的评价实施盲法(检出偏倚);⑤为不完整的结果数据(失访偏倚);⑥为选择性的结果数据(报告偏倚);⑦为其他偏倚

图1 纳入研究的偏倚风险图

2.4 HFNC效果评价

2.4.1 HFNC和COT预防术后呼衰对患者呼吸支

持升级率的影响(图2):有5篇文献^[2, 12-13, 15-16]描述了HFNC与COT预防术后呼衰对患者呼吸支持升级率的影响,各研究间无明显异质性($I^2=12\%$),故采用固定效应模型进行Meta分析。结果显示,试验组呼吸支持升级率较对照组明显降低($OR=0.55$, $95\%CI=0.39 \sim 0.76$, $P=0.0003$)。

2.4.2 HFNC和COT预防术后呼衰对患者住院病死率的影响(图3):有3篇文献^[2, 12, 16]描述了HFNC与COT预防术后呼衰对患者住院病死率的影响,各研究间无明显异质性($I^2=0\%$),故采用固定效应模型进行Meta分析。结果显示,试验组与对照组住院病死率比较差异无统计学意义($OR=0.77$, $95\%CI=0.17 \sim 3.48$, $P=0.73$),但优势更偏向于试验组。

2.4.3 HFNC预防术后呼衰对患者住院时间的影响(图4):有5篇文献^[2, 12, 14-16]描述了HFNC与COT预防术后呼衰对患者住院时间的影响,各研究间存在明显异质性($I^2=56\%$),故采用随机效应模型进行Meta分析。结果显示,试验组与对照组住院时间比较差异无统计学意义($MD=-0.48$, $95\%CI=-1.37 \sim 0.41$, $P=0.29$),但优势更偏向于试验组。

2.4.4 文献发表偏倚结果(图5):纳入文献中有关呼吸支持升级率、住院时间的研究漏斗图基本对称,提示发表偏倚较小。

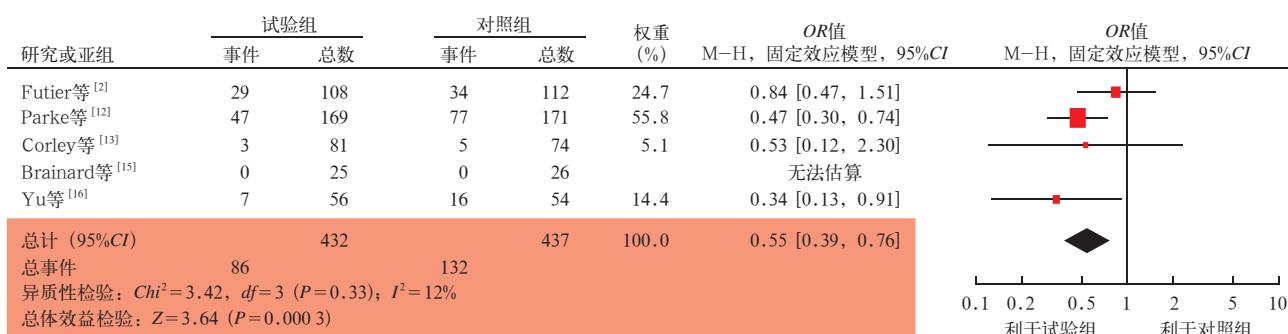


图2 HFNC与COT预防术后呼衰对患者呼吸支持升级率影响的Meta分析

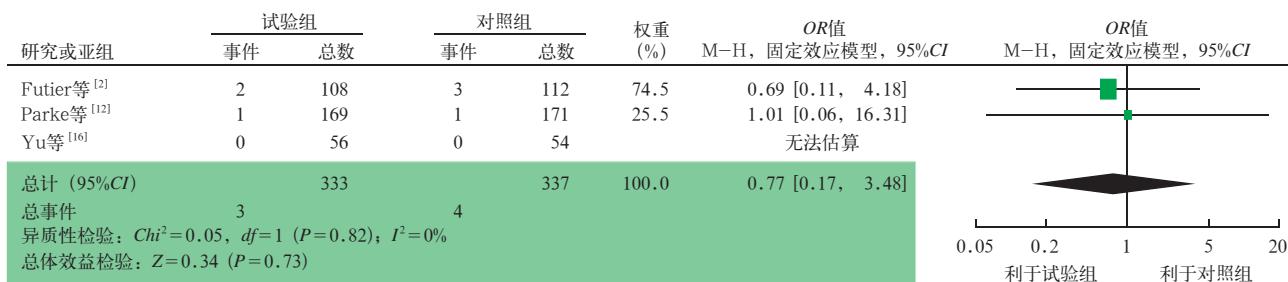


图3 HFNC与COT预防术后呼衰对患者住院病死率影响的Meta分析

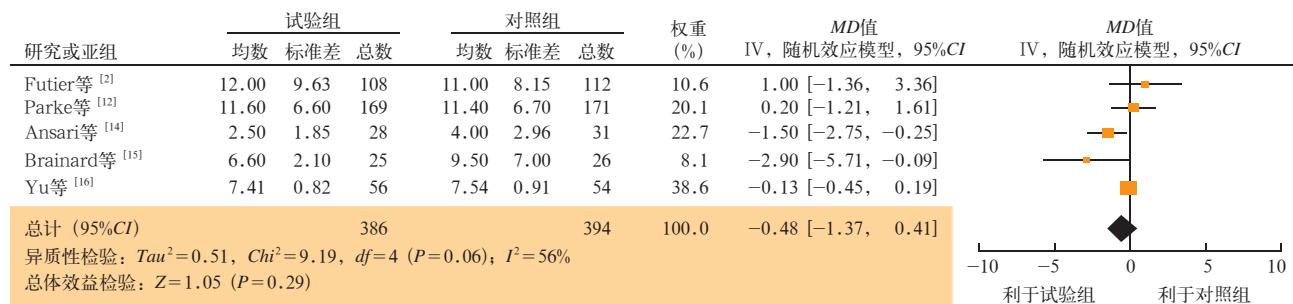


图4 HFNC与COT预防术后呼衰对患者住院时间影响的Meta分析

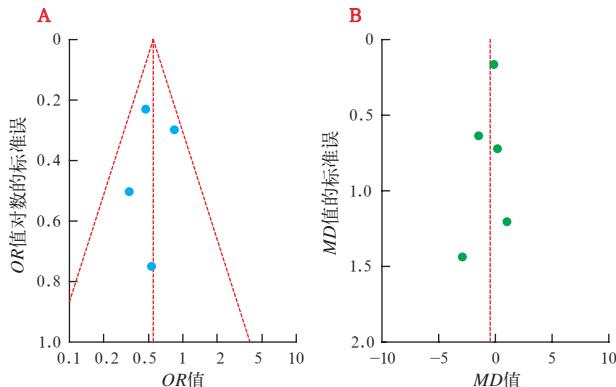


图5 HFNC与COT预防术后呼衰对患者呼吸支持升级率(A)、住院时间(B)影响的Meta分析纳入文献发表偏倚漏斗图

3 讨 论

HFNC可以输出体积浓度为21%~100%的恒定氧气,能够输送总流量最高达60 L/min的空气氧气混合气体,同时可输送温度约为37℃及相对湿度为100%的温湿气体,能改善气道黏膜表面的纤毛运动,促进分泌物排出,减少肺不张的形成,改善通气/血流比例和氧合,较普通吸氧装置更有优势^[17-18]。HFNC也可以清除鼻咽部解剖死腔残留的二氧化碳(CO₂),且流量越大清除率越高,使得下次吸气时,较少重吸收上次呼气末残留的CO₂,从而降低呼吸死腔量,减少呼吸作功^[19],提高肺泡通气量^[20];降低吸气相呼吸功耗,减轻呼吸困难症状,提供低水平气道正压^[21],在一定程度上复张肺泡,改善氧合^[22-24]。HFNC正逐渐成为治疗急性低氧性呼衰(AHRF)安全、有效且依从性良好的一种方式^[25]。

外科术后患者因疼痛易发生肺不张和急性呼吸窘迫综合征(ARDS),拔管后常发生低氧血症,选择恰当有效的呼吸支持氧疗方法能改善患者预后^[26]。传统认为NPPV是治疗术后呼衰的有效措施,但长时间使用NPPV可能导致痰液黏稠、胃胀气的发生。HFNC可在一定程度上弥补NPPV的缺点。但HFNC的适用人群尚不明确,既往研究显示各类外

科手术患者对HFNC的整体反应较好。但针对心脏手术患者的结论尚存在差异。杨毅等^[27]研究表明,NPPV可减轻心脏手术后患者的前负荷,改善氧合,降低呼吸功;牛新荣等^[28]研究表明,有创-无创序贯通气可提高心脏术后并发急性呼衰患者的撤机成功率。

为评价HFNC预防成人术后呼衰的有效性与安全性,本研究通过系统检索成人术后应用HFNC的相关文献,最终6篇英文文献纳入Meta分析,均为RCT,文献整体质量较高。5篇RCT报告了术后存在中高危呼衰风险患者的呼吸支持升级率,试验组呼吸支持升级率较对照组明显降低,结果表明,相对于COT,术后患者常规使用HFNC可降低呼吸支持升级率。Stéphan等^[29]研究显示,对于心胸外科术后存在呼衰或有呼衰风险的患者,HFNC预防拔管后再插管和呼衰的效果与间歇性双水平气道正压(BiPAP)相当。陈耿靖等^[30]研究发现,对于肺移植术后发生呼衰的患者,HFNC在改善氧合、降低再插管风险方面要优于无创通气。以上研究结果支持在类似患者中使用HFNC。但本次Meta分析显示,与COT比较,HFNC在减少术后患者住院病死率和住院时间方面并未体现出明显优势,但Meta分析结果优势更偏向于HFNC,尚需更多的研究进一步证明HFNC的益处。

综上所述,本次Meta分析显示,与COT比较,HFNC可降低术后呼衰患者呼吸支持升级率,从而减少住院费用。虽然COT、HFNC对患者住院病死率和住院时间的影响无差异,但优势倾向于HFNC。可以说明HFNC在预防术后呼衰方面安全有效。本次Meta分析由于纳入文献和病例数较少,无法对不同手术患者进一步分层分析。但文献异质性较低,证据论证可靠,可为临床提供参考依据。

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