

• 论著 •

螺旋型鼻肠管幽门后喂养预防神经重症患者呼吸机相关性肺炎：一项来自3个临床随机对照试验数据的回顾性分析

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【摘要】目的 探讨螺旋型鼻肠管幽门后喂养对神经重症患者呼吸机相关性肺炎(VAP)的影响。**方法** 回顾性分析2012年4月至2019年3月参与广东省人民医院3个幽门后置管随机对照试验(RCT)的175例机械通气超过48 h的神经重症成人患者临床资料。收集患者性别、年龄、神经系统疾病病因、基础疾病、用药情况、气管导管重插管、纤维支气管镜(纤支镜)检查、鼻肠管远端置管位置,以及患者入选临床试验时的急性生理学与慢性健康状况评分Ⅱ(APACHEⅡ)、序贯器官衰竭评分(SOFA)、格拉斯哥昏迷评分(GCS)、急性胃肠功能损伤(AGI)分级等临床资料。根据是否发生VAP将患者分为VAP组和非VAP组,比较两组各指标的差异,然后将单因素分析中 $P<0.1$ 的影响因素纳入多因素Logistic回归分析,确定VAP的危险因素。此外,根据鼻肠管远端置管位置将患者分为胃内组和幽门后组,对不同置管位置以及不同人群VAP发病进行亚组分析。**结果** ①175例机械通气神经重症患者中有42例发生VAP,VAP发生率为24.0%。②单因素分析显示, $P<0.1$ 的VAP影响因素有幽门后喂养、APACHEⅡ评分、GCS评分及纤支镜检查,其中VAP组幽门后喂养比例和GCS评分显著低于非VAP组[幽门后喂养:19.0%(8/42)比36.8%(49/133),GCS(分):5(3,7)比6(4,9),均 $P<0.05$]。多因素Logistic回归分析显示,幽门后喂养是减少VAP的独立保护因素[优势比(OR)=0.360,95%可信区间(95%CI)=0.151~0.857, $P=0.021$],纤支镜检查是VAP的独立危险因素($OR=2.210$,95%CI=1.051~4.647, $P=0.036$)。③经床旁X线证实的鼻肠管远端置管位置在胃内、十二指肠第一段(D1)、第二段(D2)、第三段(D3)、第四段(D4)及空肠段患者的VAP发生率分别为28.8%(34/118)、0%(0/4)、8.3%(1/12)、26.7%(4/15)、22.2%(2/9)及5.9%(1/17)。与胃内置管相比,幽门后各段置管患者的VAP发生率相对较低,但差异均无统计学意义(均 $P>0.05$)。④在全体患者中,幽门后组VAP发生率显著低于胃内组[14.0%(8/57)比28.8%(34/118), $OR=0.403$,95%CI=0.173~0.941, $P=0.032$]。根据年龄、性别、APACHEⅡ评分、SOFA评分及AGI分级对胃内喂养及幽门后喂养患者进行分层分析,结果显示,在SOFA<12分及AGI≥Ⅱ级的患者中,幽门后组VAP发生率均显著低于胃内组(SOFA<12分: $OR=0.392$,95%CI=0.154~0.995, $P=0.044$;AGI≥Ⅱ级: $OR=0.086$,95%CI=0.011~0.705, $P=0.006$)。**结论** 幽门后喂养可降低神经重症患者VAP发生率。

【关键词】 呼吸机相关性肺炎； 幽门后喂养； 神经重症； 自推进式鼻肠管

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Effect of post-pyloric feeding by spiral nasoenteric tubes on ventilator-associated pneumonia in neurocritical care patients: a retrospective analysis of three clinical randomized controlled trials

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【Abstract】Objective To explore the effect of post-pyloric feeding by spiral nasoenteric tubes on ventilator-associated pneumonia (VAP) in neurocritical care patients. **Methods** A retrospective study was performed to analyze the clinical data of 175 neurocritical care adult patients with mechanical ventilation (MV) more than 48 hours, who were enrolled in three randomized controlled trials (RCT) conducted by Guangdong Provincial People's Hospital for post-pyloric tube placement between April 2012 to March 2019. The following patient clinical data were collected when patients were enrolled: gender, age, neurologic diagnosis, comorbidities, medication, endotracheal reintubation, bronchoscope treatment, the distal site of nasoenteric tubes, and acute physiology and chronic health evaluation II (APACHE II) score, sequential organ failure assessment (SOFA) score, Glasgow coma scale (GCS) score, and acute gastrointestinal injury (AGI) grade assessed. Patients were divided into VAP group and non-VAP group according to the occurrence of VAP, and the differences of each index between the two groups were compared. Then the influencing factors of $P < 0.1$ were included in multivariate Logistic regression analysis to identify the potential risk factors affecting

the incidence of VAP. Furthermore, patients were divided into gastric feeding group and post-pyloric feeding group according to the distal site of nasoenteric tubes, and subgroup analysis was performed to evaluate the variety of VAP in patients with different tube sites and status. **Results** ① Forty-two patients occurred VAP in 175 MV patients, and the incidence of VAP was 24.0%. ② Univariate analysis showed the *P* value of post-pyloric feeding, APACHE II score, GCS score and bronchoscope treatment were less than 0.1, and post-pyloric feeding and GCS score in VAP group were significantly lower than those in non-VAP group [post-pyloric feeding: 19.0% (8/42) vs. 36.8% (49/133), GCS: 5 (3, 7) vs. 6 (4, 9), both *P* < 0.05]. Multivariate Logistic regression analysis indicated that post-pyloric feeding was independent protective factor [odds ratio (*OR*) = 0.360, 95% confidence interval (95%CI) = 0.151–0.857, *P* = 0.021] and bronchoscope treatment was the independent risk factor (*OR* = 2.210, 95%CI = 1.051–4.647, *P* = 0.036) for VAP. ③ The incidence of VAP was 28.8% (34/118), 0% (0/4), 8.3% (1/12), 26.7% (4/15), 22.2% (2/9) and 5.9% (1/17) respectively when tube tip in stomach, D1, D2, D3, D4 and jejunum confirmed by abdominal radiography. Post-pyloric feeding in each proportion seemed to present lower VAP rate compared with gastric feeding, however, no significant difference was found (all *P* > 0.05). ④ The incidence of VAP in post-pyloric feeding group was significantly lower than that in gastric feeding group [14.0% (8/57) vs. 28.8% (34/118), *OR* = 0.403, 95%CI = 0.173–0.941, *P* = 0.032]. Lower VAP rate appeared on patients with SOFA < 12 (*OR* = 0.392, 95%CI = 0.154–0.995, *P* = 0.044) and AGI grade ≥ II (*OR* = 0.086, 95%CI = 0.011–0.705, *P* = 0.006) fed by post-pyloric route according to the result of subgroup analysis stratified by age, gender, APACHE II score, SOFA score and AGI grade. **Conclusion** Post-pyloric feeding would decrease the incidence of VAP in neurocritical care patients on MV.

【Key words】 Ventilator-associated pneumonia; Post-pyloric feeding; Neurocritical care patient; Self-propelled nasoenteric tubes

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呼吸机相关性肺炎(VAP)是指气管插管或气管切开患者接受机械通气48 h后,或者撤机、拔管后48 h内发生的肺炎^[1],其发生率为2.5%~48.4%,病死率达13.0%~43.2%^[2]。早期识别并干预是减少VAP发生和死亡的关键。VAP预防集束化策略包括床头抬高30°~45°、减少有创通气、每日觉醒及自主呼吸试验等措施^[3]。研究表明,大多数医院的集束化策略都包含有益和潜在有害的元素^[4],其中幽门后喂养能否降低VAP发生率尚存争议^[5-8],且较少研究聚焦于重症加强治疗病房(ICU)内神经重症患者。本研究旨在探讨螺旋型鼻肠管幽门后喂养对神经重症患者VAP的影响及其危险因素,为早期干预提供依据。

1 资料与方法

1.1 研究对象:回顾性分析2012年4月至2019年3月参与广东省人民医院3个螺旋型鼻肠管幽门后置管随机对照试验(RCT)的重症患者数据。

1.1.1 纳入标准:入住ICU、年龄≥18岁及有创机械通气≥48 h的神经重症患者。

1.1.2 排除标准:胃食管反流者;胃造瘘或空肠造瘘者;鼻肠管置管前存在肺炎者;数据不全者。

1.1.3 伦理学:3个RCT研究均符合医学伦理学标准,经医院伦理委员会审批[审批号分别为2011132H、2015424H(R1)、2017186H],并在中国临床试验注册中心注册(注册号分别为ChiCTR-TRC-12001956、ChiCTR-INR-16008211、ChiCTR-INR-

17011311),所有治疗及检测均获得过患者或家属的知情同意。

1.2 数据收集:收集患者年龄、性别、神经系统疾病病因、基础疾病、用药情况、气管导管重插管、纤维支气管镜(纤支镜)检查、鼻肠管置管远端位置,入选临床试验时的急性生理学与慢性健康状况评分Ⅱ(APACHEⅡ)、序贯器官衰竭评分(SOFA)、格拉斯哥昏迷评分(GCS)、急性胃肠功能损伤(AGI)分级等临床资料。

1.3 鼻肠管置管方法:所有患者均经床旁被动等待法放置CH10型螺旋型鼻肠管,依靠患者胃肠动力使管道自推进式前行;置管后24 h经床旁X线腹部摄片证实鼻肠管远端位置,并将管道固定在患者鼻部。

1.4 病例分组:根据VAP诊断标准将患者分为VAP组和非VAP组。根据置管位置将患者分为胃内组和幽门后组。

1.5 统计学方法:采用SPSS 24.0软件进行数据处理。正态分布的计量资料用均数±标准差($\bar{x} \pm s$)表示,组间比较采用独立样本t检验;非正态分布的计量资料以中位数(四分位数)[$M(Q_L, Q_U)$]表示,组间比较采用Mann-Whitney U检验;计数资料组间比较采用 χ^2 检验或Fisher确切概率法。对影响VAP发病的指标先进行单因素分析,再将 $P < 0.1$ 的影响因素纳入多因素分析,应用Logistic多元逐步回归法(后向)确定最终进入模型的危险因素。

$P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 患者基本情况:175例患者中男性111例,女性64例;年龄18~87岁,中位年龄59(49, 69)岁;神经系统疾病病因:血管性89例(占50.8%),肿瘤性50例(占28.6%),创伤性15例(占8.6%),其他21例(占12.0%);APACHE II评分(21.2±5.5)分,SOFA评分9(7, 12)分;共有42例患者发生VAP,VAP发生率为24.0%。

2.2 VAP组与非VAP组临床资料比较(表1):VAP组患者幽门后喂养比例及GCS评分均显著低于非VAP组(均 $P < 0.05$);两组患者性别、年龄、神经系统疾病病因、基础疾病、APACHE II评分、SOFA评分、AGI分级、用药情况、气管插管重插管、纤支镜检查等临床资料比较差异无统计学意义(均 $P > 0.05$)。

表1 VAP组与非VAP组经螺旋型鼻肠管幽门后喂养神经重症患者临床资料比较

指标	VAP组 (n=42)	非VAP组 (n=133)	$\chi^2/Z/t$	P值
男性[例(%)]	28(66.7)	83(62.4)	0.250	0.617
年龄[岁, M(Q _L , Q _U)]	58(48, 69)	61(51, 70)	-1.115	0.266
神经系统疾病[例(%)]				
血管性	20(47.6)	69(51.9)	0.232	0.630
肿瘤性	15(35.7)	35(26.3)	1.382	0.240
创伤性	3(7.1)	12(9.0)	0.144	0.704
其他	4(9.6)	17(12.8)	0.321	0.571
基础疾病[例(%)]				
高血压	16(38.1)	63(47.4)	1.108	0.292
糖尿病	5(11.9)	20(15.0)	0.256	0.613
COPD	3(7.1)	3(2.3)	1.063	0.303
慢性肾衰竭	2(4.8)	6(4.5)	0.000	1.000
心力衰竭	3(7.1)	4(3.0)	0.549	0.459
冠心病	1(2.4)	8(6.0)	0.280	0.597
吸烟史[例(%)]	5(11.9)	10(7.5)	0.324	0.569
幽门后喂养[例(%)]	8(19.0)	49(36.8)	4.602	0.032
缩血管药[例(%)]	18(42.9)	55(41.4)	0.030	0.863
镇静药[例(%)]	22(52.4)	68(51.1)	0.020	0.887
糖皮质激素[例(%)]	18(42.9)	54(40.6)	0.067	0.796
气管导管重插管[例(%)]	8(19.0)	13(9.8)	2.599	0.107
纤维支气管镜检查 [例(%)]	18(42.9)	37(27.8)	3.349	0.067
APACHE II(分, $\bar{x} \pm s$)	22.5±5.5	20.7±5.5	-1.762	0.080
SOFA [分, M(Q _L , Q _U)]	9(7, 11)	9(7, 12)	-0.023	0.982
GCS [分, M(Q _L , Q _U)]	5(3, 7)	6(4, 9)	-2.534	0.011
AGI分级[例(%)]			-0.439	0.660
I级	27(64.3)	80(60.2)		
II级	13(30.9)	47(35.3)		
III级	2(4.8)	6(4.5)		

注:VAP为呼吸机相关性肺炎,COPD为慢性阻塞性肺疾病,APACHE II为急性生理学与慢性健康状况评分II,SOFA为序贯器官衰竭评分,GCS为格拉斯哥昏迷评分,AGI为急性胃肠功能损伤

2.3 VAP危险因素的Logistic回归分析(表2):将单因素分析中 $P < 0.1$ 的影响因素,即幽门后喂养、纤支镜检查、APACHE II评分及GCS评分,经多因素Logistic回归分析其所占的权重,结果显示,幽门后喂养是减少ICU神经重症患者发生VAP的独立保护因素($P < 0.05$),纤支镜检查是发生VAP的独立危险因素($P < 0.05$)。

表2 经螺旋型鼻肠管幽门后喂养的神经重症患者发生VAP危险因素的多因素Logistic回归分析

影响因素	β 值	s_{β}	$\chi^2/Z/t$ 值	P值	OR值	95%CI
幽门后喂养	-1.022	0.442	5.336	0.021	0.360	0.151~0.857
纤维支气管 镜检查	0.793	0.379	4.377	0.036	2.210	1.051~4.647
常量	-1.151	0.243	22.405	<0.001	0.316	

注:VAP为呼吸机相关性肺炎,OR为优势比,95%CI为95%可信区间;空白代表无此项

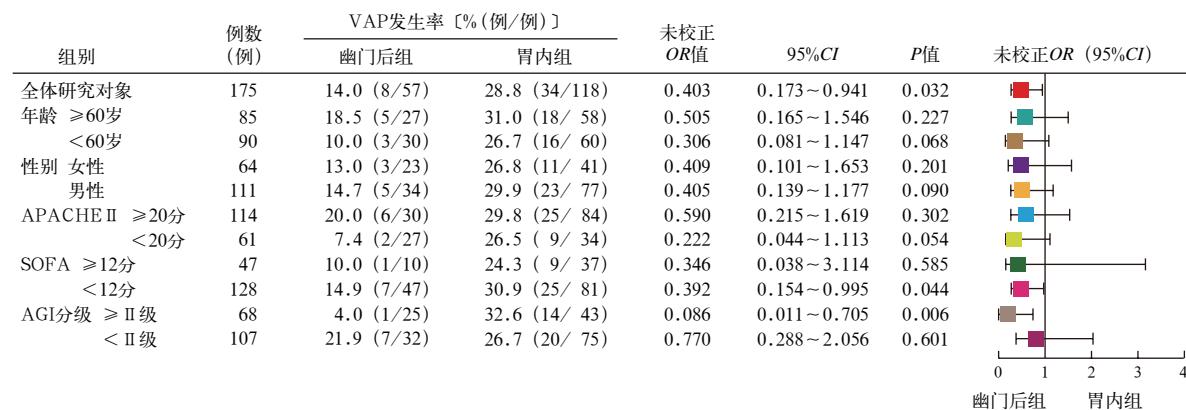
2.4 鼻肠管远端置管位置对VAP的影响(表3):鼻肠管自推进式前行后分别定位于胃内、十二指肠第一段(D1)、第二段(D2)、第三段(D3)、第四段(D4)及空肠段,其VAP发生率分别为28.8%、0%、8.3%、26.7%、22.2%及5.9%。与胃内置管患者相比,幽门后各段置管患者VAP发生率相对更低,但差异均无统计学意义(均 $P > 0.05$)。

表3 鼻肠管远端置管位置对神经重症患者发生VAP的影响

置管 位置	例数 (例)	VAP发生率 [% (例)]	未校正 OR值	95%CI	P值
胃内	118	28.8(34)	1.000	参考	
D1	4	0(0)		1.000	
D2	12	8.3(1)	0.225	0.028~1.808	0.160
D3	15	26.7(4)	0.898	0.267~3.018	0.862
D4	9	22.2(2)	0.706	0.140~3.571	0.674
空肠段	17	5.9(1)	0.154	0.020~1.211	0.075

注:VAP为呼吸机相关性肺炎,D1、D2、D3、D4分别为十二指肠第一段、第二段、第三段、第四段,OR为优势比,95%CI为95%可信区间;空白代表无此项

2.5 不同人群VAP发病的亚组分析(图1):对全体175例患者分析显示,与胃内组相比,幽门后组VAP发生率明显降低[优势比(OR)=0.403,95%可信区间(95%CI)=0.173~0.941, $P < 0.05$]。根据患者年龄、性别、APACHE II评分、SOFA评分及AGI分级对胃内喂养及幽门后喂养进行分层分析,结果显示,在SOFA<12分及AGI≥Ⅱ级的患者中,幽门后组VAP发生率均显著低于胃内组[OR值分别为0.392(95%CI=0.154~0.995)和0.086(95%CI=0.011~0.705),均 $P < 0.05$],而在其他情况下,两组VAP发生率差异无统计学意义。



注: VAP 为呼吸机相关性肺炎, APACHE II 为急性生理学与慢性健康状况评分 II, SOFA 为序贯器官衰竭评分, AGI 为急性胃肠功能损伤, OR 为优势比, 95%CI 为 95% 可信区间

图1 幽门后喂养对比胃内喂养神经重症患者 VAP 发生率的亚组分析

3 讨论

本研究中 VAP 总体发生率为 24.0%, 表明神经重症患者仍然是 VAP 的高发人群, 可能与神经重症患者长期处于意识障碍或昏迷状态、缺乏气道保护能力, 增加误吸风险有关, 也与神经重症疾病是 VAP 发病的重要危险因素相符^[9-10]。各研究间 VAP 发生率差别较大^[5, 11-13], 可能与各项研究所采用的诊断标准、干预措施、样本量、研究对象及统计学方法等差异有关。

既往许多临床试验对重症患者 VAP 的危险因素进行了研究, 发现众多医疗环境及患者自身因素对 VAP 的发生都会产生影响^[14-16]。本结果显示, 幽门后喂养是减少 VAP 的独立保护因素, 而纤支镜检查则是独立危险因素。幽门后喂养是重症患者肠内营养的重要方式, 尤其是胃潴留严重、无法耐受经胃喂养的患者, 多个指南推荐应优先选择幽门后喂养来降低反流、误吸的风险^[17]。而误吸又是 VAP 的主要危险因素之一, 因此, 幽门后喂养具有减少 VAP 的潜力。此外, 纤支镜检查属于侵入性较大的呼吸道有创操作, 可能使气道细菌定植概率增加^[11, 18]; 纤支镜操作不规范或未严格掌握适应证, 也有诱发 VAP 的可能性。这提示我们可能需要重新评估纤支镜检查的利弊, 避免不当操作, 包括纤支镜侵入性获得呼吸道标本(如支气管肺泡灌洗液(BALF))的必要性^[19]。有研究表明, 与非侵入性标本半定量培养相比, 侵入性标本定量培养对判断预后并没有优势^[2, 20]。因此, 纤支镜检查与 VAP 之间的关系值得我们进一步探讨。

本次研究中所有受试对象均采用床旁被动等待法来完成幽门后置管^[21], 因此管道远端会出现在

胃肠道的不同段位。结果显示, 与胃内置管相比, 幽门后各段置管患者 VAP 发生率相对较低, 但差异均无统计学意义。考虑到本研究已明确幽门后喂养可降低 VAP 发生率, 本组结果差异不显著可能与幽门后分段较多而各段例数较少有关, 因此需要更大样本量的研究来进一步探讨幽门后不同置管段位对 VAP 的预防作用。

神经重症患者疾病各异、状态不一, 因而对人群 VAP 发病进行亚组分析。SOFA 评分是评估患者病情严重程度的指标, 分值越高, 病情越重, 进而影响胃肠蠕动功能^[6]。本研究结果显示, 在 SOFA≥12 分的患者中, 幽门后组 VAP 发生率低于胃内组, 但差异无统计学意义。考虑到幽门后组只有 10 例患者, 且仅有 1 例发生 VAP, 因而可能是样本量严重不足或偶然性引起的差异不显著。对于 SOFA<12 分的患者, 两组 VAP 发生率 OR 值的 95%CI 非常接近界值 1, 提示可能存在统计学误差, 需持谨慎态度。AGI 分级是评估患者胃肠功能损伤严重程度的指标, 分级越高, 损伤越严重。本研究显示, 与胃内组相比, 幽门后组可显著降低 AGI≥Ⅱ 级患者的 VAP 发生率, 这与指南推荐神经重症患者应优先选择小肠内营养相符^[22]。

既往研究证实, 幽门后喂养可降低严重创伤脑病患者 VAP 发生率^[23-24]。本研究可谓是幽门后喂养预防神经重症患者 VAP 的拓展性探索。鉴于神经重症患者病情相对复杂、变化较为急骤, 常需出 ICU 进行相关检查, 给患者带来极大的安全隐患, 因此对于适合放置鼻肠管的神经重症患者, 为避免增加外出置管的风险或床旁内镜置管的负担, 可采用本研究中的床旁被动等待法来实现幽门后置管^[25-26]。

综上所述,幽门后喂养是减少VAP的独立保护因素,可降低神经重症患者VAP发生率,而纤支镜检查是VAP的独立危险因素,因此可采取相应措施来预防VAP的发生。本研究是回顾性设计,因而难以避免数据缺失、回顾偏倚等不足,证据可信度有限,需要高质量的RCT研究来证实。此外,研究人群相对特殊、管道分段也较多,因而可能存在样本量不足的情况。但本次研究不同喂养方式对神经重症患者VAP的影响,具有重要的临床意义,可为进一步研究提供一定的参考价值。

利益冲突 所有作者均声明不存在利益冲突

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