

doi: 10.13241/j.cnki.pmb.2015.17.027

高频振荡呼吸机治疗呼吸窘迫综合征致呼吸机相关性肺损伤的疗效观察

魏 兵¹ 何琳莉² 石 伟³ 刘国群¹ 谢 驰¹

(1 崇州市妇幼保健院儿科 四川 成都 611230; 2 重庆医科大学附属儿童医院呼吸科 重庆 400013;

3 四川省人民医院儿科 四川 成都 610072)

摘要 目的:观察高频振荡呼吸机在治疗呼吸窘迫综合征(NRDS)致呼吸机相关性肺损伤(VALI)患儿的临床疗效。**方法:**选择我院2012年6月~2014年10月收治的NRDS致VALI患儿83例为研究对象,采用随机数字表法将患者随机分为研究组(45例)和对照组(38例)。两组均进行一般治疗,在此基础上对照组采用常规机械通气,研究组采用高频振荡呼吸机行高频通气。观察两组患者治疗24h后pH值、二氧化碳分压(PaCO₂)、氧分压(PaO₂)、血压(BP)、心率(HR)及并发症情况。**结果:**两组患者治疗24h后pH值、PaCO₂、PaO₂及BP比较,差异均无统计学意义(P>0.05),研究组HR心率低于对照组,差异存在统计学意义(P<0.05);研究组纵膈气肿、肺损伤、间质气肿及气胸的发生率均低于对照组,差异有统计学意义(P<0.05)。**结论:**高频振荡呼吸机治疗NRDS致VALI患儿能够明显改善其症状及减少并发症的发生率,是治疗NRDS致VALI的有效的方式。

关键词: 高频振荡呼吸机;呼吸窘迫综合征;呼吸机相关性肺损伤;新生儿

中图分类号: R725.6 **文献标识码:** A **文章编号:** 1673-6273(2015)17-3301-03

Effect of High Frequency Oscillatory Ventilation in the Treatment of Ventilator-Associated Lung Injury Induced by Neonatal Respiratory Distress Syndrome

WEI Bing¹, HE Lin-Li², SHI Wei³, LIU Guo-qun¹, XIE Chi¹

(1 Department of Paediatrics, Chongzhou Maternal and Children Health Hospital, Chengdu, Sichuan, 611230, China;

2 Department of Respiration, Affiliated Children's Hospital of Chongqing Medical University, Chongqing, 400013, China;

3 Department of Paediatrics, People's Hospital of Sichuan Province, Chengdu, Sichuan, 610072, China)

ABSTRACT Objective: To explore the clinical effect of high frequency oscillatory ventilation in the treatment of newborn with ventilator-associated lung injury (VALI) induced by neonatal respiratory distress syndrome(NRDS). **Methods:** 83 cases of newborn with VALI induced by NRDS who were treated in our hospital from June 2012 to October 2014 were selected as research objective, they were divided into research group (43 newborns) and control group (38 newborns) according to the random number table method. Firstly, two groups were treated with routine therapy, then the control group was underwent conventional mechanical ventilation, while the research group was underwent high frequency oscillatory ventilation. Observed pH, PaCO₂, PaO₂ BP value and the incidence of complication between the two groups 24h after treatment. **Results:** pH, PaCO₂, PaO₂ and BP value had no significant difference between two groups (P>0.05), but the HR value in research group was significant lower than control group (P<0.05); The incidence of mediastinal emphysema, lung injury, interstitial emphysema and pneumothorax in research group were significant lower than control group(P<0.05). **Conclusion:** High frequency oscillatory ventilation in the treatment of newborn with VALI induced by NRDS can significantly improve the symptom and reduce the incidence of complication, which is an effective treatment.

Key words: High frequency oscillatory ventilation; Neonatal respiratory distress syndrome; Ventilator-associated lung injury; Newborn

Chinese Library Classification(CLC): R725.6 **Document code:** A

Article ID: 1673-6273(2015)17-3301-03

前言

新生儿呼吸窘迫综合征(neonatal respiratory distress syndrome, NRDS), 亦称肺透明膜病(hyaline membrane disease, HMD), 是新生儿常见的呼吸系统疾病之一^[1], 多发于早产儿,

其主要由患者Ⅱ型肺泡上皮细胞合成、分泌肺表面活性物质(pulmonary surfactant, PS)不足或缺乏引起患者肺不张、肺泡萎陷等临床症状, 患儿病情一般发展较快, 早期病死率高^[2,3]。患儿通常会出现呼吸困难, 甚至呼吸衰竭, 因此, 呼吸窘迫综合征患儿需要采取机械通气的方式进行治疗^[4]。但机械通气过程中产生较高压力导致呼吸机相关的肺损伤(ventilator-associated lung injury, VALI)发生, 严重影响新生儿的生命安全^[5,6]。因此, 在治疗患儿NRDS过程如何采取有效措施, 避免VALI的发生

作者简介: 魏兵(1975-), 男, 本科, 主治医师, 从事儿内外科方面的研究, E-mail: hhuuh444@126.com

(收稿日期: 2015-01-06 接受日期: 2015-01-27)

具有重要意义。目前,相关研究显示,高频振荡呼吸机在治疗 NRDS 致 VALI 患儿过程中,对患儿肺功能具有保护性作用^[7],且较常规机械通气治疗具有良好的效果,但既往在国内报道较少。本研究旨在探究常规机械通气治疗与高频振荡呼吸机治疗的疗效,现报道如下。

1 对象与方法

1.1 研究对象

以我院 2012 年 6 月~2014 年 10 月期间收治的 83 例

NRDS 致 VALI 患儿。纳入排除标准:①所有患儿均确诊为 NRDS,并且符合 VALI 的诊断标准;②所有患儿均无先天性畸形,无吸入性肺炎;③所有患儿均无其它相关严重并发症;④所有患儿家属知情同意,并签署《知情同意书》;⑤排除不满足上述标准或项目研究中途退出的患儿。采用随机数字法将所有患儿随机分为两组,其中,研究组 45 例和对照组 38 例,两组患儿间性别、胎龄、出生体重、发病时间、1min Apgar 评分及早产儿发生情况比较,差异均无统计学意义($P>0.05$),两组间具有可比性,见表 1。

表 1 两组基线资料的比较
Table 1 Comparison of basic data in two groups

分组 Groups	n	性别(男/女) Gender (male/female)	胎龄(周) Gestational age (week)	出生体重(kg) Birth weight (kg)	发病时间(h) Disease time(h)	1min Apgar 评分 1min Apgar score	早产儿(是/否) Premature infant (yes/no)
对照组 Control group	38	20/18	38.56± 2.43	2.83± 0.48	3.73± 1.14	5.32± 0.71	9/29
研究组 Research group	45	24/21	35.12± 2.61	2.81± 0.51	3.98± 1.21	5.12± 0.59	14/31
t/x ²		0.004	1.431	0.314	0.931	0.210	0.567
P		0.949	0.153	0.752	9.356	0.832	0.451

1.2 方法

所有患儿入院后检测其生命体征,并进行一般治疗,包括保暖、使用抗生素、预防感染及出血、营养支持,静脉滴注还原性谷胱甘肽,维持水、电解质及酸碱平衡以及保护患儿的各脏器功能等。在此基础上,对照组给予常规的机械通气方式治疗,使用 Drger Evita® XL 呼吸机(由德尔格医疗有限公司生产),具体参数设置如下:氧浓度为 60%~100%、呼吸频率为 30~60 次/分钟、呼气末气道正压为 0.4 kPa、吸气峰压为 2 kPa 及吸/呼比为 1:2,通气进行 30 分钟后对患儿动脉血气进行分析,根据其临床变现及时调整呼吸参数。对研究组给予高频振荡呼吸机进行高频通气治疗,使用 Sensor Medics 3100A 型高频振荡呼吸机(由美国森迪斯医学仪器有限公司提供),具体参数设置如下:振荡频率为 15 Hz、氧浓度为 60%~100%、气道压为 1.5~2 kPa、振荡压力幅度为 3.5 kPa、偏置流速 6~8L/分钟及吸/呼比为 1:3,通气进行 30 分钟后对患儿动脉血气进行分析,并根据其临床变现及时调整呼吸参数。两组患儿持续治疗过程中对其各项生命体征指标的变化变化情况进行检测,待其面色红润、各项生命体征稳定、血气分析正常、且 X 线胸片显示肺通气功

能正常后,逐步下调治疗参数,直到撤离呼吸机或进行无创性持续呼吸道正压通气治疗。

1.3 观察指标

观察两组患者治疗 24 h 后 pH 值、氧分压(PaO_2)、二氧化碳分压(PaCO_2)、血压(BP)、心率(HR)及并发症的发生情况。

1.4 统计学方法

研究所得数据采用 epidata 软件进行双人录入校对后建立数据库,所得数据采用 SPSS16.0 软件进行分析,对定量资料采用($\bar{x} \pm s$)表示。组间计量资料采用两独立样本的 t 检验,组内计量资料采用配对设计的 t 检验;计数资料采用卡方检验,检验水准 $\alpha=0.05$ 。

2 结果

2.1 两组治疗 24 h 后 PaCO_2 、 PaO_2 、BP 及 HR 比较

两组患者治疗 24 h 后 pH 值、 PaCO_2 、 PaO_2 及 BP 差异均无统计学意义($P>0.05$),研究组 HR 心率低于对照组,差异存在统计学意义($P<0.05$),见表 2。

表 2 两组患儿治疗 24 h 后 pH、 PaCO_2 、 PaO_2 、BP 及 HR 比较
Table 2 Comparison of pH, PaCO_2 , PaO_2 , BP and HR value in two groups 24 h after treatment

组别 Groups	n	pH	PaCO_2 (p/kPa)	PaO_2 (p/kPa)	HR(time/min)	BP(p/kPa)
对照组 Control group	38	7.44± 0.11	5.93± 0.93	7.55± 1.54	146± 12	5.73± 0.48
研究组 Research group	45	7.43± 0.14	6.12± 1.23	7.93± 1.73	113± 14	6.35± 0.61
t		0.013	0.133	0.521	6.394	1.321
P		0.976	0.892	0.603	0.000	0.183

2.2 两组患儿并发症发生率比较

两组患者并发症比较显示,研究组纵膈气肿、肺损伤、间质气肿及气胸的发生率均低于对照组,差异有统计学意义

($P<0.05$);间质气肿合并气胸两组间比较,差异无统计学意义($P>0.05$),见表 3。

表 3 两组患儿并发症发生率比较
Table 3 Comparison of incidence of complication in two groups

组别 Groups	n	纵膈气肿 Mediastinal emphysema	肺损伤 Lung injury	间质气肿 Interstitial emphysema	气胸 Pneumothorax	间质气肿合并气胸 Interstitial emphysema combined pneumothorax
对照组 Control group	38	6(15.79%)	18(47.37%)	6(15.79%)	7(18.42%)	1(2.63%)
研究组 Research group	45	1(2.22%)	6(13.33%)	1(2.22%)	2(4.44%)	1(2.22%)
χ^2		4.632	11.611	4.911	4.163	0.015
P		0.031	0.001	0.027	0.041	0.904

3 讨论

NRDS 是新生儿常见的呼吸系统疾病,是由 II 型肺泡上皮细胞合成、分泌 PS 不足或缺乏引起,表现为肺不张、肺泡萎陷等。患儿往往出现呼吸困难,甚至导致呼吸衰竭,因此,机械通气在 NRDS 治疗中发挥着重要的作用。研究显示,机械通气在 NRDS 治疗中仍发挥重要的作用,可以减少 NRDS 的病死率^[8]。机械通气的目的是减小患儿肺损伤、血流动力学伤害及其他不良反应的通气,维持患儿血气分析处于正常水平^[9]。但所有的机械通气对患儿肺功能均存在一定的危害^[10]。由于其通气模式为通过压力控制潮气量的大小,但因为缺乏对潮气量的监测,患儿吸气的调整较为盲目,因而,可能导致过高的压力和过长的吸气时间产生,使平均气道压力和跨肺压增加,导致肺功能损伤、发生肺气漏、坏死性气管支气管及慢性肺疾病炎等,导致 VALI 的发生^[11-13]。因此在 NRDS 呼吸机支持治疗过程中减少使用呼吸机引起的并发症受到临床医生的高度重视。并相应的出现了许多种方法和手段来减少或降低并发症的发生,包括降低跨肺压和低潮气量通气、适当的呼气末正压、PS 的应用和高频振荡呼吸机治疗等^[14,15]。其中,高频振荡呼吸机治疗现在已成为发达国家治疗 NRDS 不可缺少的方法。与常规机械通气治疗相比,具有潮气量小、气道压低、肺泡直接通气、利用高速流动的气体来增加弥散和对流、肺部区域进行不均匀性气体交换等优势^[16,17]。从而使肺组织进行气体交换更加迅速和有效,改善患儿氧合和二氧化碳排出的情况,能够有效地避免或减少肺泡因过度扩张导致的气压伤及慢性肺损伤,减少气道对氧和压力的要求^[18]。本研究选择我院 2012 年 6 月~2014 年 10 月期间收治的 NRDS 致 VALI 患儿 83 例为研究对象,探究高频振荡呼吸机治疗 NRDS 致 VALI 患儿的疗效,为临床实践提供依据。

目前,VALI 的发病原因极其复杂,牵涉到很多因素,随着临床研究成果的不断报道,Liu S 等人的研究结果表明,VALI 发生的主要因素可能是高气道压、过度增加肺容积以及肺组织过度扩张所导致的^[19]。Shetty S 等人在机械通气治疗 NRDS 过程中对患儿实施肺保护性通气策略,结果发现 VALI 的发生率明显降低,肺部气体氧合得到明显改善,血氧分压维持稳定,氧疗时间以及上机时间显著缩短^[20]。本研究显示,所有患者在治疗 24h 后,两组间 PaCO₂、PaO₂ 及 BP 不存在显著性差异(P>0.05),研究组 HR 心率低于对照组,差异存在统计学意义(P<0.05),说明两种方式在改善 NRDS 致 VALI 患儿血流动力学方面不存在差异,但研究组在改善心率上存在更明显的优势,说明高频振荡呼吸机较机械通气更具有优势,与相关研究一致^[21]。此

外,本研究结果显示,研究组纵膈气肿、肺损伤、间质气肿及气胸的发生率均低于对照组,差异有统计学意义(P<0.05);间质气肿合并气胸两组间比较,差异无统计学意义(P>0.05),提示高频振荡呼吸机能够明显恢复患儿的肺通气,改善循环系统,且可以明显减少并发症的发生。国外 John J 等人的报道也证实肺功能保护通气策略,可以减少 VALI 肺出血等并发症的发生及病死的发生,能够显著改善患儿的呼吸状况^[22]。

综上所述,采取高频振荡呼吸机治疗 NRDS 能够降低 VALI 的发生,且高频振荡呼吸机治疗在 NRDS 致 VALI 上能够明显改善患儿的血气指数、肺通气的恢复及减少并发症的发生率,是治疗 NRDS 致 VALI 的有效的方式。

参考文献(References)

- [1] Liu J Md PhD, Cao H Md, Wang H Md, et al. The Role of Lung Ultrasound in Diagnosis of Respiratory Distress Syndrome in Newborn Infants[J]. Iran J Pediatr, 2014, 24(2): 147-154
- [2] Gyamfi-Bannerman C, Son M. Preterm premature rupture of membranes and the rate of neonatal sepsis after two courses of antenatal corticosteroids[J]. Obstet Gynecol, 2014, 124(5): 999-1003
- [3] Mullooney T, Manson D, Kim R, et al. Primary ciliary dyskinesia and neonatal respiratory distress[J]. Pediatrics, 2014, 134(6): 1160-1166
- [4] 马希刚, 马辉. 20 例急性呼吸窘迫综合征的诊断和治疗 [J]. 宁夏医学院学报, 2000, 22(5): 367-368
Ma Xi-gang, Ma Hui. Diagnosis and treatment of 20 cases of patients acute respiratory distress syndrome [J]. Journal of Ningxia Medical College, 2000, 22(5): 367-368
- [5] Thall PF, Nguyen HQ, Zohar S, et al. Optimizing Sedative Dose in Preterm Infants Undergoing Treatment for Respiratory Distress Syndrome[J]. J Am Stat Assoc, 2014, 109(507): 931-943
- [6] Zaccagni HJ, Timpa JG, O'Meara LC, et al. Long-term membrane oxygenator use to support an infant with acute respiratory distress syndrome on biventricular assist device [J]. Interact Cardiovasc Thorac Surg, 2013, 17(1): 196-198
- [7] Fröhlich MR, Meier MT, Staudacher D, et al. Prevention of ventilator associated pneumonia at the University of Zurich intensive care unit. Ventilator associated pneumonia-an intensive problem[J]. Krankenhpf Soins Infirm, 2014, 107(9): 30-31
- [8] Pérez LA, González DM, Alvarez KM, et al. Nasal CPAP versus mechanical ventilation in 28 to 32-week preterm infants with early surfactant administration[J]. Biomedica, 2014, 34(4): 612-623
- [9] Premnath D, Kent AL, Bajuk B, et al. Does timing of initial surfactant treatment make a difference in rates of chronic lung disease or mortality in premature infants? An observational regional study [J]. J Matern Fetal Neonatal Med, 2014, 8:1-8

- increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review [J]. *Am J Obstet Gynecol*, 2012, 207(1): 14-29
- [9] Aguirre J, Baulig B, Dora C, et al. Continuous epicapsular ropivacaine 0.3% infusion after minimally invasive hip arthroplasty: a prospective, randomized, double-blinded, placebo-controlled study comparing continuous wound infusion with morphine patient-controlled analgesia[J]. *Anesth Analg*, 2012, 114(2): 456-461
- [10] Ross PA, Smith BM, Tolo VT, et al. Continuous infusion of bupivacaine reduces postoperative morphine use in adolescent idiopathic scoliosis after posterior spine fusion [J]. *Spine (Phila Pa 1976)*, 2011, 36(18): 1478-1483
- [11] Strazisar B, Besic N. Comparison of continuous local anaesthetic and systemic pain treatment after axillary lymphadenectomy in breast carcinoma patients-a prospective randomized study[J]. *Radiol Oncol*, 2013, 47(2): 145-153
- [12] Forastiere E, Sofra M, Giannarelli D, et al. Effectiveness of continuous wound infusion of 0.5% ropivacaine by On-Q pain relief system for postoperative pain management after open nephrectomy [J]. *Obstet Gynecol*, 2008, 101(6): 841-847
- [13] Morgan SJ, Jeray KJ, Saliman LH, et al. Continuous infusion of local anesthetic at iliac crest bone-graft sites for postoperative pain relief. A randomized, double-blind study [J]. *J Bone Joint Surg Am*, 2006, 88(12): 2606-2612
- [14] Kristensen BS, Fenger-Eriksen C, Pedersen KV, et al. Wound infusion of bupivacaine following radical retropubic prostatectomy: a randomised placebo-controlled clinical study [J]. *Eur J Anaesthesiol*, 2013, 30(3): 124-128
- [15] Clark EA, Varner M. Impact of preterm PROM and its complication on long-term infant outcomes [J]. *Clin Obstet Gynecol*, 2011, 54(2): 358
- [16] Jones HE, Harris KA, Azizia M, et al. Differing Prevalence and Diversity of Bacterial Species in Fetal Membranes from Very Preterm and Term Labor[J]. *PLoS One*, 2009, 4(12): 8205-8205
- [17] Queiros da Mota V, Prodhom G, Yan P, et al. Correlation between placental bacterial culture results and histological chorioamnionitis: a prospective study on 376 placentas [J]. *Clin Pathol*, 2013, 66(3): 243-248
- [18] C. Loubert, A. Hinova, R. Fernando. Update on modern neuraxial analgesia in labour: a review of the literature of the last 5 years. *Anaesthesia*, 2011, 66(3): 191-212
- [19] Cheng SL, Bautista D, Leo S, et al. Factor affecting fetal bradycardia following combined spinal epidural for labor analgesia: a matched case-control study[J]. *J Anesth*, 2013, 27(2): 169-174
- [20] Kuczkowski KM. Severe persistent fetal bradycardia following subarachnoid administration of fentanyl and bupivacaine for induction of a combined spinal-epidural analgesia for labor pain [J]. *J Clin Anesth*, 2004, 16(1): 78-79

(上接第 3303 页)

- [10] Duman N, Tü zü n F, Sever AH, et al. Nasal Intermittent Positive Pressure Ventilation With Or Without Very Early Surfactant Therapy For The Primary Treatment Of Respiratory Distress Syndrome [J]. *J Matern Fetal Neonatal Med*, 2014, 10: 1-22
- [11] Sadeghnia A, Tanhaei M, Mohammadizadeh M, et al. A comparison of surfactant administration through i-gel and ET-tube in the treatment of respiratory distress syndrome in newborns weighing more than 2000 grams[J]. *Adv Biomed Res*, 2014, 31(3): 160
- [12] Fröhlich MR, Meier MT, Staudacher D, et al. Prevention of ventilator associated pneumonia at the University of Zurich intensive care unit. Ventilator associated pneumonia - an intensive problem [J]. *Krankenpfl Soins Infirm*, 2014, 107(9): 30-31
- [13] Myers A, Bernstein JA, Brennan ML, et al. Perinatal features of the RASopathies: Noonan syndrome, cardiofaciocutaneous syndrome and Costello syndrome[J]. *Am J Med Genet A*, 2014, 164(11): 2814-2821
- [14] Reuter S, Moser C, Baack M. Respiratory distress in the newborn[J]. *Pediatr Rev*, 2014, 35(10): 417-428
- [15] Myers A, Bernstein JA, Brennan ML, et al. Perinatal features of the RASopathies: Noonan syndrome, cardiofaciocutaneous syndrome and Costello syndrome[J]. *Am J Med Genet A*, 2014, 164(11): 2814-2821
- [16] Hirayama T, Nagano O, Shiba N, et al. Mean Lung Pressure during Adult High-Frequency Oscillatory Ventilation: An Experimental Study Using a Lung Model [J]. *Acta Med Okayama*, 2014, 68(6): 323-329
- [17] Zhu F, Zeng N, Luo Y, et al. Effects of different position during high frequency oscillatory ventilation on oxygenation and hemodynamics of dogs with severe smoke inhalation injury [J]. *Chinese Journal of Burns*, 2014, 30(1): 51-55
- [18] Gao Z, Liu L, Liu S, et al. High-frequency oscillatory ventilation in patients with acute respiratory distress syndrome: a meta-analysis[J]. *National Medical Journal of China*, 2014, 94(27): 2110-2114
- [19] Liu S, Huang Y, Wang M, et al. Effects of high-frequency oscillatory ventilation and conventional mechanical ventilation on oxygen metabolism and tissue perfusion in sheep models of acute respiratory distress syndrome[J]. *Chin Med J*, 2014, 127(18): 3243-3248
- [20] Shetty S, Greenough A. Neonatal ventilation strategies and long-term respiratory outcomes[J]. *Early Hum Dev*, 2014, 90(11): 735-739
- [21] Alzahrany M, Banerjee A, Salzman G. The role of coupled resistance-compliance in upper tracheobronchial airways under high frequency oscillatory ventilation [J]. *Med Eng Phys*, 2014, 36(12): 1593-1604
- [22] John J, Bhaskar P, Lone RA, et al. Use of high-frequency ventilation to wean off cardiopulmonary bypass in a patient with pulmonary hemorrhage after failure of conventional ventilation[J]. *J Clin Anesth*, 2014, 26(8): 699-701