Original Article

DOI: 10.4274/tpa.585

High-frequency oscillatory ventilation in newborn: three years of experience

Aytuğ Atıcı, Selvi Gülaşı, Yalçın Çelik, Ali Haydar Turhan, Mehmet Ali Sungur*

Mersin University Medical Faculty, Department of Pediatrics, Division of Neonatology, Mersin, Turkey

**Mersin University Medical Faculty, Department of Biostatistics and Medical Informatics, Mersin, Turkey*

Summary

Aim: The aim of this study was to evaluate the indications, effectiveness and complications of high-frequency oscillatory ventilation (HFOV) in infants who were ventilated with HFOV in the last three years.

Material and Method: The study was conducted in the neonatal intensive care unit of Mersin University Hospital. Medical files of 40 infants who were ventilated by HFOV between January 2008 and December 2010 were evaluated retrospectively. The babies who died within the first four hours of HFOV were excluded. Conventional mechanical ventilation modes, duration of ventilation, complications, indications for HFOV, blood gases and changes in ventilator settings during HFOV were recorded. Chi-square test was used for the statistical analysis of the data. The significance level for all data was set at $p<0.05$.

Results: Hemoglobin-oxygen saturation significantly increased after one hour of HFOV application and pH significantly increased after four hours of HFOV application. pCO_2, FiO_2 and amplitude values significantly decreased after one hour of HFOV application ($p< 0.05$). The mean values of peak inspiratory pressure (PIP) and mean airway pressure (MAP) were 25.9 and 10.6 cm H_2O, respectively at the time of switching from conventional ventilation to HFOV.

Conclusions: The study revealed that more than half of the babies who had pneumothorax or needed more than 25 cm H_2O of PIP to maintain tidal volume but failed to improve blood gases during conventional mechanical ventilation could be saved and discharged by using HFOV. *(Turk Arch Ped 2012; 47: 18-22)*

Key words: High-frequency oscillatory ventilation, newborn

Introduction

Although efficent use of ventilators in neonatal intensive care units has increased, respiratory failure due to lung diseases continues to be a significant reason of mortality and disabilities in newborns.

Volume controlled ventilation methods were started to be used more widely after the report that pressure controlled traditional artificial ventilation methods increased the frequency of chronic lung disease (CLD). However, controlling only tidal volume was not enough to decrease the frequency of lung damage and CLD. Therefore, mixed methods (volume targeted-pressure limited) which both controlled tidal volume and limited the pressure while giving this volume were developed (1). Since this efficient and lung-protecting ventilation method was inadequate in some severe lung diseases, new ventilation methods were required (2).

High-frequency oscillatory ventilation (HFOV) is an artifical ventilation method which is applied using small tidal volumes and respiratory rates more higher than the physiological limits. The aim of high-frequency oscillatory ventilation is to produce a lower pressure in the alveoli and to decrease the possibility of lung damage related to volume applications (3). A piston pump or diaphram is used in high-frequency oscillatory ventilation devices which provides active movement of gas inside the lung or outside the lung. Since small tidal volumes formed by this piston pump or diaphragm are oscillated, pressure and volume changes in the airway are minimal. Thus, healthy lung areas are aerated better, while damaged lung areas are not stretched extremely. High-frequency oscillatory ventilation is usually used in conditions where traditional or hybrid artificial respiratory methods are inadequate and the risk of air leak in the lungs is increased. Besides, it was proposed that high-frequency oscillatory

Address for Correspondence: Selvi Gülaşı MD, Mersin University Medical Faculty, Department of Pediatrics, Division of Neonatology, Mersin, Turkey
E-mail: selvigulasi@mynet.com **Received:** 05.03.2011 **Accepted:** 10.19.2011

ventilation accelerated improvement in damaged lung tissue, decreased development of CLD, shortened the time of mechanical ventilation and did not cause to increase in the frequency of intraventricular bleeding (IVB) and periventricular leucomalacia (PVL) (4).

In this study, the infants in whom we used HFOV in the last 3 years were examined and reasons of application, problems faced during application and the efficiency of HFOV were evaluated.

Material and Methods

The files of 40 infants in whom HFOV was applied between January 2008 and December 2010 in Mersin University Medical Faculty Neonatal Intensive Care Unit were examined retrospectively. Gestational ages, birth weights, gender, APGAR scores, reasons of respiratory failure, states of surfactant application and patent ductus arteriosus were recorded. Initial artifical ventilation method and settings related to mechanical ventilation applied by traditional methods, artificial ventilation times, development of air leak during this process, times of switching to HFOV, reasons of switching to HFOV, pH, blood gases, oxygene saturation and FiO_2 values at the time of start of HFOV were recorded. In the process of application of HFOV, pH, blood gases, heart rate and blood pressure values and changes made in HFOV application accordingly at the 1st, 4th, 12th, 24th and 48th hours, development of air leak, use of inotropics, total artificial ventilation time and artificial ventilation time with HFOV, the type of HFOV device, time of hospitalization of the infant, development of intraventricular bleeding, periventricular leucomalacia, CLD and retinopathy of prematurity during hospitalization and mortality rates were recorded. Chronic lung disease was considered as persistence of oxygen requirement at the 28th day after birth in infants with a gestational age of 32 weeks and older and at the 36th week after insemination in infants with a gestational age of 32 weeks or younger. In cases where the mean blood pressure was lower than the gestational age value, inotropic treatment was started. High-frequency oscillatory ventilation was applied using Draeger Babylog 8000 plus (Draeger Medical, Lübeck, Germany) and SLE 5000 (Specialized Labrotories Equipment Ltd, U.K.) devices.

Infants who died before the fourth hour of high-frequency oscillatory ventilation were excluded from the study. The data of the patients were entered into SPSS v.11,5 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, U.S.A.) program. The distribution of the data was examined using Shapiro-Wilks test and non-parametric methods were preferred, since there was no normal distribution. Friedman test and Wilcoxon Signed Ranks test were used to examine variation by time in terms of variables measured. Chi-square test was used for analysis of categorical data. Categorical data were given as number and percent, numerical data were given as mean and standard deviation, median and the least-the highest value. A p value of <0.05 was considered to be statistically significant.

Results

Five of 40 infants included in the study were excluded from the study, since they died before the fourth hour of HFOV application. 24 of the remaining 35 infants were preterm (68.5%) and 11 were term (31.5%). The general characteristics of the infants are summarized in Table 1.

The main reasons of respiratory failure in the infants are shown in Table 2. The most common reason in preterm infants was found to be respiratory distress syndrome (RDS). Times of traditional artifical ventilation applied before HFOV, times of HFOV and total time of mechanical ventilation are given in Table 3. 58.3% of the preterm infants who were applied high-frequency oscillatory ventilation and 54.5% of the term infants who were applied high-frequency oscillatory ventilation were discharged.

When artifical ventilation was started in the infants, the mean values for pH, PCo_2, FiO_2 and oxygen saturation were 7.2, 60 mmHg, 79% and 86%, respectively. Initially, Synchronized Intermittent Mandatory Ventilation+Volume Guarantee, SIMV+VG (34.3%), Pressure Support Ventilation+Volume guarantee, PSV+VG (20%), Synchronized Intermittent Positive Pressure Ventilation+Volume Guarantee, SIPPV+VG (14.3%) and Continue Positive Airway Pressure, CPAP (14.3%) methods

Table 1. General characteristics of the patients

	Preterm (n: 24)	Term (n: 11)
Gestational age, weeks*	30.4±4.1	38.5±0.8
Birth weight, grams*	1466.9±725.3	2773.2±591.2
Apgar score at the first minute*	5.6±1.7	2.0±3.5
Apgar score at the fifth minute*	7.4±1.5	5.0±2.0
Male gender, n (%)	14 (58.3)	4 (36.4)
Steroid administration before birth, n (%)	7 (29.2)	0 (0.0)
Surfactant administration, n (%)	17 (70.8)	1 (9.1)
Presence of PDA, n (%)	18 (75)	6 (54.5)

* values are given as mean ± standard deviation (SD).
PDA: Patent ductus arteriosus

Table 2. Reasons of respiratory failure

Reason of respiratory failure	Preterm n (%)	Term n (%)
RDS	17 (70.8)	0 (0.0)
Pneumoniae	1 (4.2)	1 (9.1)
PPHN	3 (12,5)	1 (9.1)
Pneumothorax	1 (4.2)	1 (9.1)
Sepsis	1 (4.2)	1 (9.1)
Perinatal asphyxia	1 (4.2)	2 (18.2)
Other	0(0.0)	5 (45.5)

RDS: Respiratory distress syndrome, PPHN: Persistent pulmonary hypertension

were used and HFOV was applied directly in 17.1% of the infants. Two of six infants who were applied HFOV directly had severe pulmonary hypertension and four had pneumothorax. In infants who were decided to be ventilated with HFOV while being ventilated with traditional methods, mean peak inspiratory pressure (PIP) was found to be 25.9 H_2O and mean airway pressure (MAP) was found to be 10.6 cm H_2O. While the most common reason for switching to HFOV was high PIP requirement to provide the desired tidal volume in preterm infants, the most common reason in term infants was the fact that saturation did not increase, although high oxygen was given (Table 4).

Air leak (pneumothorax, penumomediastinum) developed in 7 (20%) of the patients who were ventilated with traditional artifical ventilation. 6 of them were preterm infants. Air leak developed in one patient (2.9%) among infants who were ventilated with high-frequency oscillatory ventilation. Hypotension which required inotropic use developed in 60% of the patients who were switched to high-frequency oscillatory ventilation.

Blood gases at the 0th, 1st, 12th, 24th and 48th hours of high-frequency oscillatory ventilation and changes made in the amplitude, frequency and MAP values accordingly are shown in Table 5. It was found that oxygen saturation value increased significantly one hour after high-frequency oscillatory ventilation was started and pH value increased significantly 4 hours after high-frequency oscillatory ventilation was started. pCO_2, FiO_2 and amplitude values decreased significantly after one hour. *A statistically significant increase was found in pH monitored after

Table 3. Times of artifical ventilation methods (hours)

Times of artifical ventilation methods (hours)	Preterm median (the lowest-the highest)	Term median (the lowest-the highest)	p value
Traditional artifical ventilation before HFOV	35 (0-864)	12 (0-168)	0.067
HFOV application	69 (8-656)	72 (13-1800)	0.540
Artificial ventilation during the whole hospitalization time	227 (34-1320)	166 (22-1800)	0.316

HFOV: High-frequency oscillatory ventilation

Table 4. Reasons for switching to high-frequency oscillatory ventilation

Reason for applying HFOV	Preterm infants (n: 24)	Term infants (n: 11)	p
The fact that saturation did not increase, although high oxygen was given n (%)	10 (41.7)	7 (63.6)	0.227
No improvement in respiratory acidosis n (%)	4 (16.7)	2 (18.2)	0.912
High PIP requirement to apply the desired tidal volume n (%)	13 (54.2)	5 (45.5)	0.632
Development of air leak n (%)	7 (29.2)	2 (18.2)	0.490

HFOV: High-frequency oscillatory ventilation , PIP: Peak inspiratory pressure

Table 5. Blood gases at the 0th, 1st, 4th, 12th, 24th and 48th hours and changes made in the amplitude, frequency and MAP values accordingly

	0. hour (n: 24)	1st hour (n: 24)	4th hour (n: 24)	12th hour (n: 24)	24th hour (n: 24)	48th hour (n: 24)
pH	7.23	7.29	7.33*	7.34	7.32	7.33
PCO_2	55	44**	40	41	40	40
Saturation(%)	90.5	94***	93	94	94	92
FiO_2 (%)	100	70§	48§	38	43	40
Amplitude (SLE, mbar)	33	30†	30	27	22†	23
Frequency (Hz)	10	10	10	10	11	10
MAP (cm H_2O)	14.5	15	15	15	14‡	14

* A statistically significant increase was found in pH monitored after the fourth hour compared to the pH value measured during switching to HFOV (p:0.001).

** A statistically significant decrease was found in PCO_2 at the first hour compared to the PCO_2 value measured during switching to HFOV (p:0.001).

*** It was observed that oxygen saturation during switching to HFOV increased significantly at the first hour (p:0.007).

§ It was observed that FiO_2 value during switching to HFOV decreased significantly at the first hour ($p<0.05$). The difference between the first hour and the fourth hour was also significant ($p<0.05$).

† It was observed that the amplitude value during switching to HFOV decreased markedly at the first hour (p:0.037). A further decrease was found at the 24th hour (p:0.003).

‡ It was observed that there was no difference in MAP value during switching to HFOV at the first hour (p:0.093). However, the decrease at the 24th hour was significant (p:0.002).

the fourth hour compared to the pH value measured during switching to HFOV (p:0.001).

It was found that HFOV was applied in 5 (14.3%) of 35 patients who were included in the study in 2008, in 12 patients (34.3%) in 2009 and in 18 patients (51.4%) in 2010. A statistically significant increase in the frequency of HFOV application was observed in 2010 compared to 2008 and 2009 ($p<0.05$).

Reintubation was not required in preterm infants (8.3%) and 2 term infants (18.2%) who were extubated successfully at the end of high-frequency oscillatory ventilation without switching to traditional artificial ventilation methods.

Intraventricular bleeding was found in 6 (25%) of 12 infants in whom ultrasonographic examination was performed among preterm infants who required high-frequency oscillatory ventilation. Periventricular leucomalacia was found in 8 (33.3%). No imaging method was performed in 12 infants. Retinopathy of prematurity developed in five (20.8%) of these infants and CLD developed in 7 (29.2%). No statistically significant difference was found in comparison of the years of 2008, 2009 and 2010 in terms of development of intraventricular bleeding, periventricular leucomalacia, retinopathy of prematurity and CLD. HFOV was applied in 14 preterm infants in 2008 and 2009 and in 10 preterm infants in 2010. The rate of surfactant application was found to be significantly higher in 2010 (90%) compared to 2009 and 2008 (57.1%) ($p<0.05$).

Disccusion

Artifical ventilation is a common treatment method which is frequently used in lung diseases. However, damage due to pressure, volume and atelectasia may occur in the lungs (5,6). Nevertheless, contradictory results have been reported in clinical studies in which HFOV and traditional artificial ventilation methods were compared (7,8). The designs of these clinical studies are different (presence or absence of surfactant application, methods for keeping the lungs open, type of artificial ventilation devices). In most of these studies, tidal volume is not monitored. Despite an experience of 20 years, no consensus about justifications for application of HFOV and the mode of application of HFOV has yet been instituted.

There are limited studies about the cirteria for switching to HFOV from traditional artificial ventilation methods. In a study where HFOV was used as early rescue treatment in near-term and term infants with respiratory failure, HFOV was started in infants when FiO_2 exceeded 50%, MAP exceeded 10 cm H_2O, the required PIP to provide a tidal volume of 5-7 ml/kg was above 24 cm H_2O and a marked decrease in MAP value and improvement in oxygenation was found at the 48th hour of HFOV (9). In our study, mean values of FiO_2, the required PIP to apply 4-6 ml/kg tidal volume and MAP during switching to HFOV were found to be 79%, 25.9 cm H_2O and 10.6 cm H_2O, respectively. In our study, the most common reason for switching to HFOV (51.4%) was high pressure requirement to apply the desired tidal volume. The second most common reason was lack of increase in saturation, although high oxygen was given (48.6%). As in other studies, a decrease was observed in oxygen requirement, pCo_2 and amplititude values at the first hour of HFOV, improvement in pH was observed at the fourth hour and decrease in MAP was observed at the 24th hour in our study. When preterm infants were examined, pH was observed to be improved and pCO_2, FiO_2 and amplitude values were observed to be decreased one hour after switching to HFOV. Decrease in MAP was observed to be prominent after the 24th hour. This shows that HFOV application is also effective in preterm infants.

The results of two studies which compared traditional artificial ventilation methods with HFOV in near-term newborns with severe lung disease showed that there was no difference in terms of mortality, development of CLD, air leak, IVB, PVL and hospitalization time (10,11). In our study, development of air leak was found with a rate of 20% during traditional artificial ventilation and with a rate of 2.9% during HFOV.

Recent studies emphasized direct extubation without switching to traditional artificial ventilation methods in patients in whom HFOV is applied. In a retrospecive study performed by Van Velzen et al. (12), it was found that direct extubation was performed successfully with a rate of 90% in infants who were applied HFOV with a MAP value below 8 cm H_2O and a FiO_2 value below 30%. In this study, extubation was not performed before the first week ended after birth. Before extubation caffeine treatment was started in all infants. Dexamethasone was administered in all infants who had a possibility of unsuccessful extubation and extubated infants were supported by nasal CPAP. In our study, there were 4 infants (11.4%) who were directly extubated. 3 of these were supported with nasal CPAP after extubation. One did not need CPAP and oxygen. No infant was given caffeine, aminophylline or steroid treatment. One of these infants had severe pneumonia, two had air leak (one penumothorax and one pneumomediastinum) and one had PPHN. In the infants in our study, mean MAP was found to be 7 cm H_2O and mean FiO_2 value was found to be 30% at the time of direct extubation after HFOV.

During high-frequency oscillatory ventilation, increased pleural pressure, decreased venous return and decreased heart output are an expected result because of high MAP. Derdak et al.(13) observed no difference between the groups in terms of heart rate, mean blood pressure and heart output in the first 72 hours of artificial ventilation in patient groups who were applied HFOV and traditional artificial ventilation in their study. In our study, the rate of starting inotropic agent because of hypotension after HFOV was started was found to be 60%.

In studies which suggested high-frequency oscillatory ventilation decreased inflammation in the lung and thus development of CLD, early rescue treatment was advocated. In a randomized clinical study performed by Dani et al. (14) in preterm infants younger than 30 weeks of gestational age, infants who needed artificial ventilation were randomly assigned to HFOV and PSV+VG groups. Before surfactant administration tracheal aspirate fluid was taken from the infants between the 6-18th hours and 24-48th hours and IL-1β (interleukin 1β), IL-8 and IL-10 levels were examined.

Inflammatory cytokine levels were found to be significantly lower in the group in whom early HFOV was applied compared to the PSV+VG group. Similarly, Honda et al.(15) found IL-8 level to be markedly low in the bronchoalveolar lavage fluid in infants in whom HFOV was applied in their study which compared HFOV with traditional artificial ventilation methods and proposed that application of HFOV at an early period played a regulatory role in airway inflammation. However, in a randomized clinical study performed by Lista et al.(16) which compared volume targeted (5ml/kg) artificial ventilation methods with HFOV in terms of development of inflammation in the lung in preterm infants (gestational age 25-32 weeks), IL-6, IL-8 and TNF (tumor necrosis factor) levels in tracheal aspirate fluid obtained on the first, 3rd and 7th days of life in infants who were applied volume targeted artificial ventilation were found to be markedly lower compared to infants who were applied HFOV and it was proposed that volume targeted artificial ventilation methods protected the lung. In our study, CLD was found with a rate of 22.9%, but it was not possible to examine the effect of HFOV on development of CLD in this retrospective study, since lung diseases and the gestational ages of the infants were heterogeneous.

In a study which compared the neurodevelopmental outcomes in preterm infants with RDS who were treated with high-frequency oscillatory ventilation and traditional artificial ventilation at the age of two, better neuromotor outcomes were observed with HFOV use compared to traditional artificial ventilation, although the frequency of IVB was reported to be increased with HFOV (17). There are very few studies performed on this subject and prospective studies with long-term follow-up are needed. It was also not possible to obtain such a result in our study.

Conclusively, it was shown that more than half of the infants who had no improvement in blood gases, although the PIP value needed to provide the tidal volume was increased to 25 cm H_2O or who developed pneumothorax while being ventilated by traditional methods could improve and could be discharged with HFOV application in this study. To evaluate development of CLD, lung functions and cognitive-motor ability in the long-term in infants ventilated with high-frequency oscillatory ventilation prospective studies with larger patient groups are needed.

Conflict of interest: None declared.

References

1. Keszler M, Abubakar KM. Volume guarantee ventilation. Clin Perinatol 2007; 34: 107-16.
2. Clark RH, Slutsky AS, Gerstmann DR. Lung protection strategies for ventilation in neonate. What are they? Pediatrics 2000; 105: 112-4.
3. Atıcı A, Özkan H. Yenidoğan bebeğin mekanik ventilasyonu.Yüksek hızda titreşimli ventilasyon (HFOV). 1. Baskı, 2011: 66-7.
4. Courtney SE, Durand DJ, Asselin JM, et al. High-frequency oscillatory ventilation versus conventional mechanical ventilation for very low birth weight infants. N Eng J Med 2002; 347: 643-52.
5. Dreyfuss D, Saumon G. Ventilator induced lung injury: lessons from experimental studies. Am J Respir Crit Care Med 1998; 157: 294-323.
6. Corbridge TC, Wood LD, Crawford GP, Chudoba MJ, Yanos J, Sznajder JI. Adverse effect of large tidal volume and low PEEP in canine acid aspiration. Am Rev Respir Dis 1990; 142: 311-5.
7. Pardou A, Vermeylen D, Muller MF, Detemmerman D. High-frequency ventilation and conventional mechanical ventilation in newborn babies with respiratory distress syndrome: a prospective randomized trial. Intensive Care Med 1993; 19: 406-10.
8. Rimensberger PC, Beghetti M, Hanquinet S, Berner M. First intention high-frequency oscillation with early lung volume optimization improves pulmonary outcome in very low birth weight infants with respiratory distress syndrome. Pediatrics 2000; 105: 1202-8.
9. Ben Jaballah N, Mnif K, Khaldi A, Bouziri A, Belhadj S, Hamdi A. High-frequency oscillatory ventilation in term and near-term infants with acute respiratory failure: early rescue use. Am J Perinatol 2006; 23: 403-12.
10. Rojas MA, Lozano JM, Rojas MX, et al. Randomized, multicentre trial of conventional ventilation versus high-frequency oscillatory ventilation for the early of respiratory failure in term and near-term infants in Colombia. J Perinatol 2005; 25: 720-4.
11. Clark RH, Yoder BA, Sell MS. Prospective, randomized comparison of high-frequency oscillation and conventional ventilation in candidates for extracorporeal membrane oxygenation. J Pediatr 1994; 124: 447-54.
12. van Velzen A, De Jaegere A, van der Lee J, van Kaam A. Feasibility of weaning and direct extubation from open lung high-frequency ventilation in preterm infants. Pediatr Crit Care Med 2009; 10: 71-5.
13. Derdak S, Mehta S, Stewart TE, et al. High-frequency oscillatory ventilation for acute respiratory distress syndrome in adults: A randomized, controlled trial. Am J Respir Crit Care Med 2002; 166: 801-8.
14. Dani C, Bertini G, Pezzati M, et al. Effects of pressure support ventilation plus volume guarantee vs. high-frequency oscillatory ventilation on lung inflammation in preterm infants. Pediatr Pulmonol 2006; 41(3): 242-9.
15. Honda R, Ichiyama T, Sunagawa S, Maeba S, Hasegawa K, Furukawa S. Inhaled corticosteroid therapy reduces cytokine levels in sputum from very preterm infants with chronic lung disease. Acta Pediatr 2009; 98: 118-22.
16. Lista G, Castoldi F, Bianchi S, Battaglioli M, Cavigioli F, Bosoni MA. Volume guarantee versus high frequency ventilation: lung inflammation in preterm infants. Arch Dis Child Fetal Neonatal Ed 2008; 93(4): F252-6.
17. Trufferd P, Llado JP, Escande B, et al. Neuromotor outcome at 2 years of very preterm infants who were treated with high-frequency oscillatory ventilation or conventional ventilation for neonatal respiratory distress syndrome. Pediatrics 2007; 119: 860-5.