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Comparing High-Frequency Ventilation and Conventional Ventilation on Morphology of Brain, Kidney and Liver in Preterm Babies with Respiratory Distress

Abstract

Background: The increase in the ventilator rates by conventional mechanical ventilation (CMV) is limited by a minimum amount of time needed for a complete inspiration and expiration. In preterm babies with respiratory distress syndrome, it may not be sufficient to manage the hypercapnia and hypoxia associated. High-frequency ventilation (HFV) can be considered as a substitute for CMV in premature infants by increasing the ventilator rate further and reducing the tidal volume. The current study evaluates the efficacy and effects on brain, liver and kidney morphology of HFV in preterm babies with respiratory distress.

Methods: This prospective and analytical study was conducted from December 2011 to January 2013 on 83 preterm babies' with an initial provisional diagnosis of respiratory distress that needed respiratory support at birth or soon after admission. Initial and follow up blood gas (BG) and cranial U/S, and renal and hepatic function tests were done.

Results: The study was conducted on 83 preterm babies, aged less than 37 weeks of gestation, who were divided into control (40) and study (43) groups. The study group showed significantly higher PEEP and PIP values than control in CMV and were shifted to HFV thereafter. The control group needed only CMV. After the intervention, statistically significant improvement in arterial blood gas parameters with respect to blood pH, pCO_2 and pO_2. The mean blood pH was found to be 7.386 ±0.039, with increase in mean pO_2 (before shift =45.44±4.36 vs. after shift=40.56 ±2.597 mm Hg respectively, p= 0.01) and decrease in mean pCO_2 (before shift= 38.23±0.03 vs. after shift=42.87 ± 6.915 mm Hg respectively, p=0.01). We can say that HFV helped to reduce acidosis, hypoxia, and hypercapnia in the neonates in the study group.

In terms of renal functions, the serum sodium content marginally increased with HFV (After shift= 136.00±3.910 vs. before shift=135.00±5.686 mol/l, p=0.000), Significant increase in mean 24-hour urinary creatinine from their initial CMV values after subjecting them to HFV (before shift 14.509± 4.874 mg/dl vs after shift 15.340±7.054 mg/dl, p=0.002). In terms of hepatic functions, significant difference was observed after intervention was detected with higher PT in HFV group (0.01); on the other hand, no significant difference regarding ALT, PTT and fibrinogen between study and control groups was detected after HFV intervention. Brain ultra-sound scan (BUSS) results showed that the intraventricular haemorrhage (IVH) was reduced in the HFV group as compared to the CMV group. BUSS outcome also showed that there is a significant correlation between IVH and surfactant medication.

Conclusion: Rescue HFV improved oxygenation, ventilation, lung recruitment and better oxygenation indices and there was no increased incidence of IVH. In addition, HFV had no deleterious effect on other organs such as the brain, kidney and liver.

Keywords: Preterm; HFV; CMV; BG; Respiratory distress; Cranial U/S; Creatinine; ALT

Research Article

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Abbreviations: HFV: High-Frequency Ventilation; IVH: Intraventricular Haemorrhage; CMV: Conventional Mechanical Ventilation; PEEP: Peak End-Expiratory Pressures; RDS: Respiratory Distress Syndrome; NICU: Neonatal Intensive Care Unit; ABG: Arterial Blood Gas

Introduction

The preterm infants with respiratory distress have a poor prognosis and may depend upon numerous prenatal and postnatal factors and some of the complications that follow may be cerebral palsy, broncho pulmonary dysplasia, necrotising enter colitis and intraventricular haemorrhage (IVH) [1]. The respiratory distress requires mechanical ventilation support which can be executed by various techniques [2]. Numerous studies have tried to compare the two methods of mechanical ventilation: conventional mechanical ventilation (CMV) and high-frequency ventilation (HFV) with no clear consensus of the advantage of one over other [3,4]. Both low and high peak end-expiratory pressures (PEEP) during CMV can cause harm to the baby and finding an ideal mechanical ventilation technique is a challenge [5]. High-frequency ventilation (HFV) is one such alternative technique which has some of the advantages of using small tidal volumes, the

ability to manage both ventilation and oxygenation independently, and use of safer mean airway pressures [6]. Studies analysed of preterm babies with respiratory distress have shown a significant reduction in chronic lung disease in babies who received HFV and no surfactant as compared to CMV [7].

Older studies conducted on canines have not shown any difference in the renal, lung and cardiac blood flows when either HFV or intermittent positive pressure ventilation was administered. The ventilator-synchronous fluctuations in ICP on IPPV, reduced on HFV at normal ICP and eliminated at elevated ICP [8]. Mechanical ventilation can have an effect on renal perfusion and function and a review conducted on the same concluded that injury to one organ may initiate or aggravate the injury to the other [9]. As not enough literature is available to understand the effect of HFV on the morphology of brain, kidney and liver in infantile RDS, the current study aims to investigate the benefits of HFV as compared to CMV on morphology of these organs in preterm babies with respiratory distress syndrome (RDS).

Methodology

The study was conducted at Neonatal Intensive Care Unit (NICU) in Latifa Hospital (LH), Dubai, United Arab Emirates (U.A.E.), where preterm babies were enrolled from December 2011 to January 2013. Patients were divided into 2 groups: Study group wherein babies were on CMV and needed HFV at any stage during the hospital stay due to the failure of CMV or worsening of the condition. The control group babies required a conventional mode of ventilation only. Preterm neonates with birth weight <1.8 kg and necessity of mechanical ventilation due to the failure of CMV were included in the study. However, neonates with congenital cardiac malformation, perinatal asphyxia, chorioamnionitis, severe sepsis, or those with the preterm administration of dexamethasone were excluded from this study.

Babies on the following ventilator settings were shifted to HFV: FiO_2> 60%, Respiratory rate >50/ minutes, Positive end-expiratory pressure (PEEP) > 6cm H_2O, Peak aspiratory pressure (PIP): 22 mbar for those < 1000 grams, and 24 mbar for those between 1000 -1500 grams, 25 mbar for those >1500 grams, and deterioration of blood gas (Hypercarbia and/ or Hypoxemia) or if clinically indicated. Thorough perinatal history and clinical examination conducted for all the babies. The babies underwent complete haematological and biochemical investigations along with a regular cranial ultrasound to rule out intraventricular haemorrhage or peri-ventricular leukomalacia, renal and liver disorders.

To evaluate the intraventricular haemorrhage and peri-ventricular leukomalacia, BUSS was conducted and babies divided into normal (who did not develop IVH) and abnormal (who developed signs of IVH). Babies were also classified into negative (babies who did not develop IVH at any stage during the hospital stay) and positive (babies who developed any grade of IVH during the hospital stay).

Results of HFV intervention were further classified into favourable (stationary and the regressive cases) and unfavourable (progressive cases). The "stationary" group are those babies with normal BUSS or developed any grade of IVH that did not progress during the hospital stay. The "progressive" are group of babies who had normal BUSS initially or had any grade of IVH that progressed to a higher grade of IVH during the hospital stay. The "regressive" group are those babies who had any grade of IVH during the hospital course but regressed to a lesser degree during the hospital stay.

All standard procedures were followed to conduct the hematological and biochemical tests and monitor kidney, liver function and coagulation profile tests. Blood samples were withdrawn from either an umbilical venous catheter (UVC) or peripheral intravenous access using sterilized plastic disposable syringes after the first 12 hours of life as a base line, also immediately before and 24 hours after changing the mode of ventilation to HFV in the study group as well as the control group. The kidney function in the preterm babies was assessed by evaluating urinary alpha 1-microglobulin (α1-m) (for proximal tubular function), and 24 hours urine volume. The distal tubular reabsorption capacity was investigated by assessing fractional excretion of sodium (FeNa). FeNa<1% revealed prerenal azotemia and FeNa >1% depicted acute tubular necrosis (ATN). Liver function tests include plasma alanine transaminase, prothrombin time (PT), partial thromboplastin time (PTT) and fibrinogen.

Statistical Analysis

Statistical analysis were conducted using Statistical Package (version 16) for the Social Sciences (SPSS). Results of quantitative data were expressed as the mean and standard deviation (mean ± SD). Results of qualitative data were expressed as number and percentage. Unpaired t-test was used to compare a quantitative variable between two independent groups in parametric data. Paired t-test was used to compare a quantitative variable between two dependent groups in parametric data. Pearson correlation coefficient (r) was used to correlate between many variable groups. Levels of statistical significance were set as: $p > 0.05$: considered as non-significant; $p < 0.05$: considered as significant, $p < 0.01$: considered as highly significant. Ethical approval for the research was taken before starting the study and informed consent were signed by the parents.

Results

Patient disposition and baseline characteristics

A total of 83 preterm babies were enrolled out of which, 43 were on CMV and needed HFV at any stage during the hospital stay due to the failure of CMV or worsening of the condition. Another group of 40 preterm babies required a conventional mode of ventilation only. The mean gestational age of the babies was 27.47 (±2.41) weeks in the study group and 27.43 (±2.22) weeks in the control group. Mean birth weight recorded for the study and control groups was 0.91 (±0.25) kg and 0.89 (±0.20) kg respectively (Table 1).

The sex ratio was almost equal. The most common indication in the babies who were shifted to HFV was persistent high PCO_2 (20 babies, 46.5%) followed by persistent desaturation in 20.9% babies. There was no statistically significant difference between control and study groups regarding baseline characteristics, clinical data, mode of delivery and medications used (Table 1).

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Table 1: Demographic and baseline characteristics in Study (N=43) and Control groups (N=40).

	Study Group		Control Group
Gestation(weeks), Mean (±SD)	27.47 (±2.41)		27.43 (±2.22)
Birth Weight (kgs), Mean (±SD)	0.91 (±0.25)		0.89 (±0.20)
Height (cm), Mean (±SD)	24.45 (±1.84)		24.38 (±1.51)
Medication			
Betamethasone, N (%)	Yes	23 (53.5%)	19(47.55%)
	No	20 (46.5%)	21(52.5%)
Surfactant, N (%)	1	17 (39.5%)	21 (52.5%)
	2	24 (55.8%)	17 (42.5%)
	3	2 (4.7%)	2 (5.0%)
Mode of Delivery, N (%)	VD	20 (46.5%)	18 (45.0%)
	CS	23 (53.5%)	22 (55.0%)
Apgar Score, Mean (SD)	1 min	6 (4)	6 (3)
	5 min	8 (2)	8 (2)
Mean Heart Rate (SD) (per minute)		162.58 (6.86)	158.58 (3.89)
Mean BP (mm Hg)		34.98 (23.07)	38.88 (4.61)
Mean temp (◦C)		36.87 (0.14)	36.92 (0.15)
Respiratory Rate (Breath Per Minute)		59.77 (5.34)	42.5 (10.86)
pH		7.25 (0.07)	7.32 (0.08)
pCO_2 (mm of Hg)		66.84 (10.77)	46.70 (8.62)
pO_2(mm of Hg)		32.93 (6.78)	39.15 (2.64)
HCO_3 (mmol/L)		18.63 (2.15)	20.45 (2.91)

Comparison of Ventilator settings between HFV and CMV patients

The shift from CMV to HFV showed a significant correlation with hypoxia, high PIP and PEEP values, and higher FiO_2 requirement. There was no correlation with inspiratory time and duration of ventilation (Table 2). The mean PIP was comparatively higher in the study group (20.74 mbar±1.482) than in the control group (17.56 ±1.44). The mean PEEP value was also higher for the study group as compared to the control group (5.44 ± 0.544 vs. 5.15 ± 0.362 mbar respectively, p=0.004). The mean oxygen saturation values were significantly lower in the study group than in the control group (89.63 ± 2.024 vs. 92.88 ± 2.11 respectively, p= 0.000). The fraction of inspired oxygen (FiO_2) was found to be higher in the study group than in the control group (35.58 ± 7.195 vs 23.50 ± 4.718 respectively, p=0.000). The highly significant difference was detected in the PIP, PEEP and FiO_2 in the babies before they were shifted to HFV. Non-significant difference was detected regarding Ti (inspiratory time) and ventilation duration (p=0.59 & 0.73 respectively). Once the baby was shifted to HFV, the respiratory parameters showed an improvement.

Table 2: Comparison between study groups regarding ventilator settings at point of shift to HFV.

	Study Group (43)Mean(SD),	Control Group (40), Mean(SD)	p-value
Mean O_2 Sat	89.63(2.02)	92.88(2.11)	0.000**
PIP	20.74(1.48)	17.56(1.44)	0.000**
PEEP	5.44(0.54)	5.15(0.36)	0.004**
Inspiratory time	0.28(0.02)	0.27(0.02)	0.59
FiO_2	35.58(7.19)	23.50(4.72)	0.000**
Ventilator duration (days)	5.56(1.56)	5.68(0.99)	0.73

*Significant at the 0.05 level
**Significant at the 0.01 level

The mean HFV settings were: mean airway pressure (MAP) was 11.40 ±1.16 mbar; frequency was 5.53 ± 0.83 Hz; the amplitude of 93.49 ±8.83 and FiO_2 24.36 ±1.96. The mean ventilator duration of HFV was 5.84 ±3.11 days. Prior to HFV intervention, arterial blood gas condition in the study group neonates was acidosis with a mean pH of 7.246 ±0.07; also the neonates were suffering from hypoxia (Mean pO_2=32.93 ± 6.78 mm Hg) and hypercapnia (Mean pCO_2 = 66.84 ±10.77 mm Hg).

The babies' ABG showed improvement after the shift to HFV (Figure 1). The mean blood pH was found to be 7.386 ±0.039, with increase in mean pO_2 (45.44 ±4.36 vs. 40.56 ±2.597 mm Hg respectively, p= 0.01) and decrease in mean pCO_2 (38.23±0.03 vs 42.87 ± 6.915 mm Hg respectively, p=0.01) as compared to when the babies were given CMV initially (Table 2).

Comparison of Brain ultrasound between study and control groups

At the start of HFV intervention, the incidence of IVH was more in the study group. We observed more abnormal IVH in

the study group (41.9%, n=18) as compared to the control group (27.5%, n=11). However, after shifting to HFV, IVH progression was noticed to be less in the study group, out of 18 cases of IVH in the study group, 77.8% showed marginal improvement in IVH condition (Study = 77.8%, N=14) vs. control= 72.7%, N=8) though the improvement was not significant. The results were statistically not significant but after shifting to HFV, IVH did not progress and stayed stable in the majority of patients (Table 3).

A significant correlation was observed between IVH and surfactant medication (p=0.02) after HFV intervention. In the neonates receiving one dose of surfactant, 78.9% had normal BUSS, 10.5% had regressive IVH and the remaining 10.5% were stationary. No significant correlation was observed between IVH and the modes of delivery (vaginal or caesarean) and the dexamethasone doses (Table 4).

Table 3: Comparison between both group regarding brain ultrasound scan (BUSS) findings before and after High frequency ventilation intervention.

					P value
			Study Group (43)	**Control group (40)**	
Buss (at the start of HFV)	Normal (-ve)	N (%)	25(58.1%)	29(72.5%)	0.35
	Abnormal (+ve)	N (%)	18 (41.9%)	11 (27.5%)	
Total			43(100%)	40 (100%)	
			Study group-Abnormal (18)	Control group-Abnormal (11)	
Buss (after HFV)	Unfavourable	N (%)	4(22.2%)	3(27.3%)	0.76
	Favorable	N (%)	14 (77.8%)	8 (72.7%)	
Total			18(100%)	11 (100%)	

*Significant at the 0.05 level
*Significant at the 0.01 level

Normal ultrasound: no IVH; Unfavourable BUSS: Progressive cases of IVH; Favourable BUSS: Stationary & regressive cases of IVH

Table 4: Outcome of Brain ultrasound scan (BUSS) according to the various risk factors.

Variables		**BUSS**				
		Normal N (%)	**Progressive N (%)**	**Regressive N (%)**	**Stationary N (%)**	**P-value**
Mode of Delivery	VD	29 (76.3)	3 (7.95)	4 (10.5)	2 (5.3)	0.21
	CS	25 (55.5)	8.9 (26.7)	12(26.7)	4(8.9)	
Medication:	1 dose	25 (59.5)	4 (9.5)	9 (21.4)	4 (9.5)	0.72
Betamethasone	2 doses	29 (70.7)	3(7.3)	7(17.1)	2(4.9)	
Medication:	1 dose	30 (78.9)	0	4(10.5)	4(10.5)	0.02*
Surfactant	2 doses	22 (53.7)	7(17.1)	10 (24.4)	2(4.9)	
	3 doses	2(50)	0	2(50)	0	

*Significant at the 0.05 level
**Significant at the 0.01 level

CS= Caesarean section; VD: vaginal delivery; Normal ultrasound: no IVH; Unfavorable BUSS: Progressive cases of IVH; Favorable BUSS: Stationary & regressive cases of IVH;

Comparison of Kidney function results between study and control groups

In the current study, the 24-hour serum creatinine levels showed a slight decrease in the study group after HFV-shift (0.856±0.200 in study group vs. 0.807 ±0.201 mg/dl in control group respectively). The mean 24-hour urinary creatinine showed a significant increase after shifting the baby from CMV to HFV mode (before shift 14.509 ± 4.874 mg/dl vs. after shift 15.340 ±7.054 mg/dl, p=0.002). After HFV shift, the serum sodium content also marginally improved (after shift= 136.00 ±3.910 vs. before shift=135.00 ±5.686 mol/l, p=0.000), and the urinary sodium content was reduced (After shift= 53.70 ± 25.07 vs. before shift= 57.30 ±23.964 mol/l). The study group showed high fractional excretion of sodium (FeNa) in the preterm babies, recorded as 1.4616 (±1.057) % at the time of shift to HFV. After HFV shift, FeNa was reduced to 1.308 (±1.00) %. No statistically significant difference was observed between both groups regarding other renal functions (Table 5).

Table 5: Comparison between study and control groups regarding kidney function after intervention.

	Study (43) Mean(SD)	Control (40) Mean (SD)	p-value
Na	136.00 (3.91)	135.70(6.53)	0.79
K	6.529(0.76)	4.150(0.61)	0.27
Urea	31.77(28.92)	38.83(27.51)	0.03
Creatinine	0.807(0.20)	0.785(0.21)	0.98
Fe Na	1.308(1.00)	1.512(0.68)	0.12
Uα1m	98.34(86.61)	97.34(63.61)	0.97
U Na	53.70(25.08)	46.73(22.93)	0.25
U Creatinine	15.340(7.05)	14.50(3.76)	0.54

*Significant at the 0.05 level

**Significant at the 0.01 level

Na= serum sodium, K= serum potassium; Fe Na= Fractional excretion of sodium; Uα1m= Urinary α1-microglobulin; U Na=Urinary sodium; U Creatinine= urinary Creatinine.

Comparison of Liver function results among study and control groups

The mean PT in the study group babies was elevated significantly following HFV intervention (before HFV, PT=15.944 ±2.25 vs. after HFV PT=16.244 ±3.50 seconds, p=0.01). The mean PTT values were reduced (48.774 ±22.94 vs. 48.563 ±32.74 seconds). Serum ALT levels were also altered (before the shift, 22.74 ±40.93 units/L vs. after shift 13.98 ±7.76 units/L). However, the change in ALT, PTT and fibrinogen was not so significant (Table 6).

Table 6: Comparison between Both groups regarding liver function after intervention.

	Study (43) Mean(SD)	Control (40) Mean(SD)	P-value
ALT	13.98(7.76)	13.18(10.45)	0.13
PTT	48.563(32.74)	38.47(6.47)	0.15
PT	16.244(3.50)	14.47(1.72)	0.01*
Fibrinogen	288.84(68.62)	311.08(93.99)	0.3

**Significant at the 0.01 level

ALT= Plasma alanine transaminase; PTT= Partial thromboplastin time; PT= Prothrombin time.

Discussion

Our study was conducted on 83 preterm babies and has shown that HFV can be considered as an alternate option to manage the respiratory distress in neonates in addition to CMV. HFV after its introduction was initially applied to some of the critical cases of neonates which were not amenable to treatment with CMV [6]. Abnormal PEEP and PIP values with CMV laid emphasis on the need for early regular blood gases and shift to HFV to avoid an excess drop in the pO_2 that is incriminated in periventricular leukomalacia (PVL). Based on optimal lung volume strategy, the survival of HFOV-ventilated infants had been reported to be significantly higher in the premature babies, despite having more risk factors for death [6].

Moreover, our study has observed that the preterm babies who were put on HFV after a failed CMV developed no major morphological changes in the brain, kidneys and liver. The difference in PIP, PEEP and FiO_2 values in several neonates was the main cause of shifting them to HVF. This shifting was applied in the current study to the worsening neonatal cases that were later on categorised as the study group.

This study shows that rescue HFV improved oxygenation, ventilation, lung recruitment and improved oxygenation indices. No dysfunction of other organs such as kidney and liver were observed in babies on HFV. The HIFO Study Group found improvement in respiratory condition in 182 preterm infants having less than 35 weeks gestation and had or was at risk of developing a pulmonary air leak [10].

Some studies have shown that HFV had improved gas exchange in newborn with ARDS and better pulmonary function ratios with a decrease in FiO_2 requirement [11,12]. In our study we found that HFV improved lung function, mechanics, hence improving the respiratory status of the baby with chronic lung disease. The study also stressed on the early consistant use of HFV for better and continued efficacy.

We also observed that HFV lead to a reduction of progression of IVH as observed from the BUSS reports. IVH-induced mortality rates were similar among both HFV and CMV groups. A meta-analysis study conducted on 9 studies showed an association of

HFV with an increased risk of PVL but not with IVH or severe IVH as compared to CMV [13].

A study on adult patients compared the effect of pressure support ventilation like CMV to volume control ventilation like HFV on renal function. Up to the extent of our knowledge we do not have any data in preterm babies. Mechanical ventilation has the propensity to increase the intrathoracic pressure and decrease the cardiac output with a subsequent effect on free water, sodium and creatinine clearance. The results showed no significant difference in creatinine clearance, fractional excretion of volume or urine volume among the two groups. The study concluded that volume control ventilation had no adverse effects on renal parameters as compared to pressure control ventilation [14].

Our study also observed no statistically significant difference in the renal functions between the study and control groups. Any slight decrease in serum creatinine along with an increase in urinary creatinine levels in the study group after HFV – intervention may indicate improved creatinine clearance in such babies and highlight the benefit of HFV in renal function. Hyponatraemia increases the risks and severity of respiratory distress in the neonates, which has been associated with an increased risk of developing chronic lung disease [15]. Our study showed that the serum sodium levels normalized in the HFV –group babies which hold well in providing relief from Hyponatraemia. A low urinary sodium or low FeNa following HFV intervention indicates a maintained renal tubular reabsorption capacity, but these indices cannot be specifically correlated to tissue damage [16].

Lung injury secondary to respiratory distress can also lead to hepatic dysfunction [17]. The current study also examined the liver function tests of both groups on CMV and HFV respectively. No significant difference was observed between the two groups. The only observed significant difference was a decrease in PTT in the study group after HFV intervention,this might benefit HFV in maintaining normal liver functioning in preterm babies. Otherwise No significant difference was observed between the two groups. Animal studies have reported that mechanical ventilation can cause inflammation in lungs and other distal organs as well as cause elevations of serum ALT, liver cell apoptosis and microscopic signs of hepatic damage [18,19].

A study on pigs compared the hepatic effects of strategies using high airway pressure like pressure controlled ventilation (PCV) to high frequency oscillatory ventilation (HFOV) and found out that aspartate aminotransferase increased fivefold in the PCV group and threefold in HFOV group with a respective creatine kinase increased by twofold and fourfold respectively [20]. The study further concluded that high airway pressure PCV and HFOV did not because liver dysfunction or damage with the possible cause of elevated enzymes being extra hepatic in origin [20].The hepatic dysfunction independently increases the length of intensive care unit stay and mortality and can influence the patient outcome [21]. Accordingly, mechanical ventilation method which does not cause significant liver dysfunction could be a good option for these high risk group patients with respiratory distress.

The main strength of the study was the effort to assess all the aspects of HFV from efficacy to the safety in terms of effects on brain morphology and on liver and kidney functions of these patients. The existence of the comparator arm in which the babies continued with CMV made the design of the study stronger. The main limitations of the study were a lesser number of included patients, and long term follow up not being available especially on the neurodevelopment outcomes.

Conclusion

The evidence from the literature regarding the advantage for HFV has been inconclusive till now with some evidence available from a meta-analysis of 15 randomized trials of HFV versus 14 studies on CMV in smaller or more premature babies not proving the superiority of efficacy of HFV over CMV [22]. On the other hand some studies have shown HFV to be efficient and safe and can be used for improving survival of preterm neonates under respiratory distress as compared to CMV in the neonates [21-23]. Our study concluded that HFV could be considered important mechanical ventilation option in preterm babies with RDS. The main advantages of HFV was improving pulmonary dysfunction along with minimal effects on the morphology of brain, and functions of the liver and kidneys. Going forward larger studies on the preterm babies will be required to develop a consensus or practice guideline for approaching HFV as the first option for mechanical ventilation in this patient group.

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