

## Original Research Article

# Volume guarantee ventilation in premature neonates with respiratory distress: a comparative study

Sudheer K. A.<sup>1</sup>, Sunil B.<sup>2\*</sup>, P. K. Rajiv<sup>3</sup>, Mathew Kripail<sup>4</sup>, E. Nithya<sup>2</sup>

<sup>1</sup>Consultant Neonatologist, Aster CMI Hospital, Bangalore, Karnataka, India

<sup>2</sup>Department of Paediatrics, Kempegowda Institute of Medical Sciences, Bangalore, Karnataka, India

<sup>3</sup>Department of Paediatrics, Prime Hospital and Medical centers, Dubai, UAE

<sup>4</sup>Child health Department, Sultan Qaboos University Hospital, Muscat. Oman

**Received:** 04 September 2019

**Accepted:** 03 October 2019

### \*Correspondence:

Dr. Sunil B.,

E-mail: docsunilb@gmail.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** Respiratory distress syndrome (RDS) occurs in about 50% of preterm infants born at less than 30 weeks of gestational age. Surfactant therapy and mechanical ventilation have been the standard of care in the management of RDS. Objective of this study to compare the time required to achieve successful extubation criteria in Volume guarantee mode of ventilation to that with Time cycled pressure-limited mode of ventilation and the duration of mechanical ventilation between them in preterm neonates ventilated for respiratory distress syndrome.

**Method:** The study was done at Neonatal intensive care unit, Amrita Institute of Medical Sciences and Research Centre, Kochi, Kerala over a period of 2 years. Total of 37 inborn preterm neonates between 26 weeks to 32weeks with RDS requiring mechanical ventilation were included in 2-year study period with 18 babies in 1st year study period ventilated with SIPPV mode and 19 babies in 2nd year study period on SIPPV-VG mode of ventilation. Analysis was done using SPSS v. 16 software.

**Results:** In the present study the neonates receiving SIPPV-VG ventilation had stable and equivalent gas exchange at significantly lower MAP and PIP compared to neonates receiving SIPPV -TCPL. Also, neonates receiving SIPPV-VG had achieved significantly faster extubation criteria than SIPPV-TCPL and hence lesser duration of ventilation.

**Conclusion:** Our study concludes that Volume Guarantee ventilation achieves near stable tidal volume delivery by auto-weaning peak inspiratory pressures thereby promoting early extubation and hence reducing volutrauma and barotrauma in contrast to TCPL mode.

**Keywords:** Respiratory distress syndrome, SIPPV-VG, SIPPV-TCPL, Volutrauma

## INTRODUCTION

Worldwide, the rates of preterm delivery are increasing, with 1-2% of babies being born before 28 weeks' gestation.<sup>1</sup> Increased VLBW infant survival rates have paralleled improvements in prenatal, obstetric, and

neonatal care such as increased use of prenatal corticosteroid treatment, prenatal antibiotic treatment, early surfactant therapy and parenteral nutrition.<sup>2-4</sup> Bronchopulmonary dysplasia (BPD) continues to remain as a major morbidity in very low birth weight infants with an incidence of 20% among survivors. The incidence of bronchopulmonary dysplasia (BPD) has not changed,

probably as a consequence of a demographic shift with more immature babies surviving.

The underlying pathophysiology of BPD appears to differ for the current population of preterm infants compared to that described by Northway et al in 1967 and management strategies should be targeted to limit ventilator-induced lung injury.<sup>5-8</sup> Recent randomised trials on use of non-invasive ventilation, such as nasal continuous positive airway pressure and nasal intermittent positive pressure ventilation has shown a significant decrease in post-extubation failure as well as trend towards reduced incidence of BPD. Non-invasive ventilation as a primary mode of therapy is successful only in approximately fifty percent of these extremely premature babies.<sup>9,10</sup> Randomized controlled trials comparing conventional

mechanical ventilation and high-frequency ventilation, using 'optimal ventilator strategies', have shown no significant difference in rates of BPD.<sup>11</sup> Ventilator induced lung injury (VILI) is considered an important risk factor in the development of bronchopulmonary dysplasia (BPD).<sup>12</sup> There is experimental observations which revealed that it is actually the volume of gas delivered to the lungs that is more likely to be the primary determinant of lung damage during mechanical ventilation.<sup>13</sup> Evidence for the importance of volutrauma also comes from the adult acute respiratory distress syndrome network trial.<sup>14</sup> VILI is primarily caused by over distension (volutrauma) and repetitive opening and collapse (atelectrauma) of terminal lung units.<sup>15</sup>

Lung-protective ventilation should therefore aim to reduce tidal volumes, and recruit and stabilize atelectatic lung units (open lung ventilation strategy). If volutrauma is indeed important in the development of VILI then volume-controlled ventilation (VCV) may have advantages over Time cycled pressure limited ventilation (TCPLV) which is traditionally being used in neonates.<sup>16,17</sup> Since the introduction of microprocessor-based ventilators, however, it is now possible to ventilate even the smallest of babies using volume controlled ventilation. This use has been facilitated by the development of sensitive and accurate flow sensors and servo-controlled mechanics allowing accurate measurement and tracking of gas flow to avoid over-expansion (volutrauma) or under-expansion (atelectotrauma) of the lungs and damage attributable to airway flow that is too high or too low (rheotrauma). This development may have advantages particularly in newborns who have respiratory distress syndrome (RDS) in whom lung compliance may rapidly change in response to the disease process or treatment, such as surfactant therapy.<sup>18</sup>

Volume Guarantee in Dragor Babylog 8000 plus ventilator is a combined ventilator modality perhaps best described as a double or dual loop synchronized modality that ventilates using Time cycled pressure limited (TCPL) breaths with continuous flow, but it allows the

pressure to be adjusted up to a clinician set maximum using microprocessor technology to guarantee tidal volume delivery. The auto-feedback method, based on the previous breaths, aims to guarantee tidal volume delivery within a set range. The starting tidal volume target is usually 4 to 6 mL/kg. The maximum pressure limit is usually set about 20% greater than the pressure needed to deliver this tidal volume consistently. The peak pressure achieved by the ventilator thus varies between the baseline pressures (PEEP) and the set peak inspiratory pressure (PIP). Potential advantages of VG mode has been revealed by many studies which include 1) more stable tidal volume delivery and less risk for volutrauma, because the clinician can limit tidal volume delivery; (2) Equivalent gas-exchange with lower peak inspiratory and mean airway pressure with stable PaCo<sub>2</sub> levels (3) auto-weaning of peak inspiratory pressure, which results faster weaning and decreases in total duration of mechanical ventilation.<sup>19</sup>

This present study is aimed for assessing the feasibility and efficacy of Volume Guarantee (VG) ventilation in preterm neonates with respiratory distress syndrome in comparison with the traditional Time Cycled Pressure Limited (TCPL) ventilation which was practiced in our unit.

## METHODS

The study was done at Neonatal intensive care unit, Amrita Institute of Medical Sciences and Research Centre, Kochi, Kerala. This 24 bedded, Level 3 NICU is a tertiary care referral centre with approximately 600 to 800 sick neonatal admissions per year, cared under two full time Consultant Neonatologist with back up of experienced pediatric cardiology and pediatric surgery team.

All inborn preterm neonates between 26 weeks to 32 weeks at birth with respiratory distress syndrome severe enough to warrant assisted mechanical ventilation and exogenous surfactant replacement formed our study population.

Study was conducted by 2 years from March 2008 to February 2010. Two-year study period was divided into 2 phases. In the 1st year of study period (March 2008 to Feb 2009) we used Synchronized intermittent positive pressure ventilation without Volume guarantee mode (SIPPV) alone and during 2nd year study period (March 2009- Feb 2010) we used SIPPV with Volume Guarantee (SIPPV-VG) as ventilation mode in Dragor Babylog 8000 plus ventilator.

### *Sample size and sample technique*

Study Hypothesis was that the neonates assigned to Volume Guarantee mode of ventilation would require 33% less time to achieve the primary objective to predetermined extubation criteria compared to Time

cycled pressure limited ventilation similar to previous clinical trial and to demonstrate significance ( $<0.05$ ) with a power of 0.8 calculated sample size was 50 Neonates, 25 in each group. But reviewing the previous 2yr (2005-2007) case records of NICU at Amrita institute of Medical sciences where antenatal steroids and Early CPAP was practiced in all at high risk premature neonates, the assisted ventilation and surfactant use in inborn babies was on average 16 babies per year only. So, recruiting 50 babies was considered not feasible in 2 years study period.

So, the study was designed as a prospective cohort study with a total study period of 2 yrs with a protocol to include minimum of 30 consecutive neonates, at least 15 babies in each year.

The study was approved by the institute ethical committee and informed consent was obtained from either the father or a guardian of each participating neonate.

Total of 37 preterm babies fulfilling inclusion criteria were included in 2 year study period with 18 babies in 1st year study period ventilated with SIPPV mode and 19 babies in 2nd year study period on SIPPV-VG mode of ventilation.

#### **Data collection technique and tools**

For all the neonates with RDS ventilated with Dragor Babylog 8000 plus a Ventilator chart was maintained. Ventilator set and measured parameters on DragorBabylog8000plus ventilator were recorded every hour. Vital parameters including temperature, heartrate, respiratory rate, NIBP, SPO2 was continuous monitored using Spacelab monitor.

Measured values like, required PIP and MAP to achieve consistent target tidal volume( $V_{te}$ ) of 4ml/kg, minute ventilation (MV), in VG mode were recorded taking average of three consistent measured value observed by senior NICU nurse for period of 10 minutes when baby is in sleep or quiet awake state. ABG was done periodically (4-6th hrly) and as and when clinically indicated.

All neonates underwent Echo by 48hrs and/or when clinically indicated to document significant PDA requiring treatment. Neurosonogram was done on day 3, day 10 of life and at discharge to document IVH and PVL. All neonates underwent ROP screening programme as per unit protocol. All complications during ventilation were documented and necessary steps taken to prevent progression. The neonates who died during study period were investigated and discussed in mortality meeting. The cause of death and complication it had prior to death were properly documented.

#### **Data collected**

Data of baseline characteristics of study participants – included birth weight, gestational age, Presence of IUGR (weight  $<10$ th on Lubchenko percentile), Apgar score at 1minute, delivery

room management (oxygen, bag and mask, intubation), X-ray chest (grade of RDS), arterial blood gas,  $FiO_2$  requirement and Downe's score at admission.

Data of maternal variables included -multiple births, pregnancy induced hypertension (PIH),

preterm premature rupture of membrane (PPROM), Gestation diabetes, fetal distress with doppler abnormality, caesarean section and antenatal steroids.

#### **Data of Ventilator chart included**

- a) CPAP duration, Maximum CPAP pressure and  $FiO_2$  requirement before intubation, Age in hours at intubation and ventilation, surfactant dose, mode of ventilation, target volume.
- b) Periodic documented variables-Set and measured Peak inspiratory pressure (PIP) and Mean airway pressure, Minute ventilation (MV),  $FiO_2$  requirement and ABG values  $PaO_2$ ,  $PaCO_2$  and calculated  $AaDO_2$

#### **Outcome variable**

- a) Time required to achieve successful extubation criteria that is a consistent Mean airway pressure below 8cm H<sub>2</sub>O and  $AaDO_2$  below 100 mm HG for minimum of 6hrs) in each mode.
- b) Total duration of ventilator support, CPAP support and Nasal cannula O<sub>2</sub>.
- c) Complication – Patent ductus arteriosus (clinical and Echo proven), pneumothorax, culture positive sepsis, intraventricular hemorrhage (USG grading), necrotizing enterocolitis (NEC modified Bells staging), bronchopulmonary dysplasia, periventricular leukomalacia PVL (neuro sonogram at discharge), retinopathy of prematurity (ROP stage) and mortality were documented.

#### **Data analysis**

Data generated was entered in MS Office excel sheet. Analysis was done using SPSS v. 16.

Results are expressed as frequency and proportions for categorical variables and for continuous variables mean, standard deviations, median and interquartile ranges were derived.

Proportions were compared using Chi-square test of significance.

Mann-Whitney U test was used to determine whether there was a statistical difference between two ventilator groups in the measured parameters and continuous

variables. In above statistical tests the “p” value of less than 0.05 was accepted as indicating statistical significance.

**RESULTS**

In present prospective cohort study period, the incidence of RDS among inborn babies less than 32wks was 66.6% and 71.7% in two study period respectively.

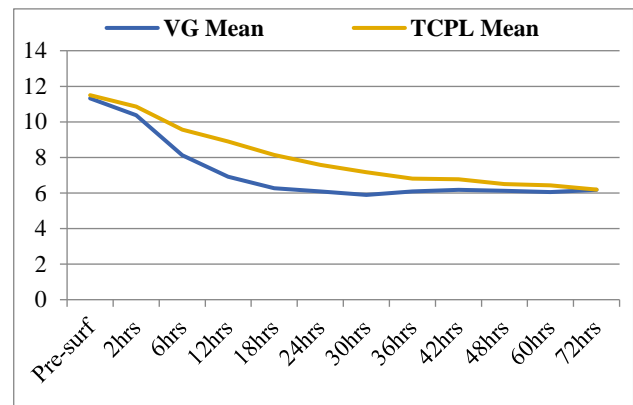
**Table 1. Maternal and perinatal characteristics of neonates in 2 study groups.**

Patient profile	SIPPV+VG	SPPV-TCPL	P value
Sex (M/F)	13/6	10/8	>0.05
IUGR	7(36.8%)	4 (22.2%)	>0.05
LSCS	17 (89.5%)	11 (61%)	>0.05
Antenatal steroids (any)	18 (94.7%)	16 (88.8%)	
Complete course (2 doses)	11 (57.8%)	10 (55.5%)	>0.05
Incomplete (1 dose)	7 (36.8%)	6 (33.3%)	
Not received	1 (5.3%)	2	
Multiple pregnancy	5(26.3%)	5(27.7%)	>0.05
Twins	3	2	
Triplets	2	3	
PROM >12hrs	8	7	>0.05
Preeclampsia	10	7	>0.05
Fetal Doppler abnormality	8	8	>0.05
GDM	3	2	>0.05
Resuscitation (any)	10 (52.6%)	10 (55.5%)	
Bag and mask	2	5	
Intubated	8 (42.1%)	5(27.7%)	>0.05
Chest compression	0	0	
APGAR 1 min <3	0	0	
APGAR 5 min <5	0	0	

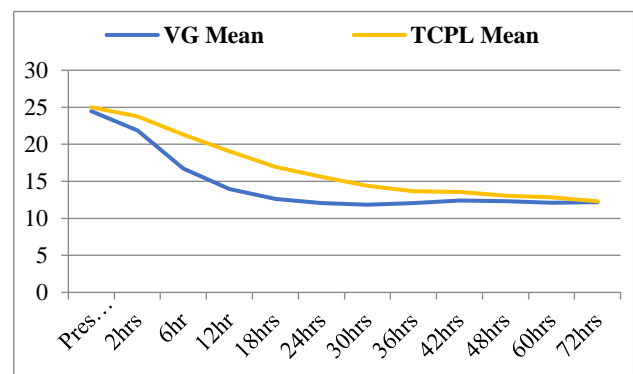
During 2 yrs study period total of 107 (69.4%) babies were diagnosed as Respiratory distress syndrome(RDS) and 24% ( 37/154) had severe RDS requiring ventilator support and surfactant. Early CPAP was successful in 65.4% in RDS babies.

Antenatal steroid coverage during 2yr study period was 70.8%(109/154) but among babies with severe RDS the coverage was 56.7% (21/37). There was male preponderance for severe RDS, 23 out of 37 babies (62.1%) were male babies. (Table 1)

In this prospective cohort study on VG vs TCPL ventilation in a closely matched population of preterm infants weighing <32 weeks with severe RDS requiring mechanical ventilation and surfactant babies in SIPPV plus VG mode of ventilation had stable and equivalent gas exchange at significantly lower Mean airway pressure as shown in and Figure 1 (MAP) and Peak inspiratory pressure (PIP) as shown in Figure 2, compared to babies on SIPPV (TCPL)mode. Time based mean ,median and interquartile range values of PIP and MAP in VG mode was consistently lower when compared to TCPL mode and was statistically significant (p<0.05) between 1st 42 hours of post surfactant period.



**Figure 1: Graphical representation of time based mean values of MAP during first 72 hours in two study group.**



**Figure 2: Graphical representation of time based mean Peak Inspiratory Pressures (PIP) in two study groups during first 72hrs.**

Infants assigned to SIPPV plus VG mode of ventilation achieved the arbitrary success criteria of MAP <8cm and AaDo2 <100mm HG maintained for 6hrs, faster than infants randomised to SIPPV mode which was statistically significant (p <0.001) implying faster weaning of airway pressure in Volume Guarantee mode and statistically significant decrease in duration of mechanical ventilation.(Table 2)

**Table 2: Primary outcome -Time required to achieve success criteria of target MAP (<8cmH20) and AaDo2 (<100mmHg) sustained for 6hrs and duration of ventilation.**

Variable	Group	N	Mean(Hrs)	S.D	Median(Hrs)	IQR-(25-75 <sup>th</sup> )	P value
Target MAP (Achieved at hrs)	VG	19	12		12	12-18	<0.001
	TCPL	18	23.6		30	30-37.5	
Target AaDo2 (Achieved at hrs)	VG	19	14.86		12	12-18	0.01
	TCPL	18	33.66		24	18-30	
Duration ventilation Hrs	VG	17	60.2	19.6	56	44-79	0.024
	TCPL	16	76.0	15.9	75	62-88.5	

The incidence of complication of prematurity in ventilated babies in both modes were comparable with no statistical difference except that in TCPL(SIPPV) mode one baby suffered pneumothorax and two babies had BPD compared to nil incidence in SIPPV plus VG mode.

## DISCUSSION

In this prospective cohort study, the incidence of RDS among inborn babies less than 32wks was 66.6% and 71.7% in two study period. During 2yrs study period total of 107 (69.4%) babies had RDS at birth and 24% (37/154) had severe RDS requiring ventilator support and surfactant. Early CPAP was successful in 65.4% in RDS babies. Antenatal steroid coverage during 2yr study period was 70.8% (109/154) but among babies with severe RDS the coverage was 56.7% ( 21/37).There was male preponderance for severe RDS, 23 out of 37 babies (62.1%) were male babies.

Our results are comparable with multicentre randomised control trials. The reason for high success of CPAP is probably the beneficial role of high antenatal steroid coverage and early initiation of CPAP to maintain functional residual capacity (FRC). Male preponderance for severe RDS as was observed in our study was also noted by Sandri et al, who analysed the need for surfactant based on gender which was more in male babies (relative risk 1.9; 95% confidence interval 1.13 to 3.20) and need for mechanical ventilation was also higher for male (relative risk 2.85, 95% confidence interval 1.26 to 6.44).<sup>20</sup>

In this prospective cohort study on VG vs TCPL ventilation in a closely matched population of preterm infants weighing <32 weeks, infants assigned to SIPPV plus VG mode of ventilation achieved the arbitrary success criteria of MAP <8cm and AaDo2< 100mm Hg maintained for 6hrs, faster than infants randomised to SIPPV mode which was statistically significant (p <0.001) implying faster weaning of airway pressure in VG mode. Total duration of ventilation was also significantly less (p<0.05) in VG mode compared to TCPL (SIPPV) mode. Present study results are comparable with other studies done by Sinha et al, Lista et al, and Cochrane database review.<sup>21-23</sup>

In this present study, the babies on SIPPV VG mode had stable PaCO<sub>2</sub> with less fluctuation. The mean and median values of PaCO<sub>2</sub> in VG mode was in the higher normal range of 35-55mmHG compared to SIPPV mode where mean and median values were in lower normal range. The babies in SIPPV mode had more out of range values (7.4% vs 1.1%) with more hypocarbia events (6.4% vs 0.56%) and also had high minute ventilation (MV) compared to babies on SIPPV VG mode. Similar conclusions were drawn in clinical trials by Cheema et al, Kezler et al, and Dawson et al, with VG mode reducing the incidence of hypocarbia by 50% with stable tidal volume delivery.<sup>24-26</sup>

This above observations can be explained on basis that in volume targeted ventilation during the phase of rapid improvement in lung compliance following surfactant administration, or /and when babies make a significant contribution from spontaneous effort, the machine auto weaned the PIP and MAP in real time targeting set tidal volume, so that equivalent stable gas exchange occurred at significantly lower MAP and PIP, avoiding hyperventilation with higher tidal volume. On the other hand, in SIPPV mode the PIP and MAP was manually weaned based on ABG and visual tidal observation. Hence they had unstable tidal volume with tendency for hyperventilation and lower PaCO<sub>2</sub> which is harmful for both lung and brain. The present study results with SIPPV VG with target VT = 4ml/kg showed stability of PaCO<sub>2</sub> in higher normal range throughout the study period with faster weaning of ventilator pressure and early extubation thus has an advantage of less risk for ventilator induced lung injury (VILI). The stability in PaCO<sub>2</sub> has potential advantage in preventing intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL) as noted in clinical trial by Fabres et al.<sup>27</sup>

In our present study SIMV or SIMV VG was chosen as weaning mode during recovery period of RDS (Fio<sub>2</sub><30% and MAP <8) and babies in SIMV VG had stability with gas exchange with sustained lower MAP and PIP. Harrare et al, in their study conclude that use of SIMVVG as weaning mode during recovery period resulted in automatic weaning of the mechanical support and enhancement of the spontaneous respiratory effort

while maintaining gas exchange relatively unchanged in comparison to conventional SIMV.<sup>28</sup> The proposed mechanism by which SIMV-VG may benefit mechanically ventilated preterm infants is of their spontaneous inspiratory effort. Down regulation of PIP when VT mechanical breath remains at or above the physiologic level releases the infant's own respiratory drive from the suppression caused by superimposed ventilation and averts over inflation pressures that increase the risk of baro- and volutrauma. In addition, prevention of excessively low tidal volumes, attributable to sudden deterioration in the inherent mechanical characteristics of the respiratory system of VLBW babies, can preserve alveolar gas exchange and prevent atelectasis.

## CONCLUSION

The incidence of severe RDS requiring surfactant and mechanical ventilation has drastically reduced following higher antenatal steroid coverage and CPAP application early in course of RDS.

- Apart from prematurity, male gender and low antenatal steroid coverage are high risk factors for severe RDS.
- In premature babies who were ventilated and received surfactant for severe RDS, Volume Guarantee (VG) mode of ventilation achieved stable and equivalent gas exchange at lower peak inspiratory and mean airway pressures compared to TCPL mode.
- Weaning occurs in real-time in VG mode, rather than intermittently in response to blood gases or intermittent observation of delivered tidal volume in TCPL mode and hence VG mode achieved significantly faster weaning and reduced duration of mechanical ventilation.
- Volume Guarantee ventilation achieves near stable tidal volume delivery during phase of rapid improvement in lung compliance by auto-weaning peak inspiratory pressures and thus avoiding hyperventilation with higher tidal volume in contrast to TCPL mode. Hence VG mode avoids fluctuation in PaCO<sub>2</sub> values preventing hypocarbia events which is harmful to both brain and lung.

Hence Proper training of residents and nursing staff about VG mode ventilation regarding working principles, limitations and trouble shooters is essential.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Munson ML. Births: final data for 2003. National Center for Health Statistics, Centers for Disease Control and Prevention, 2005. Natl Vital Stat Rep. 2005 Sep 8;54(2):1-116.
2. Lemons JA, Bauer CR, Oh W. Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, January 1995 through December 1996. NICHD Neonatal Research Network. Pediatrics 2001;107(1):e1.
3. Stoll BJ, Hansen NI, Bell EF, Shankaran S, Laptook AR, Walsh MC, et al. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. Pediatr. 2010 Sep 1;126(3):443-56.
4. Horbar JD, Soll RF, Edwards WH. The Vermont Oxford Network: a community of practice. Clinics in perinatol. 2010 Mar 1;37(1):29-47.
5. Bancalari E, Claure N. Definitions and diagnostic criteria for bronchopulmonary dysplasia. Semin Perinatol. 2006;30(4):164-70.
6. Jobe AJ. The new BPD: an arrest of lung development. Pediatric research. 1999 Dec;46(6):641.
7. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respiratory and Critical Care Med, 2001;163(7): 1723-1729.
8. Northway WH Jr, Rosan RC, Porter DY. Pulmonary disease following respirator therapy of hyaline-membrane disease: bronchopulmonary dysplasia. N Engl J Med. 1967; 276(7):357-68.
9. Polin RA, Sahni R. Continuous positive airway pressure: Old questions and new controversies. J Neonatal Perinat Med. 2008;1(1):1-10.
10. Morley CJ, Davis PG, Doyle LW et al, COIN Trial Investigators, Nasal CPAP or intubation at birth for very preterm infants. N Engl J Med. 2008; 358(7):700-8.
11. Nelson Claire and Eduardo Bancalari, New modes of mechanical ventilation in the preterm newborn: evidence of benefit, Arch Dis Child Fetal Neonatal Ed. 2007 November; 92(6): F508-12.
12. Baraldi E, Filippone M. Chronic lung disease after premature birth. New England J Med. 2007 Nov 8;357(19):1946-55.
13. Dreyfuss D, Soler P, Basset G, Saumon G. High inflation pressure pulmonary edema: respective effects of high airway pressure, high tidal volume, and positive end-expiratory pressure. Am Rev Respir Dis. 1988 May;137(5):1159-64.
14. The Acute Respiratory Distress Syndrome Network. Ventilation with low tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Eng J Med. 2000; 342(18):1301-1308. 26
15. Dreyfuss D, Saumon G. Role of tidal volume, FRC, and end-inspiratory volume in the development of pulmonary edema following mechanical ventilation. Am Rev Respir Dis. 1993;148:1194-203.
16. Ramanathan R, Sardesai S. Lung protective ventilatory strategies in very low birth weight infants. J Perinatol. 2008 May; 28(1):S41-6.

17. Donn SM, Sinha SK. Minimising ventilator induced lung injury in preterm infants. *Archives of Disease in Childhood-Fetal and Neonatal Edition.* 2006 May 1;91(3):F226-30.
18. Jaideep Singh, Sunil K. Sinha, S.M. Donn, Volume-Targeted Ventilation of Newborns. *Clin Perinatol.* 2007;34(1):93-105.
19. Martin Keszler, Kabir M. Abubakar, Volume Guarantee Ventilation, *Clin Perinatol.* 2007;34(1): 107-16.
20. Sandri F, Plavka R, Ancora G, Simeoni U, Stranak Z, Martinelli S, et al. Prophylactic or early selective surfactant combined with in CPAP in very preterm infants. *Pediatric.* 2010;125:e1402-9.
21. Sinha SK, Donn SM, Gavey J, McCarty M. Randomised trial of volume controlled versus time cycled, pressure limited ventilation in preterm infants with respiratory distress syndrome. *Arch Dis Child Fetal Neonatal Ed.* 1997;77(3): F202–F205.
22. Lista G, Colnaghi M, Castoldi F, Condo V, Reali R, Compagnoni G, et al. Impact of targeted-volume ventilation on lung inflammatory response in preterm infants with respiratory distress syndrome. *Pediatr Pulmonol.* 2004; 37(6):510-4.
23. McCallion N, Davis PG, Morley CJ. Volume-targeted versus pressure-limited ventilation in the neonate. *Cochrane Database Syst Rev.* 2005; CD003666.
24. Cheema IU, Ahluwalia JS. Feasibility of tidal volume-guided ventilation in newborn infants: a randomized, crossover trial using the volume guarantee modality. *Pediatr.* 2001;107:1323-8.
25. Keszler M, Abubakar KM. Volume guarantee: stability of tidal volume and incidence of hypocarbia. *Pediatr Pulmonol.* 2004;38(3):240-5.
26. Dawson C, Davies MW. Volume-targeted ventilation and arterial carbondioxide in neonates. *J Paediatr Child Health.* 2005; 41(9-10): 518-21.
27. Fabres J, Carlo WA, Phillips V, et al. Both extremes of arterial carbondioxide pressure and the magnitude of fluctuations in arterial carbon dioxide pressure are associated with severe intraventricular haemorrhage in preterm infants. *Pediatrics.* 2007; 119(2):299-305.
28. Herrera CM, Gerhardt T, Claure N, Everett R, Musante G, Thomas C. et al. Effects of volume-guaranteed synchronized intermittent mandatory ventilation in preterm infants recovering from respiratory failure. *Pediatr.* 2002; 110:529–533.

**Cite this article as:** Sudheer KA, Sunil B, Rajiv PK, Kripail M, Nithya E. Volume Guarantee ventilation in premature neonates with respiratory distress: a comparative study. *Int J Contemp Pediatr* 2019;6:2559-65.