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Volume Guarantee Versus Pressure Limited Ventilation in Reduction of BPD (Bronchopulmonary Dysplasia) Incidence and Sequels in Preterm Infants

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ABSTRACT

Background: Multiple studies have indicated significant advantages of VTV over PLV that are clearly obvious in lowering the concatenated outcomes of bronchopulmonary dysplasia, decreased value of pneumo-thorax, and lower rate of extreme intraventricular hemorrhage.

Aim and objectives: This research paper aimed to make a comparison of the actual effect and reliability of VTV over PLV in reducing bronchopulmonary dysplasia in preterm newborns.

Subjects and methods: A retrospective analysis applied on data collected from intubated preterm newborns less than thirty-seven weeks gestational age, who were in need of mechanical ventilation in a category III of intensive care unit for neonates (NICU). The number of recruited infants was 100 in total. They were enrolled in the present work and required mechanical ventilation. Congenital malformations were exclusion criteria for selected preterm infants.

Results: No significant differences among groups based on sex, birth weight, gestational age or even underlying illness. However, significant difference among studied groups based on hospitalization and duration of MV.

Conclusion: The use of VG ventilation is widely regarded as the standard therapeutic approach for preterm neonates with respiratory distress syndrome (RDS) who require mechanical ventilation. While this study did not find any notable disparities in neonatal morbidity and mortality, it did observe that VG ventilation resulted in considerably reduced durations of ventilation and hospitalisation compared to PC ventilation among infants with greater gestational ages.

Keywords: Ventilation, Neonatal morbidity, Gestational age, Congenital malformations.

INTRODUCTION

For the newborns, cycled time, limited pressure ventilation has employed in many NICUs. This type of ventilation utilizes a predetermined amount of O_2 gas and a predetermined peak inspiratory pressure for a specific time period. The utilization of positive pressure lung ventilation (PLV) has resulted in the documentation of two phenomena: Overexpansion, also known as volutrauma, and under-expansion or collapse [(1)].

It has also been observed that the master factor of ventilator-induced lung injury is VT, not inflation pressure . Ventilation volume-targeted can help to adjust and preserve a healthy VT [(2)]. At using of VT as a control factor, pressure of inflation drops as lung acquiescence and efforts of patient inspiratory improve, allowing for actual time pressure weaning. Excessive VT can be avoided by lowering pressure in real time, given the low duration of "mechanical ventilation" [(3)].

Multiple studies have demonstrated that VTV (Volume Targeted Ventilation) has a reduced likelihood of mortality or bronchopulmonary dysplasia (BPD), a lower incidence of "pneumothorax", decreased "hypocarbia", and a lower mean occurrence of acute intraventricular haemorrhage/"periventricular leukomalacia", in comparison with PLV (Pressure Limited Ventilation) [(4)]. In a comprehensive systematic analysis, **McCallion and colleagues [(5)]** compared volume-objected ventilation to pressure-limited ventilation using 4 randomized trials involving 178 preterm newborns recruited during the first 72 hours after birth. Volume guided ventilation reduced the time of ventilation and even the incidence of pneumothorax and serious (Grade 3 or 4) IVH, according to a meta-analysis of the experiments. At 36 weeks after PMA, there was a marginally statistically significant decline in the amount of BPD among survived patients.

After undergoing ventilation as well as a high availability of oxygen for RDS, a subset of preterm newborns had chronic lung illness, which was being recorded in 1967. Bronchopulmonary dysplasia (BPD) that has recently been defined as the requirement for supplemental oxygen gas at either two time points: 28 days after delivery or 36 weeks after gestation [(6)]. In additional to oxygen reliance at 36 weeks' postmenstrual phase, the new definition considers total time of oxygen supplementing, the necessity for the positive case of pressure ventilation or nasal constant positive airway pressure (CPAP), and MV. Poor alveolarization, altered bronchial microvasculature, and pulmonary fibrosis are the histological characteristics in BPD. Lung immaturity, fetal growth restriction, infections, oxidative stress, in-utero irritation, and mechanical ventilation have all been linked to the formation of BPD [(7)].

Compressive stress ('barotrauma') used to be a source of concern for lung damage. Many investigations, however, have found that collapses of lung and over-distension (also known as atelectasis) are

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really the primary causes of infection in the newborn lung. Animal analysis shows high PIP in an experimental animal where a cast was utilized to minimize chest wall compliant and therefore VT back up this theory. In the mice that were shielded against high VT, histological analysis revealed a considerable reduction in respiratory infections [8].

A randomized controlled study (RCT) comparing two breathing techniques, high VT at 12 mL/kg over low VT at 6 mL/kg, in individuals possesses severe lung damage provided more support. When interim important aspects a considered decrease in both fatality and breathing durability in the low VT groups, the study was called off early. During the progression and intervention of RDS, lung compliance varies fast and dramatically. Adaptive ventilation methods may improve lung reliability and reduce lung damage. Furthermore, maintaining steady minute volume ventilation to minimize abrupt variations in the CO2 concentration in bloodstream ($PaCO_2$) and maintain cerebral blood supply and reduce brain injury [9].

The goal of this investigation was to assess safety of VTV and its benefits against PLV in reducing BPD in preterm newborns.

MATERIAL AND METHODS

Study design: The present study was retrospective analyzed data obtained from a cohort of intubated premature infants, babies who were born at 37 weeks or less and needed help breathing in a level III neonatal intensive care facility.

For certain preterm children ventilated in period 1, PLV type (Servo Ventilator 300) was employed (From February 1st 2019 to February 28th 2020).

For those preterm children ventilated throughout period 2, from March 1, 2020, to March 1, 2021, the Babylog VN 500 from Dräger was used as the VTV mode.

Inclusion criteria: The present study included 100 premature newborns who needed mechanical ventilation.

Exclusion criteria: Term babies and babies with congenital abnormalities were not included in the study.

Throughout period 1, PLV was utilized on 50 preterm newborns with an average weight of birth (BW) of 1.38 ± 0.62 kg (ranged between 0.40 -2.35 kg) as well as a mean gestational age (GA) of 27.42 ± 3.0 week (range 31.1-34.6 weeks). Throughout period 2, VTV has been used on 50 preterm newborns with an average BW of 1.39 ± 0.64 kg (ranging 0.45 – 2.70 kg) and a mean GA of 28.49 ± 3.12 week (ranging 23.5-34.6 weeks). Every infant in the NICU had their pulse rate, respiration average, pressure of blood, and levels of oxygen measured (Nihon Kohden, Nihon Kohden Company, Japan). "Respiratory distress disorders "(RDS) (34 infants), newborn pneumonia (10 infants), "hypoxic-ischemic encephalopathy" (4 cases), and meconium aspiration disorders (two cases) were always the basic illnesses in the PLV subgroup. RDS (33 infants), newborn pneumonia (11 infants), three patients of each HIE, and MAS were always the basic illnesses in the group of VTV.

For 5 infants in the PLV subgroup and 6 children in the group of VTV who suffered from pulmonary hypertension, inhaled nitric oxide (iNO) treatment was utilized. An echocardiographic evaluation was performed on all patients receiving iNO therapy, Doppler imaging was used to examine the tricuspid ejection jet, the shunt path of the patent ductus arteriosus, and the atrial shunt pathway. High pulmonary artery pressures, right-to-left or bilateral PDA, or patent foramen oval shunting were all echocardiographic indicators of pulmonary hypertension in all patients treated with iNO treatment.

Ventilation strategy: Babies in PLV subgroup were maintained in the assist control mode conditions as during the acute phase of distress. The following have been the original setup: PEEP 5 up to 8 cm H_2O, PIP 12 up to 25 cm H_2O tailored to the patient's chest movement and eliminating of CO_2, rate to 30 breaths (bpm) and inspiratory time was 0.4 seconds. The ventilator type was modified from A/C to synchronized intermittent obligatory ventilation mode (or SIMV) as once babies had recovered from their severe respiratory disease. The goal was to keep arterial blood gas values such pH between 7.25 and 7.45, PaO_2 between 50 and 70 mm Hg, $PaCO_2$ between 35 and 55 mm Hg, and SpO_2 between 90 and 95% constant. Extubation was considered if the essential ventilator parameters were met: PIP = 16 cm H_2O, PEEP = 5 cm H_2O, rate at 20 bpm, and FiO_2 0.3. The newborns were kept on nasal bubbles CPAP after being extubated, with 5 to 6 cm H2O administered by short bi-nasal prongs.

The ventilation settings were chosen using the guide for newborn VTV protocols (Klingenberg et al. and Keszler et al. practical). For preterm newborns, the VT was chosen initially at 4.0 up to 6.0 mL/kg. Neither group received either sedation or muscle relaxants during the research period.

Arterial blood analysis was performed to examine $PaCO_2$ and PaO_2. For all research neonates under 72 hours old, arterial blood gas was monitored every 12 hours, also every 24 hours till extubation. $PaCO_2$ 35 mmHg was categorized as hypocarbia, whereas $PaCO_2$ greater than 60 mm Hg was described as hypercarbia. Hypocarbia and hypercarbia were detected by using the results of the arterial blood gas study. The arterial blood gas analyzer determined that hypoxemia existed when the patient's SpO_2 was 80% or lower for at least 20 seconds, or when the patient's PaO_2 was 50 mm Hg or lower.

The diagnosis of RDS was established through the utilization of radiological and clinical evidence. Bronchopulmonary dysplasia (BPD) is characterized as the inability to pass a test period of breathing room air, with or without the aid of a ventilator, at 36 weeks from

the start of the mother's last menstrual cycle. This occurs following treatments with an inspired oxygen fraction (FiO_2) more than 0.21 for a minimum duration of 28 days. The culture of positive blood that also was treated with antibiotic medications for at least 7 days was considered sepsis.

Intraventricular hemorrhage (IVH) was identified on cranial ultrasonography, and the patient was further classified as having IVH with or without ventricular dilatation and intracerebral (parenchymal) hemorrhage. Pulmonary bleeding symptoms included blood in the endotracheal tube and reports of central or distributed ground glass opacities on chest x-rays. The global grading for ROP was used to determine the stage of retinopathy of prematurity (ROP). ROP stages were described as ROP stages 3 to 5. The ridge with fibro-vascular extensions into the vitreous was present in stage 3 ROP, fractional retinal detachment was present in fourth stage ROP, and total retinal detachment was present in the fifth stage.

Ethical approval: The research proposal received a comprehensive ethical assessment from Faculty of Medicine, Menoufia University and has been evaluated in compliance with the ethical principles and criteria specified in the Declaration of Helsinki.

Statistical analysis

Data analysis was carried out using version 20.0 of the IBM SPSS software program that was supplied into the computer (Armonk, NY: IBM Corp). To check the normality of variable distributions, we used The Kolmogorov-Smirnov test, while Chi-square test was employed to analyze comparisons between categories for categorical data (Fisher or Monte Carlo). For regularly distributed quantitative data, and for comparing two groups, the student t-test was applied. For non-regularly dispersed quantitative variables, the Mann Whitney test was employed to compare two groups. The significance of the acquired findings was assessed at a 5% level.

RESULTS

There was really no statistically significant difference between the two groups in the terms of sex, birth weight, gestational age or underlying condition (Table 1).

Table (1): comparing between the investigated groups based on different parameters

	PLV (n = 50)		**VTV (n = 50)**		**Test of Sig.**	**P**
	No	**%**	**No**	**%**		
Sex						
Male	26	52.0	30	60.0	χ^2=	0.420
Female	24	48.0	20	40.0	0.649	
Birth weight (kg)						
Mean ± SD.	1.38 ± 0.62		1.39 ± 0.64		U=	0.923
Median (Min. – Max.)	1.43 (0.4 – 2.35)		1.4 (0.45 – 2.7)		1236.0	
Gestational age (weeks)						
Mean ± SD.	27.42 ± 3.0		28.49 ± 3.12		t=	0.084
Median (Min. – Max.)	27.35 (23.1 – 34.6)		29.1 (23.5 – 34.6)		1.748	
Underlying disease						
RDS	34	68.0	33	66.0		
Neonatal pneumonia	10	20.0	11	22.0	χ^2=	^{MC}p=
HIE	4	8.0	3	6.0	0.548	1.000
MAS	2	4.0	3	6.0		

χ^2: **Chi square test** MC: **Monte Carlo** **t: Student t-test** **U: Mann Whitney test** SD: **Standard deviation** p: p value for comparing between the studied groups *: Statistically significant at $p \leq 0.05$

In terms of getting inhaled NO, pulmonary HTN or receiving 2nd or more surfactant dose treatments, there was no significant difference between the two groups (Table 2). Also, in table of contents (2), there was a substantial difference between the two groups regarding the durations of MV and hospitalization as well as episodes of hypocarbia and hypercarbia.

Table (2): comparing between the investigated groups based on different parameters.

	PLV (n = 50)		VTV (n = 50)		Test of Sig.	P
	No	**%**	**No**	**%**		
Receiving Inhaled No						
No	45	90.0	44	88.0	χ^2= 0.102	0.749
Yes	5	10.0	6	12.0		
Evidence of pulmonary HTN						
No	45	90.0	44	88.0	χ^2= 0.102	0.749
Yes	**5**	**10.0**	**6**	**12.0**		
Maximum iNO concentration P.P.M	**(n = 5)**		**(n = 6)**			
Mean ± SD.	14.4 ± 1.14		12.67 ± 1.37		t= 2.253	0.051
Median (Min. – Max.)	14.0 (13.0 – 16.0)		13.0 (11.0 – 14.0)			
Receiving 2nd or more surfactant doses						
No	27	54.0	29	58.0	χ^2= 0.162	0.687
Yes	23	46.0	21	42.0		
Duration of hospitalization (days)						
Mean ± SD.	24.46 ± 2.8		19.35 ± 2.6		U= 153.0*	<0.001*
Median (Min. – Max.)	12.50 (5.0 – 44.0)		8.0 (4.0 – 40.0)			
Duration of ventilation, D						
Mean ± SD.	14.52 ± 1.87		10.58 ± 1.59		U= 153.0*	<0.001*
Median (Min. – Max.)	14.50 (10.0 – 17.0)		10.0 (9.0 – 17.0)			
Fio2 less than 30% at 28 d						
YES	14	28	9	18.0	χ^2= 1.412	0.2354
NO	36	72	41	82		
Episodes of hypocarbia						
Mean ± SD.	4.74 ± 1.16		3.72 ± 1.16		t= 4.399*	<0.001*
Median (Min. – Max.)	5.0 (2.0 – 6.0)		4.0 (1.0 – 5.0)			
Episodes of hypercarbia						
Mean ± SD.	1.86 ± 0.78		0.82 ± 0.69		U= 465.50*	<0.001*
Median (Min. – Max.)	2.0 (1.0 – 3.0)		1.0 (0.0 – 2.0)			

χ^2: Chi square test **t: Student t-test** **U: Mann Whitney test** SD: **Standard deviation**
p: p value for comparing between the studied groups *: Statistically significant at $p \leq 0.05$

There was no statistically significant difference between them regarding Fio2 < 30% at 28 ds.
Although there was significant difference between both groups based on BPD and death rates was recorded (Table 3), the difference between both groups regarding the other complications like pulmonary hemorrhage, air leakage syndromes, severe ROP, sepsis, IVH or periventricular leucomalacia were insignificant.

Table (3): Comparison between the two investigated groups based on different parameters

	PLV (n = 50)		VTV (n = 50)		χ^2	P
	No	%	No	%		
Death						
No	40	80.0	48	96.0	6.061*	0.014*
Yes	10	20.0	2	4.0		
BPD						
No	31	62.0	43	86.0	7.484*	0.006*
Yes	19	38.0	7	14.0		
Pulmonary hemorrhage						
No	38	76.0	43	86.0	1.624	0.202
Yes	12	24.0	7	14.0		
Severe ROP						
No	43	86.0	45	90.0	0.379	0.538
Yes	7	14.0	5	10.0		
Laser therapy						
No	47	94.0	49	98.0	1.042	FEp= 0.617
Yes	3	6.0	1	2.0		
Sepsis						
No	44	88.0	46	92.0	0.444	0.505
Yes	6	12.0	4	8.0		
IVH grade 1-2						
No	46	92.0	47	94.0	0.154	FEp= 1.000
Yes	4	8.0	3	6.0		
IVH grade 3-4						
No	44	88.0	46	92.0	0.444	0.505
Yes	6	12.0	4	8.0		
Periventricular leukomalacia						
No	45	90.0	47	94.0	0.543	FEp= 0.715
Yes	5	10.0	3	6.0		
Air leakage syndrome						
No	44	88	46	92	0.44	0.505
Yes	36	72.00	41	82.00		

χ^2: **Chi square test** , FE**: Fisher Exact** , p: p value for comparing between the studied groups, *: Statistically significant at $p \leq 0.05$

DISCUSSION

Mechanical ventilation continues to serve as the primary approach for managing "respiratory distress syndrome" (RDS) in neonates. [9] Nevertheless, numerous investigations conducted throughout the course of time have provided evidence indicating that breathing can result in lung injuries, including barotrauma, volutrauma, atelectotrauma, and biotrauma. These issues have the potential to result in enduring consequences, specifically bronchopulmonary dysplasia (BPD). To mitigate the occurrence of lung damage caused by ventilation, contemporary newborn ventilators offer volume-guaranteed (VG) modes as an alternative to the conventional pressure-controlled ventilation (PCV) method [10].

The objective of the novel technique is to provide a consistent tidal volume despite variations in compliance and resistance. Consequently, a decreased occurrence of hypercarbia or hypocarbia results in the generation of a comparatively more constant "partial pressure of carbon dioxide" ($PaCO_2$). The volume guarantee (VG) mode also enables automated weaning, wherein the peak

inspiratory pressure is automatically adjusted to achieve the desired tidal volume as the patient's lung compliance improves. Nevertheless, a significant obstacle in implementing a dual control mode of ventilation, such as volume guarantee (VG), is the potential interference caused by leaks. These leaks might either mistakenly trigger an assisted breath or result in dyssynchrony between the patient and the ventilator. The prevalence of leak issues is higher in newborns compared to adults due to the utilization of unsealed tubes. The efficacy of VG ventilation in infants, particularly in extremely preterm newborns, is contingent upon the extent of concurrent leakage [(11)].

Taking into consideration the aforementioned context, the primary objective of this research endeavor was to conduct a comparative analysis between VG ventilation and typical PC ventilation. The focus of this comparison was to evaluate the length of mechanical ventilation, as well as the resulting newborn morbidity and mortality.

Regarding the demographic data, there was no distinction between the two groups in terms of sex, birth weight, gestational age, or the related cause. In terms of getting inhaled NO, pulmonary HTN or receiving 2nd or more surfactant dose treatments, there was no significant difference between the two groups. Despite randomization, there was an imbalance in BW, GA, and prenatal steroid usage in **Chowdhury's** [(12)] trial. The median GA/BW of patients in the PLV group was lower than that of patients in the VTV group (26 w/856 g against 28 w/1016 g). **Chowdhury** [(12)] compensated for this disparity in his published study, but the unadjusted results were used in this review.

Wheeler *et al.* [(13)] also found no statistically significant differences between the two groups in terms of sex, birth weight, or gestational age.

The total number of days of ventilation and length of hospital stay across all age and weight groups were significantly different between the two groups, as shown in our study. In the prior trial, **Wheeler *et al.*** [(13)] found that the VG group had a significantly shorter total duration of breathing in newborns with a gestational age of 31-34 weeks. The observed decrease in the peak inspiratory pressure (PIP) in the volume guarantee (VG) pattern, in response to increased lung compliance, which facilitates quicker discontinuation of mechanical ventilation (MV), may explain the inconsistency observed in this situation. While there was a decrease in the overall duration of breathing in the higher gestational age category, there was no significant alteration observed in the ventilation period among infants in the lower gestational age range of 27-30 weeks. Another study, **Khashaba *et al.*** [(14)] reported a substantial reduction in hospitalization times for VG ventilation what is new in our study is that the significant difference was reported to all preterm babies whatever the gestational age or birth weight. This shorter duration of ventilation and total hospitalization duration has a great effect on the patient sequalae as well as economic and social outcomes.

Our results showed a highly significant difference between the two groups with respect to hypocarbia and hypercarbia episodes. In their study, **Herrera *et al.*** [(15)] saw a notable reduction in both peak and mean inspiratory pressure while utilizing SIMV+VG ventilation as opposed to the conventional pressure-controlled ventilation method. The authors of this study reached the conclusion that the utilization of modest levels of mechanical support in the SIMV+VG mode of ventilation decreases the likelihood of "ventilator induced lung injury" and the subsequent morbidity. In terms of BPD and death, our study found a substantial difference between the two groups. Although, we found no significant differences between the two groups in terms of the occurrence of severe ROP, IVH grade 3, PVL, sepsis, pulmonary hemorrhage and pneumothorax. In a prior study conducted by **Wheeler *et al.*** [(13)], a notable observation was made regarding the occurrence of VG mode failure in preterm infants with a gestational age ranging from 27 to 30 weeks (i.e., weighing less than 1000 g). This pattern was found to be very consistent throughout the various groups studied. The bigger disparity between delivered and estimated tidal volume was a primary cause of failure. In the prior study, it was discovered that the equipment's applied anatomic dead zone has a significant impact in tidal volume release in the 23-32-week gestational age group. VTV patterns were associated with a lower risk of death or birth defects when applied at 36 weeks of pregnancy. **Wheeler *et al.*** [(13)] found that VTV modes reduced the incidence of pneumothorax, mean days of ventilation, hypocarbia, grade 3-4 intraventricular hemorrhage, and the combined outcome of periventricular leukomalacia or grade 3-4 intraventricular hemorrhage (Typical RR 0.53, NNT). Multiple factors contribute to the development of prematurity-related conditions such retinopathy of prematurity, intraventricular hemorrhage, periventricular leukomalacia, and bronchopulmonary dysplasia.

Prolonged exposure to elevated levels of oxygen and reduced levels of carbon dioxide has been associated with detrimental effects on vital organs, including the brain, retina, and lungs, particularly in preterm infants. Based on recent research findings, it is advisable to aim for an oxygen saturation range of 90-95% in order to mitigate the risk of developing retinopathy of prematurity (ROP) and bronchopulmonary dysplasia (BPD). This study established a correlation between the dependence on ventilators and the risk of retinopathy of prematurity (ROP). It was observed that the length of mechanical ventilation had an impact on the likelihood of ROP development, with an average odds ratio of 1.06.

Nevertheless, there is still a dearth of evidence regarding the relationship between ventilator mode and the occurrence of retinopathy of prematurity (ROP).

CONCLUSION

Although both PLV and VG ventilations are considered the main standards of therapy in preterm infants with RDS who are in need for mechanical ventilation, in the present study, no statistically significant difference was observed in neonatal morbidity and mortality. However, a significant reduction was observed in the duration of ventilation and hospital stay in the VG ventilation group compared to the PC ventilation group, specifically among infants with lower gestational age. A notable disparity was observed in terms of occurrences of hypercarbia and hypocarbia.

ABBREVIATIONS

AC: Assist Control, **BPD:** "Bronchopulmonary Dysplasia" **CPAP:** "Continuous Positive Airway Pressure", **FiO2:** "Fraction of Inspired Oxygen" **HIE:** Hypoxic Ischemic Encephalopathy **iNO:** Inhaled Nitric Oxide **IVH:** ntraventricular hemorrhage, **MAS:** "Meconium Aspiration Syndrome" **MV:** "Mechanical Ventilation", **NICU:** "Neonatal Intensive Care Unit" **$PaCO_2$:** Partial pressure of carbon dioxide , **PaO_2:** Partial pressure of oxygen **PC:** Pressure Control, **PDA:** Patent ductus Arteriosus, **PEEP:** Positive End Expiratory Pressure **PIP:** Peak Inspiratory Pressure **PLV:** Pressure limited Ventilation **PMA:** Postmenstrual Age, **Pulmonary HTN:** Pulmonary Hypertension, **RDS:** Respiratory distress Syndrome **RCT:** Randomized Control Trial **ROP:** Retinopathy of Prematurity, **SIMV:** Synchronized Intermittent Mechanical Ventilation, **SpO_2:** Oxygen saturation, **VG:** Volume Guarantee, **VT:** Tidal volume **VTV:** Volume Targeted Ventilation.

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REFERENCES

1. **Klingenberg C, Wheeler K, McCallion N *et al.* (2017):** Volume-targeted versus pressure-limited ventilation in neonates. DOI: 10.1002/14651858.CD003666.pub4
2. **Reiterer F, Schwaberger B, Freidl T *et al.* (2017):** Lung-protective ventilatory strategies in intubated preterm neonates with RDS. Paediatric respiratory reviews, 23: 89-96.
3. **Bugedo G, Retamal J, Bruhn A (2017):** Driving pressure: a marker of severity, a safety limit, or a goal for mechanical ventilation? Critical care, 21 (1): 1-7.
4. **Chen L J, Chen J Y (2019):** Volume-targeted versus pressure-limited ventilation for preterm infants. Journal of the Chinese Medical Association, 82 (10): 791-794.
5. **McCallion N, Davis P G, Morley C J (2005):** Volume-targeted versus pressure-limited ventilation in the neonate. https://pubmed.ncbi.nlm.nih.gov/16034906
6. **Gisondo C , Donn S (2020):** Bronchopulmonary Dysplasia: An Overview. Research and Reports in Neonatology, 10: 67.
7. **Davidson L , Berkelhamer S (2017):** Bronchopulmonary dysplasia: chronic lung disease of infancy and long-term pulmonary outcomes. Journal of clinical medicine, 6 (1): 4.
8. **Enomoto M, Keszler M, Sakuma M *et al.* (2017):** Effect of volume guarantee in preterm infants on high-frequency oscillatory ventilation: a pilot study. American journal of perinatology, 34 (01): 26-30.
9. **Aversa S, Marseglia L, Manti S *et al.* (2016):** Ventilation strategies for preventing oxidative stress-induced injury in preterm infants with respiratory disease: an update. Paediatric Respiratory Reviews, 17: 71-79.
10. **Krishna G, Ann Skariah T, Lewis Edward L (2019):** Volume-guaranteed ventilation versus pressure-controlled ventilation in preterm infants with respiratory distress syndrome: a randomized controlled trial. Iranian Journal of Neonatology, 10 (2): 42-46.
11. **Keszler M (2019):** Volume-targeted ventilation: one size does not fit all. Evidence-based recommendations for successful use. Archives of Disease in Childhood-Fetal and Neonatal Edition, 104 (1): F108-F112.
12. **Chowdhury A, Chowdhury O, Patel D (2013):** Randomised Trial of VolumeTargeted Ventilation versus Pressure-Limited Ventilation in Acute Respiratory Failure in Prematurely Born Infants. Neonatology, 104: 290–4
13. **Wheeler K, Klingenberg C, McCallion N *et al.* (2017):** Volume-targeted versus pressure-limited ventilation in the neonate. https://doi.org/10.1002/14651858.CD003666.pub3
14. **Khashaba M, El-Mazahi M, Nasef N (2015):** Volume guarantee ventilation in the weaning phase of preterm infants. Egyptian Pediatric Association Gazette, 63: 10. 1016/j.epag.2015.08.001.
15. **Herrera C, Gerhardt T, Claure N *et al*. (2002):** Effects of volume guaranteed synchronized intermittent mandatory ventilation in preterm infants recovering from respiratory failure. Pediatrics, 110 (3): 529-33