



A COMPARATIVE STUDY TO COMPARE THE EFFECT OF VOLUME GUARANTEE VENTILATION AND PRESSURE LIMITED VENTILATION ON REQUIRED DURATION OF VENTILATION IN PRETERM INFANTS

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ABSTRACT

Background: Volume guaranteed (VG) is a novel mode, best described as a dual loop synchronized modality that ventilates with time cycled pressure limited ventilation. It provides automatic adjustment of the peak inspiratory pressure for ensuring a minimum set tidal volume. There are limited data about the effects of VG ventilation on required duration of ventilation and short term neonatal outcomes in preterm infants with respiratory distress syndrome (RDS).

Objective: The objective of this study was to evaluate the effect of VG ventilation on required duration of ventilation.

Methods: This prospective randomized comparative study was conducted at level III b NICU of Deenanath Mangeshkar Hospital & Research Center, Pune between May 2016 to April 2017. Forty six preterm infants who required mechanical ventilation were randomly divided into 2 groups [SIPPV group (n=23) and SIPPV + VG group (n=23)]. Required duration of mechanical ventilation was recorded. Post extubation CPAP duration and duration of oxygen requirement were also recorded.

Results: There were no significant differences between two groups in terms of demographic features. Infants ventilated with VG mode had shorter duration of ventilation (statistically not significant). Extubation failure was observed less frequently with SIPPV + VG mode of ventilation. Post extubation duration of CPAP requirement and duration of oxygen requirement were significantly less (p-value <0.05) in infants ventilated with VG mode.

Conclusion: In conclusion, in our study VG ventilation significantly reduced duration of CPAP and oxygen requirement in preterm infants. A trend in reduction in required duration of ventilation was also observed with VG mode of ventilation. This data favours the use of VG ventilation in respiratory support of premature infants.

KEYWORDS : SIPPV-Synchronized Intermittent Positive Pressure Ventillation, VG- Volume Guarantee

I. INTRODUCTION

Mechanical ventilation (MV) is an important tool in the care of critically sick and preterm infants as very low birth weight (VLBW) infants may require MV therapy during their hospitalization (1,2). Synchronized mechanical ventilation is used now a days. The principal advantages of synchronized mechanical ventilation such as decreased work of breathing, more comfort to patient, less need of sedation, earlier weaning process have been well documented (3). There is wide acceptance of synchronized mechanical ventilation in NICU.

The two most widely used modalities of synchronized mechanical ventilation are Synchronized Intermittent Mandatory Ventilation (SIMV) and Assist/control (AC)/synchronized intermittent positive pressure ventilation (SIPPV). SIPPV is a Time Cycled Pressure Limited mode in which every spontaneous breath is supported by the preset peak inspiratory pressure (PIP) and the ventilation rate is triggered by the patient's respiratory rate. SIPPV typically uses a minimal mandatory back up breaths to support the infant during periodic breathing or apnea (4).

During IPPV, the tidal volume delivered to the patient is dependent on lung compliance and resistance, the patient's inspiratory effort, as well as the applied ventilator pressure. Improving lung mechanics, either because of surfactant administration or during recovery phase of respiratory distress syndrome (RDS), can lead to delivery of inadvertently large tidal volume(5). Large variations in tidal volume and alveolar ventilation not only raise the possibility of volutrauma, could also lead to hypocarbia with its recognized deleterious effects on cerebral blood flow (6).

Hypoventilation due to insufficient tidal volume delivery due to increased resistance, airway obstruction can lead to inefficient gas exchange, increased work of breathing, agitation, increased risk of IVH. High inflation pressures or losses in alveolar volume due to insufficient ventilation can play a role in the development of lung injury in preterm infants.

It is now clear that volume is an important contributor to ventilator-induced lung injury (7), and as such, there is a growing interest in directly controlling tidal volume (VT) during mechanical ventilation in infants.

Volume targeted ventilation is a modality aimed at reducing the variability by adjusting the peak pressure or duration of the mechanical breath to maintain tidal volume (8). Modalities of volume targeted ventilation include volume controlled (VC), volume-assured pressure-support (VAPS), pressure-regulated volume-controlled (PRVC) and volume guarantee (VG) (8).

Volume guarantee (VG) is one such mode that may be combined with any standard synchronized mode such as SIPPV, SIMV or PSV mode. It is best described as a dual loop synchronized modality that ventilates with time cycled pressure limited ventilation but allows pressure to be adjusted to deliver a tidal volume in a clinician chosen range. The addition of volume guarantee to one of these modes enables the clinician to set a mean tidal volume to be delivered, as well as the standard ventilator settings of PIP, positive end expiratory pressure (PEEP), inspiratory time and respiratory rate. (8)

Volume guarantee mode of ventilation has been designed to combine the advantages of pressure-limited ventilation with the advantages of volume- controlled ventilation, without the inherent disadvantages of either of these modalities when used on their own. (8)

Our study aims to assess the effectiveness of addition of volume guarantee to SIPPV mode, in reducing the duration of ventilation in comparison to SIPPV mode of ventilation.

II..MATERIAL AND METHODS

Study Site: NICU Deenanath Mangeshkar hospital & research centre, Pune Maharashtra.

Study Population: Preterm infants admitted to NICU requiring mechanical ventilation.

Study Design: A prospective, randomized, comparative study

Sample Size with Justification: A sample size of 23 patients per group is needed to detect a reduction of 60% in mean duration of ventilation in preterm infants receiving SIPPV + Volume Guarantee (SIPPV+VG) mode of ventilation (36 hrs) compared to group of preterm infants receiving SIPPV mode of ventilation, with 80% power and 5% level of significance using a two-sample t-test (one tailed), assuming a mean duration of ventilation to be 96 ± 80 hrs in SIPPV group reported from the literature.

Articles cited for estimation of sample size:

Nuray Duman, Funda Tuzun, Sumer Sutcuoglu, Cemile Didem Yesilirmak, Abdullah Kumral & Hasan Ozkan. Impact of volume guarantee on synchronized ventilation in preterm infants: a randomized controlled trial. *Intensive Care Med.* (2012)38:1358-1364. (9)

Formula for estimating sample size with substitution of values used:

$$nA = (1 + 1/k) [\Sigma(zA + z1 - B) / (MA - MB)]^2$$

Where

- $K = n_1/n_2$ is the matching ratio = 1
- Σ is standard deviation = ± 80 hrs
- B is Type II error, meaning 1 - B is power; $Z_{1-\beta}$ = Represents the desired power (typically 0.84 for 80% power).
- A is Type I error = 5% ; Z_α = Represents the desired level of statistical significance (typically 1.64 for one tailed test)
- difference in means = $(MA - MB) = 96 - 36$ hrs

Time Frame to Address the Study: May 2016 – April 2017.

Inclusion Criteria:

1. Preterm babies of gestational age less than 37 wks requiring mechanical ventilation.

Exclusion Criteria:

1. Major congenital cardiac, respiratory or central nervous system malformation
2. Craniofacial malformations
3. Intraventricular hemorrhage, grade III/IV.
4. Pulmonary hemorrhage

46 consecutive preterm infants (of consenting parents) requiring mechanical ventilation were studied for duration of ventilation during the 1 year period from 01/05/16 to 30/04/17 in NICU of Deenanath Mangeshkar Hospital & Research center.

Out of 46 infants, 23 were put to SIPPV+VG mode of ventilation and 23 infants were put on SIPPV mode of ventilation.

Mode of ventilation was assigned based on computer generated random sequence numbers.

Babies were weaned to SIMV+VG/SIMV (As per respective initial mode).

Extubation criteria were:

1. $FiO_2 \leq 0.4$,
2. Rate ≤ 20 /min,
3. PIP ≤ 18 cm H₂O, or to achieve tidal volume 4-6 ml/kg,
4. PEEP ≤ 5 cmH₂O and
5. Flow of 6-8 L/min.
6. pH > 7.25, pCO₂ ≤ 50

Babies were extubated to nCPAP.

Successful extubation was defined as no need of reintubation for at least 3 days after the first extubation attempt The reintubation criteria, extubation failure were same in both the groups and include at least one of the following: Silverman-Anderson Score >7 (99), pH <7.25, pCO₂ > 60 mmHg, SpO₂ < 88% on FiO₂ > 60%.

OUTCOME:

Primary Outcome: Duration of ventilation

Secondary Outcome:

1. Re intubation rate
2. Duration of CPAP
3. Duration of Oxygen requirement

STATISTICAL METHOD:

Statistical analysis was carried out with the help of SPSS (version 20) for Windows package (SPSS Science, Chicago, IL, USA). The description of the data was done in form of mean +/- SD for quantitative data while in the form of % proportion for qualitative (categorical) data. P-values of < 0.05 were considered significant. For quantitative data, Unpaired Student's t-test was used to test statistical significance of difference between two independent group means with respect to growth in terms of weight gain, duration of feeding and time to discharge between two independent groups. For comparison of categorical variables (i.e to examine the associations between qualitative/quantitative variables), chi-square test was used if the number of elements in each cell were 5 or higher and Fisher's exact test, otherwise. To compare proportions between two treatment groups or between pre & post treatment within a group, Z test of proportions was used.

III. RESULTS

Our study was conducted over period of 1 year from May 2016 to April 2017 in our level III b NICU at a tertiary care hospital. Total 46 preterm newborns requiring mechanical ventilation after birth were included in our study. Out of those, 23 neonates received SIPPV mode of ventilation and other 23 received SIPPV + VG mode of ventilation.

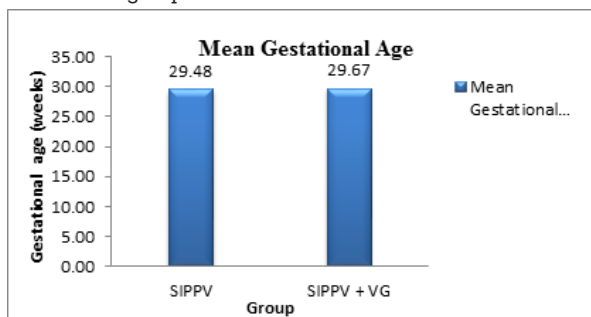
Out of 46 enrolled neonates in the study, 18 (39.13%) were female [8 (34.78%) in SIPPV group & 10 (43.48%) in SIPPV + VG group]. 28 preterm neonates (60.87%) were male in our study [15 (65.22%) in SIPPV group & 13 (56.52%) in SIPPV + VG group]. P value 0.763.

Table 1: Mean Gestation age wise distribution of preterm neonates

Group	Number of patients	Gestational age (weeks)		p-value
		Mean	SD	
SIPPV	23	29.48	3.18	0.828
SIPPV + VG	23	29.67	2.73	

Mean gestation age of enrolled neonates was 29.48 weeks (SD 3.18) in SIPPV group while it was 29.67 weeks (SD 2.73) in

SIPPV + VG group.



Graph 1: Bar-Diagram showing mean gestational age wise distribution of preterm neonates.

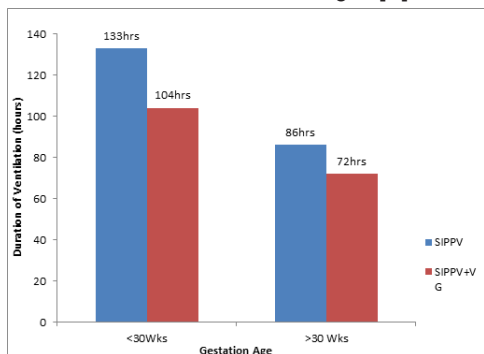
3 neonates (13.04%) died in both Non VG and VG group. P value 0.999 therefore there is no significant difference in incidence of death between SIPPV group and SIPPV + VG group.

Table 2: Mean required duration of ventilation in both groups according to gestational age

Gestation Age	Group	Required duration of Ventilation (hours)		P value
		Mean	SD	
Less than 30 Weeks	SIPPV	133.0	70.49	0.357
	SIPPV + VG	104.0	63.64	
More than 30 Weeks	SIPPV	86.0	44.36	0.328
	SIPPV + VG	72.0	60.19	

Mean required duration of ventilation in < 30 weeks of gestation age infants was 133.0 hours (SD 70.49) in SIPPV group and it was 104.0 hours (SD 63.64) in SIPPV + VG group, p value 0.357.

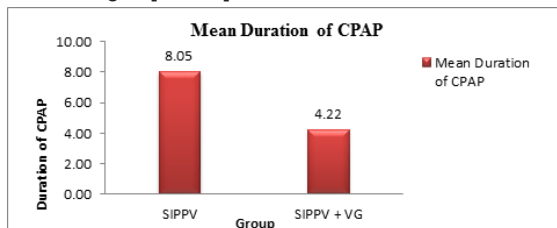
Mean required duration of ventilation in > 30 weeks of gestation age infants was 86 hours (SD 44.36) in SIPPV group and 72.0 hours (SD 60.19) in SIPPV + VG group, p value 0.32.



Graph 2: Bar-Diagram showing mean required duration of ventilation in both groups according to gestational age

CONCLUSION:-

By using 2 independent sample t-test p-value > 0.05 therefore there is no significant difference between SIPPV group and SIPPV + VG group for required duration of ventilation.



Graph 3: Bar-Diagram showing mean Duration of CPAP requirement (Post extubation).

Mean duration of CPAP requirement in SIPPV group was 8.05 days (SD 5.59) while in SIPPV + VG group mean duration of CPAP requirement was 4.22 days (SD 2.84), p value 0.013.

Conclusion:- By using 2 independent sample t-test p-value < 0.05, therefore there is significant reduction in required duration of CPAP (post extubation) SIPPV + VG group compared to SIPPV group.

Table 3: Mean required duration of CPAP (Post extubation) in both groups according to Gestation age

Gestation Age	Group	Duration of CPAP requirement (days)		P value
		Mean	SD	
Less than 30 Weeks	SIPPV	10.23	5.45	0.026
	SIPPV + VG	5.67	3.46	
More than 30 Weeks	SIPPV	3.33	1.51	0.426
	SIPPV + VG	2.78	0.67	

In patients with gestation age < 30 weeks, mean duration of CPAP requirement in SIPPV group was 10.23 days (SD 5.45) while in SIPPV + VG group it was 5.67 days (SD 3.46), p value 0.026.

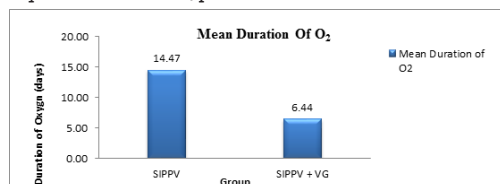
In patients with gestation age > 30 weeks, mean duration of CPAP requirement in SIPPV group was 3.33 days (SD 1.51) while in SIPPV + VG group it was 2.78 days (SD 0.67), p value 0.426 .

Table 4: Mean duration of Oxygen requirement in both groups

Group	No. of patients	Duration of O ₂ (days)		p-value
		Mean	SD	
SIPPV	19	14.47	10.66	0.013
SIPPV + VG	18	6.44	7.85	

In SIPPV group mean duration of O₂ requirement was 14.47 days with SD of 10.66.

In SIPPV + VG group mean duration of O₂ requirement was 6.44 days with SD of 7.85, p value 0.013.



Graph 5: Bar-Diagram showing mean duration of Oxygen requirement in both groups.

Conclusion:- By using 2 independent sample t-test p-value < 0.05 therefore there is significant reduction in duration of O₂ requirement in SIPPV + VG group compared to SIPPV group.

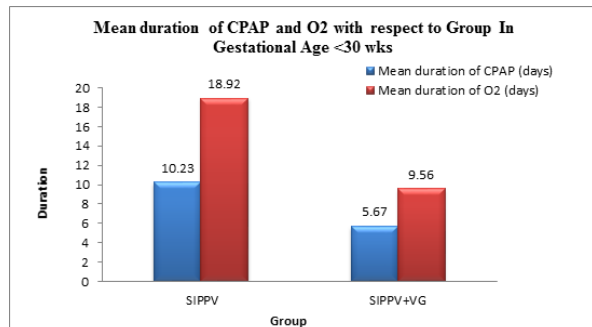
Table 5: Mean duration of Oxygen requirement in both groups according to gestation age

Gestation Age	Group	Duration of O ₂ (days)		P value
		Mean	SD	
Less than 30 Weeks	SIPPV	18.92	9.69	0.043
	SIPPV + VG	9.56	9.98	
More than 30 Weeks	SIPPV	4.83	4.56	0.05
	SIPPV + VG	3.33	3.12	

In patients with gestation age < 30 weeks, in SIPPV group mean duration of oxygen requirement was 18.92 days (SD 9.69) while in SIPPV + VG group, it was 9.56 days (SD 9.98), p value 0.043.

In patients with gestation age > 30 weeks, in SIPPV group mean duration of O₂ requirement was 4.83 days (SD 4.56)

while in SIPPV + VG group, it was 3.33 days (SD 3.12), p value 0.05.



Graph 6: Bar-Diagram showing Comparison of required duration of CPAP and duration of Oxygen requirement between both groups in gestational age < 30 weeks.

CONCLUSION:-

By using 2 independent sample t-test p-value < 0.05 therefore there is significant reduction in mean duration of CPAP requirement and duration of O₂ requirement in SIPPV + VG group compared to SIPPV group for patients with gestational age < 30 weeks.

IV. DISCUSSION

As a result of therapeutic and technological advancements in neonatology, survival of extremely premature infants has increased substantially. Respiratory support in the neonatal intensive care unit continues to evolve rapidly. Despite a shift towards non-invasive respiratory support, 64% of neonates born less than 30 weeks gestational age require mechanical ventilation during their NICU stay (10).

Our study was conducted in a tertiary level III b NICU. Forty six preterm infants with respiratory distress, requiring mechanical ventilation fulfilling inclusion and exclusion criteria were enrolled in our study. Both groups (SIPPV and SIPPV + VG) were well - matched regarding baseline characteristics i.e. birth weight, gestational age, gender, mode of delivery, requirement of resuscitation at birth, surfactant requirement and requirement of pharmacological closure of patent ductus arteriosus (PDA).

Length of mechanical ventilation:

Nuray Duman et al (11) did randomized control trial to find the impact of VG on synchronized mode of ventilation. PLV Vs VG was compared and was found that required duration of ventilation was less in VG group [79 hrs in PLV group Vs 39 hrs in VG group, p 0.19]. Another study by Guven et al (12) showed reduction in duration of mechanical ventilation when VG ventilation in combination with surfactant treatment was used in preterm infants with RDS. A trend towards decrease in duration of ventilation in VG group was also observed in a randomized control study done by M. T. Khashaba et al (13).

WanSheng Peng et al (14) did systematic review and meta-analysis to assess the effect of volume-targeted ventilation (VTV) compared with pressure-limited ventilation (PLV) in preterm infants. Meta-analysis of nine trials (15, 16, 17-19, 9, 12, 20, 21) showed that preterm infants ventilated using VTV modes had significant reduction in duration of mechanical ventilation (mean difference -2.0 days). However, significant heterogeneity was reported between the trials.

We compared effect of SIPPV and SIPPV+VG group on the duration of ventilation. We did not find significant difference between the groups (118.16±66.06 hours in SIPPV group Vs 88.0±62.3 hrs in SIPPV+VG group, p value 0.169). On subgroup analysis, no significant difference was found between both the groups in babies less than 30 weeks. Overall

a consistent trend towards reduction in required duration of ventilation was observed in SIPPV + VG group. Our results were similar to the finding of the study done by Nuray Duman et al (11) and M. T. Khashaba et al (13).

Extubation Failure:

In the study done by M. T. Khashaba et al (13), preterm infants with RDS were ventilated with SIMV + VG & PSV + VG and compared with SIMV & PSV. They found that extubation failure was significantly less in VG group. Data reporting the failure of the primary mode of ventilation in VTV and PLV groups are described in four trials (16, 17, 19, 22) in the meta analysis done by Wan Sheng Peng et al in 2014 (14). The meta-analysis demonstrated that preterm infants treated with VTV had a significantly lower failure of primarily assigned mode of ventilation compared to those treated with PLV. In our study, extubation failure was noted in lesser frequency (4.35%) in SIPPV + VG group than in SIPPV group (13.04%). Although the incidence of extubation failure was less in VG group in our study, the difference found was not significant. The results obtained in our study are similar to the findings of study done by M. T. Khashaba et al (13).

Duration of CPAP (Post extubation):

Trials on volume guarantee ventilation have shown inconsistent results on required duration of CPAP (post extubation) in preterm infants. The randomized study done by Khashaba et al (13) showed the reduction in post extubation CPAP duration when volume guarantee ventilation was used. Sirin Guven et al (12) in their randomized controlled study found the significant reduction in duration of CPAP (days) in non VG group. In their study, duration of CPAP was significantly higher in SIMV+VG group compared with SIMV group. This can be explained with faster extubation rates after surfactant replacement in infants in SIMV + VG group.

In our study, post extubation duration of CPAP requirement in SIPPV + VG group was significantly less than in SIPPV group (8.05±5.59days in SIPPV group Vs 4.22±2.84 days in SIPPV + VG group, p value 0.013). On subgroup analysis, the duration of CPAP in babies with gestational age less than 30 weeks was significantly less in SIPPV + VG group compared to SIPPV group. Similar trend was observed in babies with gestational age > 30 weeks. However, the difference found was statistically not significant.

Duration of oxygen requirement:

Clinical studies showed evidence of decrease in lung inflammation and rates of BPD with restricted use of oxygen or lower saturation targets (23, 24).

Guven et al (12) and Liu Cui-Qing et al (20) in their randomized controlled study observed significant reduction in duration of supplemental oxygen administration when preterm infants were ventilated with VG mode.

In pooled meta-analysis done by WanSheng Peng et al (14), data reporting supplemental oxygen administration in VTV and PLV groups are described in two trials (12, 22). The meta-analysis revealed reduced supplemental oxygen administration using VTV [MD of -1.68 (-2.47 to -0.88) days] compared to PLV.

In our study in SIPPV group mean duration of Oxygen (O₂) requirement was significantly less in SIPPV + VG group (14.47±10.66 days in SIPPV group Vs 6.44±7.85 days in SIPPV+VG group, p value 0.013). On subgroup analysis, we found that duration of O₂ requirement was significantly less in patients with gestational age less than 30 weeks in SIPPV +VG group. Similar trend was observed in patients with gestational age > 30 weeks and but the difference found was statistically not significant.

These findings are in agreement with the findings of studies done by Liu Cui-Qing et al (20) and Guven et al (12). The obtained results in our study are also similar to the results of a meta-analysis done by WanSheng Peng et al (14).

V.SUMMARY

Respiratory support in the neonatal intensive care unit continues to evolve rapidly. However, preterm lungs are particularly susceptible to ventilator induced lung injury (VILI). VILI is a major contributor to chronic lung disease (CLD) such as bronchopulmonary dysplasia (BPD).

A prospective, randomized, comparative study was conducted in a level III b NICU of a tertiary care hospital. This study was done in 46 preterm infants of gestational age less than 37 wks (of consenting parents) requiring mechanical ventilation in NICU, 23 in each group (Assist Control/SIPPV + Volume Guarantee and Assist Control/SIPPV).

The infants requiring mechanical ventilation in NICU were enrolled in the study group after matching the inclusion and exclusion criteria and allocated in two groups based on computer generated random sequence numbers.

Infants were ventilated by one of the two modes of ventilation and out of them, duration of ventilation and other secondary outcomes such as extubation failure, required duration of CPAP, duration of oxygen requirement were compared on this basis.

We found that the infants, ventilated with VG mode of ventilation, required less duration of ventilation in comparison to infants ventilated with SIPPV mode. However, the difference found was statistically not significant.

Incidence of extubation failure is lesser in infants ventilated with SIPPV + VG mode of ventilation in comparison to the other group. Here also, we did not find the difference statistically significant.

Required duration of nasal CPAP in post extubation period, duration of oxygen requirement was found to be significantly less in SIPPV + VG group of infants in comparison to SIPPV group of infants in our study.

Thus, volume guarantee ventilation can be used for preterm infants for reducing the required duration of ventilation, post extubation nasal CPAP and oxygen requirement.

VI.CONCLUSION

We found that the infants, ventilated with VG mode of ventilation, required less duration of ventilation in comparison to infants ventilated with SIPPV mode. However, the difference found was statistically not significant.

Incidence of extubation failure is lesser in infants ventilated with SIPPV + VG mode of ventilation in comparison to the other group. Here also, we did not find the difference statistically significant.

Required duration of nasal CPAP in post extubation period, duration of oxygen requirement was found to be significantly less in SIPPV + VG group of infants in comparison to SIPPV group of infants in our study. The significant difference was mainly observed in infants of gestational age less than 30 weeks.

Volume guarantee ventilation can be used for preterm infants for reducing the required duration of ventilation, post extubation nasal CPAP and oxygen days. By reducing the duration of ventilation, CPAP & Oxygen days in smaller premature infants, volume guarantee ventilation can be helpful in reducing the overall hospital stay in these infants.

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