Effect of change in tidal volume on left to right shunt across ventricular septal defect in children – A pilot study

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ABSTRACT

Background	:	Pulmonary vascular resistance, an important determinant of shunting across ventricular septal defects (VSD), rises at both extremes of lung volume.
Aims	:	We sought to determine the effect of changes in tidal volumes (V_T) on pulmonary blood flow (Qp), systemic blood flow (Qs), and shunt (Qp/Qs) in children with VSD.
Setting	:	Single-center teaching hospital.
Design	:	Prospective observational study.
Methods	:	Thirty children with a mean age of 11.8 ± 5 months undergoing surgical closure of VSD were studied. Hemodynamics and shunt-related parameters were assessed using transthoracic echocardiography measured at three different V_T i.e. 10, 8, and 6-ml/kg keeping the minute ventilation constant.
Results	:	Reduction in V_T from 10 to 8 to 6 ml/kg led to a reduction in gradient across VSD measuring 23.5, 20 and 13 mmHg respectively (P < 0.001). Similarly, right ventricluar outflow tract (RVOT) diameter, RVOT velocity time integral, Qp (57.3 ± 18.1, 50.6 ± 16.9, 39.9 ± 14.7 mL; P < 0.001), Qs (24.1 ± 10.4, 20.0 ± 8.7, 15.3 ± 6.9 mL; P < 0.001) and peak airway pressure (17.2 ± 1.5, 15.8 ± 1.3, 14.5 ± 1.2 cmHg; P < 0.001) showed progressive decline with decreasing V_T from 10 to 8 to 6 ml/kg, respectively. However, Qp/Qs (2.4 ± 0.4, 2.6 ± 0.4, 2.6 ± 0.4) demonstrated a minor increasing trend.
Conclusion	:	Lower V_T reduces the gradient across VSD, the pulmonary blood flow, and the peak airway pressure. Hence, ventilation with lower V_T and higher respiratory rate maintaining adequate minute ventilation might be preferable in children with VSD. Further studies are required to confirm the findings of this pilot study.
Keywords	:	Peak airway pressure, shunt (Qp/Qs), tidal volume, transthoracic echocardiography, ventilatory setting, ventricular septal defect

How to cite this article: Pathak P, Das S, Gupta SK, Hasija S, Choudhury A, Gharde P, et al. Effect of change in tidal volume on left to right shunt across ventricular septal defect in children – A pilot study. Ann Pediatr Card 2021;14:350-5.

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INTRODUCTION

Ventricular septal defect (VSD) is the most common congenital heart disease (CHD),[1] with isolated VSD constituting 20% of all CHD.[2,3] The magnitude and direction of the shunt across VSD depend upon the size of the defect and pulmonary vascular resistance (PVR) compared to systemic vascular resistance.[4,5] In patients with moderate and large VSD, increased pulmonary blood flow (Qp) results in left ventricular volume overload and pulmonary hypertension.[6]

Children with moderate and large VSD usually present with congestive heart failure and are routinely treated with diuretics, digoxin, and after-load reduction.[4,7] As part of their management, especially in the perioperative period, they may require mechanical ventilatory support.[5] The increased Qp generates higher resistance and lower compliance in the lungs and leads to high peak airway pressure (Paw), hypercarbia, and hypoxemia.[8-10] In patients on ventilation, PVR rises at both upper and lower limits of tidal volume (V_T).[11] During inspiration, lung inflation above the functional residual capacity (FRC) causes alveolar distension which in turn results in compression of alveolar vessels. Lower limits of V_T produce atelectasis, collapse of the lung, increase in dead space ventilation, hypercarbia, hypoxia, and intrapulmonary shunting.

Mechanical ventilation before initiation of cardiopulmonary bypass (CPB) is aimed at optimizing oxygenation and removal of CO_2, while avoiding barotrauma to the lungs. The ideal method of ventilation with better control of Qp is still not determined. The ventilation strategies have mostly focused on parameters influencing PVR, but the effect of V_T on PVR and shunt flow is not well studied. Therefore, in this prospective observational study, we planned to evaluate the effect of changes in V_T on VSD shunt-related parameters by echocardiography during preoperative mechanical ventilation.

METHODS

After obtaining institutional ethics committee approval and informed consent from parents or guardians of all participants, we prospectively enrolled 33 children younger than 3 years with isolated VSD who were scheduled for an elective surgical closure. Patients with concomitant CHDs were excluded from the study.

Anesthesia management

Patients were premedicated with syrup Triclofos sodium 30 mg/kg orally 1-hour before induction of anesthesia. In the operating room, 5-lead electrocardiography, pulse oximetry and noninvasive blood pressure were monitored. Anesthesia was induced with ketamine 2 mg/kg, fentanyl 3 mcg/kg and rocuronium 0.6 mg/kg. After intubation, ventilation was initiated with FiO_2 (Fractional inspiratory oxygen concentration) of 0.5 by the ventilator (Datex-Ohmeda, Avance) and V_T of 10 ml/kg of ideal body weight calculated by Mclaren method.[12] Anesthesia was maintained with sevoflurane, intermittent boluses of 0.1 mg/kg vecuronium, 2 mcg/kg fentanyl, and 50 mcg/kg midazolam. Invasive monitoring included femoral arterial pressure and right atrial pressure. Drugs were repeated during CPB. After the completion of the surgery, patients were managed in the cardiac intensive care unit as per hospital protocols.

All patients were ventilated on volume-controlled ventilation mode with V_T of 10 ml/kg body weight with Paw pressure limitation of 30 cmH_2O. A FiO2 of 0.5, I: E of 1:1.5 and positive end-expiratory pressure of zero were set to maintain an end-tidal CO_2 ($ETCO_2$) between 35 and 45 mmHg and SPO_2 >95%. The respiratory rate was adjusted accordingly to keep the minute ventilation (MV) within the normal range. The normal range of MV was calculated by multiplying V_T of 10 ml/kg with respiratory rate per minute adjusted to maintain the desired $ETCO_2$. After initially setting the V_T at 10 ml/Kg, it was changed to 8 ml/Kg and 6 ml/Kg with simultaneous adjustment of the respiratory rate to maintain a constant MV. Patients were ventilated with one set of V_T for 5 min before transthoracic echocardiography (TTE) assessment was performed. The data acquired at these settings were designated V_T10, V_T8, and V_T6, respectively.

Echocardiography examination

The echocardiographic examination was performed using a pediatric transthoracic probe of 8 or 12 MHz on an iE33 echocardiography machine (Philips; Bothell, WA, USA) to obtain the images. An independant experienced echocardiographer performed a comprehensive TTE in all patients. Echocardiography was performed following induction of anesthesia and before surgical incision under stable hemodynamic conditions. In parasternal long-axis view, VSD size [Figure 1], peak gradient across the VSD and diameter of the left ventricular outflow tract (LVOT) at the level of aortic valve were recorded.[13] In the parasternal short axis-aortic valve view, diameter of the right ventricular outflow tract (RVOT) and velocity-time integral (VTI) at the level of pulmonary annulus were calculated. Apical 5 chamber view was used to measure VTI at the level of LVOT [Figure 2]. Images were stored for offline analysis. Qp/Qs was calculated using the continuity equation: [13]

Qp/Qs = Stroke Volume (SV) $_{Right\ heart}$/SV $_{Left\ heart}$

= RVOT diameter × VTI_{RVOT}/LVOT diameter × VTI_{LVOT}

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation (SD) or median as applicable. Categorical
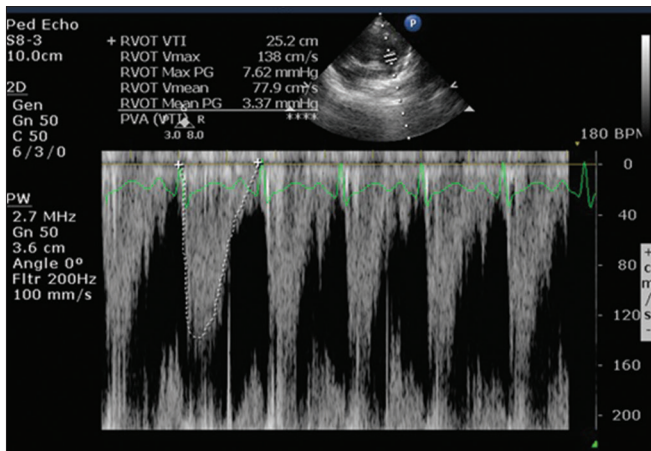
Figure 1: Parasternal short axis-aortic valve level view showing right ventricular outflow tract (RVOT), pulmonary valve and pulmonary artery. Velocity time integral at RVOT was taken at pulmonary valve level using pulse wave (PW) Doppler
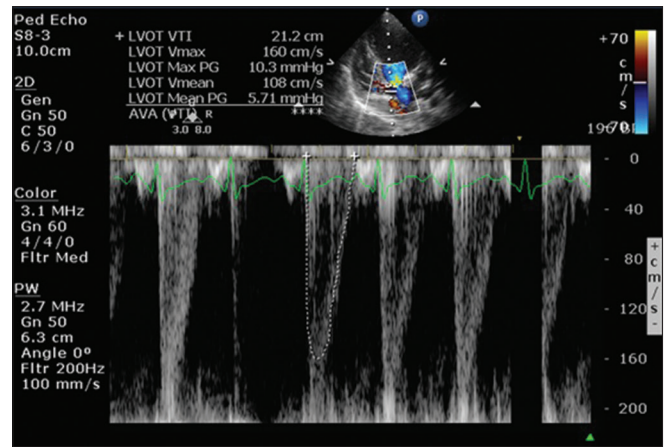

Figure 2: Apical 5 chamber (A5C) view showing left ventricular outflow tract (LVOT), aortic valve and ascending aorta. Velocity time integral at LVOT was taken at the aortic valve level using pulse wave Doppler

data were expressed as frequency (percentage). A multiple-time point comparison was done using repeated measures ANOVA followed by *post hoc* pairwise comparisons, if significant, using paired *t*-test with Bonferroni correction. Statistical analysis was performed using the R console (RStudio IDE, 250 Northern Ave, Boston, MA 02210). A $P < 0.05$ was considered statistically significant.

Sample size

An arbitrary sample size of 30 was taken for this proof-of-concept study. A retrospective statistical analysis of the study, considering the difference in mean gradient across VSD from V_T of 10 ml/Kg to 6 ml/Kg with SD of 12.5 and specified level of significance (alpha value) of 0.017 for three V_T settings, the power of the study emerged to be 96% using the online version of nMaster 2.0 software, Department of Biostatistics, CMC, Vellore, Tamil Nadu, India.[14]

RESULTS

Out of the 33 patients, we excluded 3-patients from the analysis-one patient had very high Paw at 10 ml/kg V_T and in the other two patients, $ETCO_2$ and SpO_2 could not be maintained within the desired range. Baseline demographic and hemodynamic characteristics of the patients are summarized in Tables 1 and 2. The mean age of the patients was 11.83 ± 5.5 months with 19 (63%) boys. The mean VSD diameter was 0.76 ± 0.13 cm.

Hemodynamic and respiratory parameters like HR, systolic and diastolic blood pressure, SpO_2 were comparable in all the three V_T settings [Table 2]. There was gradual reduction in the Paw when V_T was changed from 10 to 8–6 ml/Kg. Echocardiographic parameters like gradient across the VSD, RVOT diameter, RVOT-VTI, LVOT-VTI, Qp, Qs, and Qp/Qs had significant statistical

differences using repeated measures ANOVA [Table 3]. On further analysis, it was evident that there was a graded reduction in gradient from 23.5 (range 10, 51) to 20 (range 8, 50) and 13 (range 4, 44) mmHg, when V_T was reduced from 10 ml-8 ml-6 ml/Kg, respectively [Table 3]. Qp and Qs demonstrated a decreasing trend, whereas the Qp/Qs demonstrated an increasing trend $(2.4 \pm 0.4, 2.6 \pm 0.4,$ and $2.6 \pm 0.4)$ [Figure 3]. *Post hoc* analysis of the variables showed statistical significant differences on the application of pairwise comparisons using Wilcoxon signed-rank test with Bonferroni correction.

DISCUSSION

Moderate and large VSDs usually present with tachypnea, growth retardation, recurrent chest infections, and heart failure. Mechanical ventilation plays a crucial role in the ventilatory support in some of these patients presenting with acute heart failure or for pre- and peri-operatve optimization. Ventilatory strategies described have emphasized the need of eliminating factors that increase Qp, such as hyperventilation and higher oxygen administration. Higher V_T like 12–14 ml/kg produces high Paw, inflated lungs, reduction in venous return to heart, rise in stroke volume variation, and increase in PVR, which reduces Qp.[15] High Paw produces barotrauma to alveoli making ventilation difficult with repeated alarms thus leading to suboptimal V_T and hypercarbia. Besides, the resultant reduction in venous return with higher V_T may reduce the stroke volume and more inflation of lungs may interfere with the operative field.

A study by Li *et al* .[16] evaluated the effect of changing V_T on left to right shunt-related echocardiographic parameters in patients undergoing VSD repair. A prospective study,[13] estimated left to right shunt in patients with isolated VSD using Doppler echocardiography and oximetry by cardiac

catheterization. They found that the Doppler method gives the estimation of Qp/Qs with greater accuracy and enables the demonstration of the size of VSD by calculating shunt magnitude.[13] We followed the same principles of assessment of various shunt parameters by Doppler interrogation.

Our study demonstrates that the decrease in the V_T settings from 10 ml/kg to 8 ml/kg and 6 ml/kg keeping the MV constant, produces a significant decrease in the Qp as reflected by significant decrease in RVOT-VTI. There was a gradual reduction in the Paw when V_T changed from 10 ml-8 ml-6 ml. Gradient across VSD and RVOT decreased along with the reduction in V_T. A simultaneous fall in LVOT VTI led to reduction in Qs. The reduction in Qs was more than the reduction in Qp making Qp/Qs higher at lower V_T settings.

The main determinants of shunt flow across a VSD are the size of the defect, pulmonary vascular bed, the pressure difference between RV and LV, and relative resistance between pulmonary and systemic circulations.[4] The increased Qp has an important role in producing higher resistance and low compliance to the lungs.[17] The

altered lung dynamics create difficulty during artificial ventilation till the closure of VSD.

Another prospective study[18] compared the pre- and post-surgery lung functions in infants with increased Qp and evaluated the correlation between FRC, airway resistance, and lung compliance. They studied 30 pediatric patients and followed them postoperatively for 6 months. They found that infants with increased Qp had decreased pulmonary compliance, higher airway resistance, and FRC, which improved significantly after the surgical repair. These alterations in lung mechanics showed a strong correlation with the amount of pulmonary vascular enlargement and the severity of pulmonary hypertension. The result of this study stimulated us to find out the ventilator strategies for the patients with CHD having increased Qp as they pose difficulties in managing ventilation.

Li *et al.*[16] compared the VTI of left to right shunt in the pulmonary artery and descending aorta (DA) by manipulating the ventilation parameters for pediatric patients with V_T 10, 8, and 6 ml/kg. The effect on cerebral oxygen saturation ($rScO_2$) was noted by the alteration in V_T. They had similar objectives as our study to determine the ventilation strategy with the ideal range of $PaCO_2$ which could provide optimal Qp/Qs with an adequate oxygen supply for children with the left to

Table 1: Baseline patient characteristics (*n*=30)

	Mean±SD
Age (months)	11.83±5.5
Height (cm)	69.05±7.79
Weight (kg)	6.39±1.72
Sex (male:female)	19:11
Size of VSD (cm)	0.76±0.13

VSD: Ventricular septal defects, SD: Standard deviation

Table 2: Patients hemodynamic characteristics

Parameters	Tidal volumes (ml)			P
	10	8	6	
Heart rate (bpm)	136.80±5.74	136.36±5.68	137.96±7.97	0.056
SPO_2 (percentage)	100.00±0.00	100.00±0.00	100.00±0.00	1
SBP (mm of Hg)	89.56±7.60	89.76±7.23	89.86±7.49	0.57
DBP (mm of Hg)	50.20±4.79	50.36±4.18	50.03±4.44	0.62
$ETCO_2$ (cm of Hg)	36.73±1.46	37.86±1.22	41.2±1.65	0.001
Paw (cm of Hg)	17.20±1.51	15.80±1.34	14.53±1.25	<0.001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, $ETCO_2$: End tidal carbon dioxide partial pressure, Paw: Peak airway pressure, SPO_2: Oxygen saturation
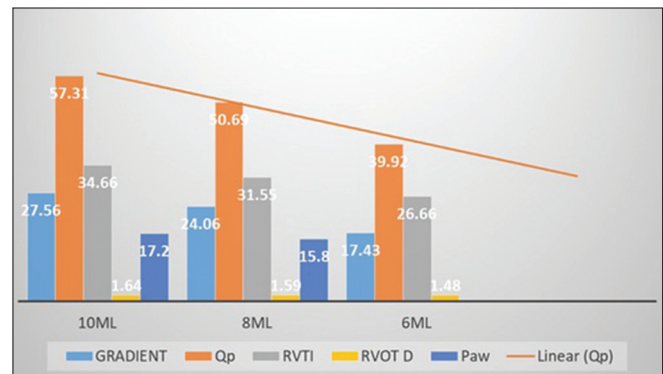

Figure 3: Showing the gradual and simultaneous reduction in gradient across VSD, Pulmonary flow (Qp), RVTI (velocity time integral at right ventricular outflow tract), RVOT D (right ventricular outflow tract diameter) and Paw (peak airway pressure) when the V_T changed from 10 ml/kg

Table 3: Patients echocardiographic characteristics

Parameters	Tidal volume ml/kg			P
	10	8	6	
RVOT D (cm)	1.64±0.26	1.59±0.28	1.48±0.28	<0.001
LVOT D (cm)	1.26±0.24	1.26±0.24	1.26±0.24	1
RVTI (cm)	34.66±8.23	31.55±7.49	26.66±6.98	<0.001
LVTI (cm)	18.80±5.75	15.61±4.82	11.95±3.86	<0.001
Qp (ml/beat)	57.31±18.15	50.69±16.95	39.92±14.73	<0.001
Qs (ml/beat)	24.15±10.45	20.02±8.79	15.33±6.97	<0.001
Qp/Qs	2.49±0.46	2.63±0.44	2.69±0.46	<0.001
Gradient (mm of Hg), median (minimum-maximum)	23.50 (10-51)	20 (8-50)	13 (4-44)	<0.001

RVOT D: Right ventricular outflow tract diameter, LVOT D: Left ventricular outflow tract diameter, RVTI: velocity time integral at RVOT, LVTI: Velocity time integral at LVOT, Qp: Pulmonary flow, Qs: Systemic flow

right shunt. They maintained a higher $PaCO_2$ to raise the PVR, which was achieved by V_T of 6 ml/kg that had decreased the left to right shunt after anesthesia and a favorable VTI_{PA}/VTI_{DA} associated with an improvement in cerebral perfusion. Li *et al.* managed a range of $PaCO_2$ 40–50 mmHg, which has a significant impact on PVR. They detected reduction in VTI_{PA}/VTI_{DA} measured by transesophageal echocardiography when the V_T was altered from 10 to 8–6 ml/kg.

Our study was different from Li *et al.* in the principle that we demonstrated the direct effect of V_T change on Qp/Qs by maintaining a constant MV. We have used TTE to calculate different hemodynamic parameters with the changes in V_T. We observed decrease in gradient across VSD, RVOT diameter, RVOT VTI, Qp, LVOT VTI, and Qs. However, we detected a slight increasing trend in Qp/Qs ratio at lower V_T. The reduction in the LVOT VTI and Qs was attributable to the decreased return of blood to the left side of the heart at lower V_T. The higher reduction in Qs compared to Qp might be the probable rationale for increasing the trend in the Qp/Qs. However, the reduction in Qs had no significant alteration in BP, HR, and clinical outcome at 3 settings of V_T.

The present study finding proposes for a lower V_T like 6–8 ml/kg and a higher respiratory rate for maintaining constant MV when mechanical ventilation is required in the preoperative and intraoperative period for VSD or L-R shunt patients. This method will reduce the Qp. The lungs will be prevented from barotrauma and hyper-inflation caused by high Paw while ventilating at higher V_T. Our study was one of the preliminary studies of its kind with clinical importance. It will guide researchers to conduct further study in this field to substantiate the findings.

Limitations of the study

A single echocardiographer had acquired all the readings, hence some intra-observer bias might not be ruled out. Examination by 2 echocardiographers might have been better. The fall in Paw at lower V_T might be possible, but we cannot differentiate between reduction in lung volume from the reduction in Qp or V_T. A higher time interval between two settings of V_T perhaps might have a better stabilization of respiratory parameters. It was not practical to get arterial blood gas with every change in V_T, hence PaCO2, PaO2, and SaO2 values were not examined during the changes in V_T.

CONCLUSIONS

To conclude, reduction in V_T from 10 ml/kg to 8 ml/kg and 6 ml/kg with adequate MV decreases the Qp besides reducing Paw and resultant barotrauma. We, therefore, propose the use of lower V_T and higher respiratory rate with adequate MV as the preferred ventilatory strategy in pediatric patients having VSD with left to right shunt.

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