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Original Article

Effect of inhaled procaterol and budesonide on right ventricular diastolic function in children with asthma

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Abstract

Objectives To study changes in parameters of right ventricular (RV) diastolic function after procaterol and budesonide inhalation in children with asthma.

Methods This was a one-group pretest-posttest design to determine changes in right ventricular diastolic function following four weeks of inhaled procaterol and budesonide administration. Subjects were children aged 8 to 18 years with frequent episodic asthma recruited consecutively at the Department of Child Health, Cipto Mangunkusumo Hospital. M-mode and 2-D echocardiography examinations were performed to determine RV isovolumetric relaxation time (IVRT), acceleration time (AT), deceleration time (DT), E wave, A wave, E/A ratio, and tricuspid annular plane systolic excursion (TAPSE). Means of the RV function parameters before and after treatment were compared using the paired t-test or Wilcoxon test.

Results There were 29 patients comprising 16 boys and 13 girls. The means or medians of the E wave, A wave, E/A ratio, acceleration time (AT), deceleration time (DT), and isovolumetric relaxation time (IVRT) before and after treatment were 0.55 and 0.55 cm/sec ($P=0.709$), 0.45 and 0.35 cm/sec ($P<0.0001$), 1.17 and 1.58 cm/sec ($P<0.0001$), 52.73 and 55.03 m/sec ($P=0.04$), 55.39 and 58.10 m/sec ($P=0.03$), and 46.50 and 70.0 m/sec ($P<0.0001$), respectively. The median pre- and post-inhalation TAPSE were 1.63 and 1.84 cm, respectively ($P<0.001$).

Conclusions In children with frequent episodic asthma, there are changes in RV diastolic functions IVRT, AT, DT, E/A ratio and A wave following procaterol and budesonide inhalation. There was no increase in E wave following inhalation. TAPSE was increased following procaterol and budesonide inhalation. **[Paediatr Indones. 2009;49:131-4]**.

Keywords: *asthma, right ventricular diastolic function, TAPSE*

Asthma is a chronic disease marked by reversible airway inflammation and obstruction. Pathophysiologically, it is caused by interaction between environmental and genetic factors causing airway inflammation. These conditions cause structural and functional changes of the airways i.e., bronchospasm, mucosal edema, and the formation of mucus plugs, resulting in symptoms and signs of cough, wheezing, and shortness of breath. Asthma is a major cause of chronic illness in children, with high morbidity and mortality rates. Currently, asthma has a prevalence of up to 7.2% worldwide.[1-4]

The rise in negative pressure during inspiration and positive pressure during expiration which exceeds the normal right ventricular preload and afterload cycle may cause an increase in intrathoracic pressure. Excessive respiratory effort in asthma may lead to increased intrathoracic pressure and lung hyperinflation, which causes an increased afterload for the right ventricle.[5-6] Chronic lung disease may contribute to an increased pulmonary arterial

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resistance, causing disturbance in right ventricular systolic and diastolic function. Theoretically, a change in right ventricular compliance will take place due to the rise in pulmonary vascular resistance, causing changes in right ventricular diastolic filling parameters. This will cause substantial changes in cardiac performance[7-12] Doppler echocardiography is a non-invasive technique to determine right ventricular diastolic function. The results of this examination is highly influenced by certain factors such as age, heart rate, and respiratory rate. Ayten *et al*[13] in Turkey evaluated changes in right ventricular diastolic filling in moderately asthmatic children age 3.5 to 13 years. Such study has never been done in Indonesia. This study aims to evaluate changes in parameters of right ventricular diastolic function after procaterol and budesonide inhalation in children with asthma.

Methods

This pre-experimental study used a one-group pretest-posttest design to determine changes in right ventricular diastolic function following four weeks of inhaled procaterol and budesonide administration. Subjects were children age 8 to 18 years with frequent episodic asthma recruited consecutively at the Pediatric Cardiology and Pediatric Respirology Divisions, Department of Child Health, Medical School, University of Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia, from February to April 2008. In this study, conventional one-dimensional M-mode echocardiography and two-dimensional echocardiography were performed to determine the right ventricular function parameters isovolumetric relaxation time (IVRT), acceleration time (AT), deceleration time (DT), E wave, A wave, E/A ratio,[14-17] and tricuspid annular plane systolic excursion (TAPSE), It is measured on four-chamber view by measuring the distance from the tricuspid annulus to the apex during systole and diastole, then calculating the maximum difference between these two measurements.

All outcome variables were recorded in a standardized form. Means of the right ventricular function parameters before and after treatment were calculated and compared using the paired t-test wherever the data fulfilled normal distribution and the Wilcoxon test when the data were not normally distributed. The level of significance was set at $P<0.05$.

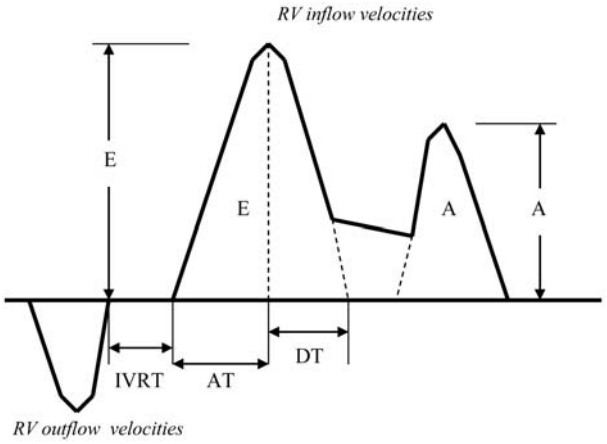

Figure 1. Schematic representation of right ventricular diastolic function parameters

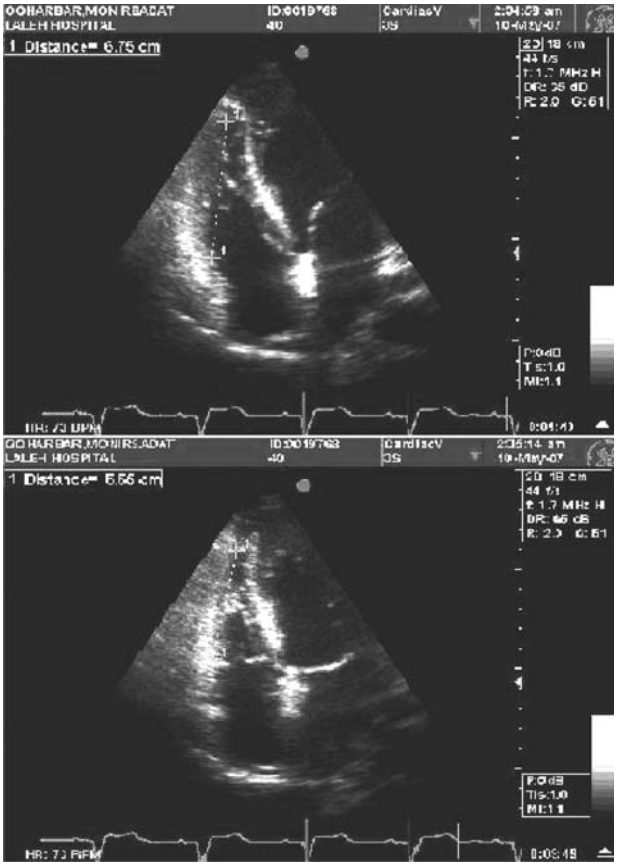

Figure 2. Measurement of TAPSE

Results

Out of 29 subjects, 16 were male. Body weight ranged from 14 to 90 kg, with a median of 29 kg. The subjects' age ranged from 8 to 18 years, with a median of 10 years. Respiratory rate was 26-44 breaths/minute (median 32 breaths/minute) pre-inhalation and 26-40 breaths/minute (median 32 breaths/minute) post-inhalation. Heart rate was 75-125 beats/minute mean (SD) : 99 (SD 13.13) beats/minute pre-inhalation and 68-115 beats/minute mean (SD) : 92 (SD 9.85) beats/minute) post-inhalation. After four weeks of inhaled procaterol and budesonide there were significant increases in IVRT, AT, E/A ratio, DT, and A wave. No post-treatment change in E-wave was noted (**Table 1**).

Table 1. Right ventricular diastolic function parameters before and after treatment

Variable	Pre-treatment		Post-treatment		P
	Median/ mean	Range/SD	Median/ mean	Range/SD	
IVRT*	46.5	34.00-75.00	70	51.30-95.00	<0.0001
AT†	52.7	8.27	55	8.60	0.04
DT†	55.4	8.75	58.1	8.39	0.03
E wave*	0.5	0.36-0.73	0.5	0.46-0.93	0.709
A wave*	0.4	0.30-0.73	0.3	0.26-0.76	<0.0001
E/A ratio†	1.2	0.16	1.6	0.23	<0.0001

*Median and range provided, Wilcoxon test used; †Mean and SD provided, T-test used

Discussion

Conventional M-mode echocardiography has been widely used to determine left ventricular size and function, but not to evaluate right ventricular function. This diagnostic tool is also highly dependent on the evaluator, and since evaluation of right ventricular diastolic function is done visually, there is a high chance of inter-observer variability.[18-19]

Right ventricular diastolic function parameters are influenced by age, heart rate, and respiratory rate. Zhendong[12] found that increased age was associated with decreased A wave and increased E/A ratio, inspiration was associated with a rise in E wave, A wave, and DT, and that tachycardia caused difficulty in interpreting E wave and A wave data. The present study found that right ventricular diastolic function is impaired in children with frequent episodic asthma, as shown by improvement in right ventricular diastolic function parameters following treatment with inhaled procaterol and budesonide.

Measurement of TAPSE is a simple echocardiographic means to evaluate right ventricular systolic function. TAPSE measurement is widely done in adult patients to evaluate right ventricular function and the prognosis of pulmonary hypertension. According to Abraham *et al*,[20] a TAPSE of <1.8 cm is indicative of impaired right ventricular function. Another study set this cutoff point at 1.5 cm.[18] Our study found a significantly increased TAPSE after inhalation therapy. Median TAPSE was 1.63 cm (range 1.43-2.30 cm) before treatment and 1.84 cm (range 1.42-2.34 cm) after treatment ($P<0.001$). To date, no reference data for TAPSE in children exists, so that we used the commonly used adult reference values of 1.7 ± 0.1 to 2.2 ± 0.1 cm.[21] In asthma, a transient depression of the right ventricle is seen during deep inspiration due to increased right ventricle afterload. This condition is thought to influence the right ventricular pumping abi1ity. Based on this theory, we assume that a change in maximum right ventricular strain capacity will take place during diastole, which can be measured by evaluation of TAPSE. A more thorough investigation on normal TAPSE values in children, particularly Indonesian children, is needed for reference in further studies.

The limitation of the study lies on its design, i.e., with the pretest-posttest design, which is a pre-experimental design, we could not exclude with certainty the role of history, maturation, testing, instrumentation or any combination of those factors. We have done our best to perform the measurements by measuring each value 3 times and calculated the average. Referring to the nature of chronicity of the condition we think that it is unlikely that there were significant changes of the clinical course of the disease. However other factors could not be excluded. With these in mind, we conclude that in children with frequent episodic asthma, there is a rise in right ventricular diastolic function parameters IVRT, AT, DT, and E/A ratio, and a decline in A wave following four weeks of treatment with inhaled procaterol and budesonide. There is no change in E wave before and after treatment. The right ventricular systolic function parameter TAPSE is increased after treatment.

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