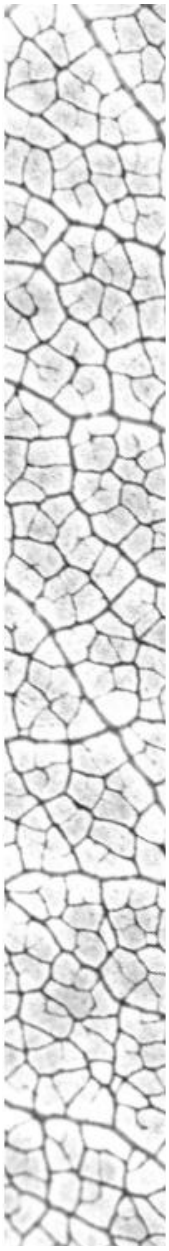

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Dimensions change and left ventricular function carvedilol post therapy due to heart failure cases in children with congenital heart disease left-to-right

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Abstract

Background: Congenital Heart Disease (CHD) is the most common congenital disorder in newborns with a prevalence of 9.1 per 1000 live births. In left-to-right PJB shunts occur excessive volume burden on the ventricles, resulting in heart failure.
Purpose: Knowing the difference in changes in the dimensions and function of the left ventricle on echocardiography after standard therapy plus placebo with the standard therapy group plus carvedilol in children with heart failure due to left-to-right CHD.
Method: Using a Randomized Controlled Trial (RCT) research design by giving a Double Blind Study treatment. Research data including comparison of initial data and final data of the two groups were analyzed by independent sample t test.
Result: The results of measurement of left ventricular mass showed a significant decrease to 40.56 ± 23.63 g / m2 (p <0.001). There was a significant decrease in left ventricular volume to 42.23 ± 20.36 m3 (p = 0.05). There was a significant increase in the mean left ventricular ejection fraction to 74.16 ± 4.10% (p = 0.03). There was an increase in the left ventricular shortening fraction to 42.18 ± 3.66% (p = 0.04).
Conclusion: There are differences in the dimensions of the left ventricular at the end of systolic (DVKI-AS), the left ventricle at the end of diastolic (VKI-AD), the thickness of the back wall of the left ventricle at the end of diastolic (DBVKI-AD), and the thickness of the interventricular septum at the end of diastolic (SIV-AD).

Keywords: congenital heart disease, heart failure, pomegranate, carvedilol, left ventricle

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INTRODUCTION

One of the most high urgency-level diseases is Heart disease (Widiyanti, et al. 2016). Congenital heart disease (PJB) is the most frequent congenital disorder in newborns with a prevalence in the last 15 years is 9.1 per 1000 live (van der Linde, et al. 2011). The most frequent complication in patients with left-to-right PJB is heart failure

On the left PJB shunts to the right there is excessive volume load on the ventricle resulting in heart failure (Pavo, & Michel-Behnke, 2017). The reduction of blood pump in heart failure leads to a compensatory mechanism of sympathical system activity and a renin-angiotension-aldosterone (RAA) system. If long lasts can cause changes in the shape and function of the heart muscle (Wahab, 2009). The standard therapy of heart failure in children with left to right PJB shunts is digitalis, diuretic, and ACE inhibitors. However, The use of these medications is temporary, namely to prepare optimal conditions prior to the operative action (Kay, Colan, & Graham, 2001).In addition, there is still no data that expresses the effectiveness of the use of these drugs in children (Hsu, & Pearson, 2009).

Long-term use of inotropic can give a destructive effect. Vasodilator therapy is then introduced with the aim of fixing hemodynamics and lowering the heart burden. ACE inhibitors are the first and antagonists to work through the obstacles on the RAA system. The concept of the and blockade was later expanded on the sympathetic nervous system, with the use of β (Lechat, 2006) inhibitors.

Carvedilol is an adrenoreceptor antagonist β1 and β2 nonselective with vasodilatory ability through the α-1 adrenoreceptor antagonist. Carvedilol also has antiproliferative effects and antioxidant activity. The use of carvedilol has been approved by the Food and Drug

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Administration (FDA) since 1997 as a therapeutic heart failure, and can be administered concurrently with digoxin, diuretics, and ACE inhibitors to reduce disease travel and lower the number of treatments and deaths associated with cardiovascular conditions (Spicer, 2001. Remme, & Swedberg, 2001). With the dose of the titration carvedilol can improve the dimensions and function of the left ventricle (Conrad, et al. 2019). Although the current carvedilol is indicated as a therapy for heart failure in adults, but only 7 studies can report the safety, effectiveness, or pharmacokinetics of the use of carvedilol in the repair of heart failure in children (Foerster, & Canter, 2008; Nishiyama, et al. 2009; Clausen, 2018).

Based on the discussion above, it is necessary to do research of randomized controlled studies to prove whether the use of carvedilol is effective in repairing the left ventricular dimensions and functions in children with left-to-right PJB of heart failure. Echocardiography is a tool used to measure the output of cardiac work by non-invasive (Kusumastuti, & Osaki, 2015). Echocardiography will specify the movement of the heart wall in the 2-dimensional (2d) echocardiographic image of (Aziz, et al. 2018). In this study, echocardiography was used to see any changes in the dimensions of the left ventricle at the end of the systolic and diastolic, the rear wall thickness of the left ventricle at the end of diastolic, thickness of ventricular septum at the end of diastolic, the left ventricular volume, left ventricular mass, Left ventricular ejection fraction, left ventricular shortening fraction, and E/A wave ratio.

METHOD

This Research used the Randomized Controlled Trial (RCT) research with the Double Blind Study treatment. There are two treatment groups that are groups with standard therapeutic plus placebo and a group with Standard therapeutic with carvedilol

Population and Sample

Samples were taken from the patient with a left to right PJB shunts that experienced heart failure which meet the criteria of inclusion and willing to follow the research, then randomly selected with the number of samples according to calculation

Data Analysis

Data on research results include comparisons of preliminary data and end data of both groups analyzed with Independent sample t test. Data before and after the treatment is analyzed by paired t test statistical test. Statistical analysis of computer programs assisted.

RESULT

A total of 30 child patients as research subjects divided into two groups, consisting of 19 (63.3%) Male and 11 (36.7%) Women, with an average age of 57.6 ± 43.57 months. By age group there were 9 (30%) Patients aged ≤ 24 months or ≤ 2 years, 14 (46.7%) Patients aged 25-83 months, 3 (10%) Patients aged 84-131 months, 4 (13.3%) Patients aged ≥ 132 months. The weight of the child in this study was 13.68 ± 6.19 kg, where there were 18 (60%) Patients with good nutrition, 9 (30%) Patients with less nutrition, and 3 (10%) Patients with poor nutrition. Based on the type of defect, 21 (70%) Patients with ventricular septal defect (DSV) and 9 (30%) Patients with a Duktus Arteriosus persistent (DAP), where as much as 3 (10%) Patients in the form of small defects, 20 (66.7%) Patients in the form of moderate defects, and 7 (23.3%) Patients in the form of large defects.

Table 1. Comparison of dimensional change and left ventricular function of echocardiography test before and after treatment in treatment group (standard therapy + carvedilol)

Parameter	Before Mean (SD)	After Mean (SD)	Mean Change (SD)	Price *P*
DVKI-AS (cm)	2,08 (0,37)	1,89 (0,48)	0,18 (0,37)	0,08 *
DVKI-AD (cm)	3,56 (0,48)	3,31 (0,57)	0,25 (0,43)	0,03 *
DBVKI-AD (cm)	0,56 (0,20)	0,52 (0,15)	0,04 (0,10)	0,14 *
SIV-AD (cm)	0,59 (0,16)	0,48 (0,14)	0,11 (0,14)	0,80 *
Left ventricular mass (g/m^2)	56,44 (34,11)	40.56 (23.63)	1,58 (13,38)	0,00 *
Left ventricular volume (m^3)	50,08 (18,96)	42,23 (20,36)	7,85 (14,74)	0,05 *
Ejection Fraction (%)	70,66 (3,87)	74,16 (4.10)	-3,50 (5,96)	0,03 *
Short Fraction (%)	39,01 (3,35)	42.18 (3.66)	-3,17 (5,43)	0,04 *
Ratio E/A	1,67 (0,29)	1,75 (0,26)	-0,07 (0,32)	0,36

*there is different mean if price p<0,05

Observations on the left ventricular dimension value at end of systolic (Dvki-as) Tcan decrease Dvki-AS after administration of carvedilol in treatment group to 1.89 ± 0.48 cm, but the decline by using the test paired T test is not statistically meaningful with the price P = 0.08. While in the control group, DVKI-AS increased to 2, 20 ± 0.47 cm (P = 0.63). There is a meaningful difference in the Carvedilol Pascaterapi in both research groups with the test results of independent t test with a price of P = 0.04, and the average difference between the two groups is-0.27.

There is a decrease in left ventricular dimensions when late diastolic (dvki-AD) means through test paired T test after administration of Carvedilol in the treatment group to 3.31 ± 0.57 cm with a price of P = 0.03. While in the control group, DVKI-AD increased to 3.82 ± 0,84 cm (Price P = 0.20). There is a meaningful difference in the carvedilol in both research groups through the results of independent T test tests with a price of P = 0.04, with the average difference of the two groups being-0.39.

There is a decline in left ventricular rear wall at the end of diastolic (DBVKI-AD) after administration of carvedilol in treatment group to 0.52 ± 0.15 cm, but the decline is not statistically meaningful with test paired T test (price P = 0.14). While in the control group, there was increased DBVKI-AD to 0.57 ± 0.18 cm (price P = 0.15). There is a meaningful difference in the carvedilol in both research groups with the test results independent t Test (price P = 0.03), and the average difference between the two groups is-0.15.

Observation results of interventricular septum at the end diastolic (SIV-AD) indicates the presence of a statistically significant decline of SIV-AD through test paired T test to 0.48 ± 0.14 cm (price P = 0,008) in the treatment group after receiving therapy carvedilol. While in the control group, there was increased SIV-AD to 0.56 ± 0.15 cm (price p= 0.80). There is a meaningful difference in carvedilol in both research groups with test results independent t, Test (price P = 0.04), and the average difference between the two groups is-0.14

The result of the measurement of the left ventricular mass value indicates a statistically significant decrease in the left ventricular mass in the treatment group after receiving therapy carvedilol with test paired t test to 40.56 ± 23.63 g/M^2 (price p < 0.001). While in the control group, there was an increase in the left ventricle mass to 76.14 ± 72.86 G/m^2 (price P = 0.16). There is a meaningful difference in the carvedilol in both research groups with independent test (price P = 0.01), and the average difference between the two groups is-35.36.

A statistically significant decrease in left ventricular volume with test paired T test to 42.23 ± 20.36 m^3 (P = 0.05) in the treatment group after receiving carvedilol therapy. While in the control group, there was an increase in the left ventricle volume to 650.05 ± 47.28 m^3 (price p = 0.20). There is a meaningful difference in the carvedilol in both research groups of independent t test results (price P = 0.03), and the average difference between the two groups is-15.66.

There is a statistically significant left ventricular ejection fraction value increase with test paired T test to 74.16 ± 4.10% (price P = 0.03) in the treatment group after receiving carvedilol therapy. While in the control group, there was a decrease in the left ventricular ejection fraction to 70.75 ± 4.45% (price P = 0.34). There is a significant difference in the carvedilol supply in both research groups of independent t test results (price P = 0.03), and the average difference between the two groups is-5.05.

There is a statistically significant increase in the left ventricular shortening fraction of the test paired T test to 42.18 ± 3.66% (P = 0.04 price) in the treatment group after receiving carvedilol therapy. While in the control group, there was a decrease in the left ventricular shortening fraction to 39.41 ± 3, 84% (price P = 0.46). There is a meaningful difference in the carvedilol in both research groups with test results independent t Test (price P = 0.04), and the average difference between the two groups is-4.00.

At the observation of the E/A ratio, the administration of Carvedilol in the treatment group contained as much as 13 (86,70%) Research subject with an E/A ratio between 1-2, and as much as 2 (13,30%) The E/A ratio > 2. As for the control group, there are 13 (86,70%) The E/A ratio between 1-2, and a total of 2 (13,30%) The subject with the E/A ratio > 2. There is an increase in the ratio of E/A after the administration of Carvedilol to the treatment group to 1.75 ± 0.26, but the increase is not statistically meaningful with test paired T test (price P = 0.36). Similarly, in the control group, there was an increase of E/A ratio to 1.74 ± 0.46 (price P = 0.67). There Is No statistical difference in the Carvedilol Pascaterapi in both research groups with the test results independent t Test (price P = 1.00), and the average difference between the two groups is-0.04.

DISCUSSION

In this study, there was a decrease in the average value of DVKI-AD in the treatment group (price P = 0,039). While the control group occurs an average increase in the value of DVKI-AD (Price P = 0,203.). There is a significant difference between the control group and the Carvedilol final treatment at the average value of DVKI-AD with the price P = 0,043. Accordingly in SIV-AD, there is a significant difference between the treatment group and the control group with the price P = 0,044, where a significant decrease in the treatment group (price P = 0,008), while the control group occurred Increase the average of the SIV-AD value (price p = 0,803).

Significant differences between treatment groups and the Carvedilol Jet control group are also present in DVKI-AS (Price P = 0.04) and DBVKI-AD (Price P = 0,038). In both research groups there was an average decline in the value of DVKI-AS, but the decrease of DVKI-AS occurred Pascaterapi carvedilol in both groups is not significant compared to before given carvedilol therapy, priced at p = 0.08 on Treatment groups; and price P = 0,635 in the control group. Likewise, with the average DBVKI-AD value, the decline that occurs after carvedilol in both groups is not significant compared to before given carvedilol therapy with the price P = 0,146 on the treatment group; and price P = 0,155 on the control group

This suggests that administering carvedilol can provide benefits to the remodeling process that occurs. There is a research conducted by Khattar et al. (2001) indicates there is a decline in the final volume of systolic through cross sectional echocardiography examination, but there is no change in the final volume of diastolic in patients with a single-jet heart failure with Carvedilol. When ACE inhibitors are added to the Carvedilol group, there is no change in the final systolic volume. However,

there was a significant decrease in the final systolic volume when carvedilol was administered to the Group YanG had been given an ACE inhibitor for 6 months (Khattar, et al. 2001).

In this study there were significant differences between treatment groups with control groups at mass average (price P = 0,016) and left ventricular volume (price p = 0,034). A decrease in mass and left ventricular volume of carvedilol in the treatment group although the decline occurred not significantly different when compared to before administered carvedilol therapy. While in the control group acquired increase in mass and left ventricular volume carvedilol in comparison with before given the carvedilol.

The important result gained in this study is that carvedilol can restore partial eccentric remodeling that is seen in the left ventricle mass and left ventricular volume in child patients with heart failure due to PJB shunts left to right. This change occurs in research subjects with a stable clinical condition.

Diastolic function of the left ventricle can be assessed by calculating (i) the peak speed and ratio of the E wave and A wave; (ii) The decelation time, which is the interval of the peak of wave E to the zero cut point from the decrease of the wave slope E; (iii) Atrial filling fraction, the velocity of wave A is integrally divided by the total speed of entry of blood flow through the mitral valve; and (iv) the time of isovolemic relaxation, which is the interval between the end speed of the final blood flow from the left ventricle with the onset of blood flow through the mitral valve taken from the echocardiography pulsed test (ekokardiografi pulsed-wave Doppler) (Nolan, et al. 2008).

In this research there were significant differences in ejection fraction (price P = 0,031) and shortening fraction (price P = 0,041) between the treatment group and the control group. There was a significant increase in ejection fraction (price P = 0,039) and shortening fraction (price P = 0,040) on the treatment group compared to the control group. The increase in ejection fraction and the shortening fraction does not found in the control group.

In this research, there was an increase in E/A ratio after administration of carvedilol in both research groups but the increase was not statistically meaningful (price P = 0,365 on the treatment group; and price P = 0,676 in the control group). There is no significant difference in the Carvedilol Pascaterapi in both research groups (price P = 1.00)

In the research conducted by Bergström et al. (2004), the administration of carvedilol in adults with heart failure diastolic and normal systolic function, can give a significant difference in the ratio of E/A and heart frequency. The decrease in heart frequency will provide a long heart diastolic filling effect so that the diastolic phase occurs longer than the systolic phase for the occurrence of diastolic filling. Carvedilol can fix the early diastolic filling phase through complex interactions between relaxation and heart space. The administration of Carvedilol is not related to the speed improvement of myocardial relaxation, but more on slowing the fast filling phase so that A normal filling pattern occurs (Bergström, et al. 2004).

CONCLUSION

There is a difference in the left ventricular dimension changes during systolic end (DVKI-AS), left ventricular dimensions at the end of diastolic (DVKI-AD), thick left ventricular rear wall at the end of diastolic (DBVKI-AD), thick interventricular septum at the end of diastolic (SIV-AD), left ventricular volume, left ventricular mass, left ventricular ejection fraction, and shortening fraction Left ventricle, but there is no difference in the E/A ratio change between standard therapy groups and carvedilol compared to standard therapy groups in children with heart failure due to the left-to-right PJB shunts.

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