

## Evaluating the Clinical Course of Patent Ductus Arteriosus after Discharge and Comparing in Therapies Techniques

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### Abstract

#### Background

Patent ductus arteriosus is an open channel between the aorta and pulmonary artery. The study aimed to evaluate the clinical course of patent ductus arteriosus after discharge and comparing in therapies technique.

#### Materials and Methods

This cross-sectional and inferential- descriptive study was performed in the hospitals of city of Zahedan-Iran in the period of one decade from 2005 to 2015. The study populations were all patients with patent ductus arteriosus (PDA) and these patients followed for at least one year after discharge from the hospitals due to the treatment with one of the Video-assisted thoracoscopic surgery (VATS), Amplatzer, surgery and medical techniques. 144 patients were assessed and the results of echocardiographic findings recorded in pre-determined data collection form and analyzed using SPSS version 15.0.

#### Results

No residuals for VATS treatment after hospital discharge, but in the Amplatzer the rate of residual was 13.3% when the higher rate of 20% was for surgery. The highest rate of residual for PDA closure was 23.5% in medical treatment. In the treatment methods comparison analysis in respect to the size left atrium-to-aorta (LA / AO) changes from one month to one year observed a significant difference in the methods of VATS, Amplatzer and Surgery in which illustrate the left heart cavities that represent a great relief due to passing time occurred.

#### Conclusion

From the study concluded that in the methods of VATS, Amplatzer and surgery a closed PDA needs time to become normal left chambers by changes in LA / AO, but in the medical method, not observed any changes in LA / AO. The results showed any residual due to VATS method after discharge from hospital, but surgery and Amplatzer had very low rates.

**Key Words:** Amplatzer, Medical treatment, PDA, Surgery, VATS.

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## 1- INTRODUCTION

Congenital heart diseases (CHDs) are principal causes of death in infants, so that its prevalence is about 8 of 1000 live births (1, 2). Patent ductus arteriosus (PDA) is a cardiovascular connection between the descending aorta and the pulmonary artery, and it happens when left subclavian artery the separated from aorta. In all types of CHD the prevalence of PDA accounted 5-10 percent (3). The incidence of PDA in full term neonates is 1 in 2.000 live births that have been reported by Schneider (4).

In term neonates mechanical ventilation and increasing of O<sub>2</sub> saturation caused a reduction in pulmonary vascular resistance and eliminating low vascular resistance in placenta increased systemic vascular resistance at birth. This process makes mechanical occlusion of PDA and ultimately remains in the form of arterial ligament. PDA based on its size (small, moderate, large) causes some symptoms such as failure to thrive, irritability, sweating, poor feeding, tachypnea, tachycardia peripheral bounding pulses, widened pulse pressure, systolic murmur with the highest severity between second and third left intercostal space and moderate to severe cardiomegaly in chest X-ray (5). Spontaneous ductus arteriosus closure is rare after infancy (6).

Therefore treating this disorder and defect is essential. The treatment types for PDA are listed as surgery, Video-Assisted Thoracic Surgery (VATS), Amplatzer and medical treatment with indomethacin, ibuprofen and paracetamol (2). Has been reported that the results of PDA closure after 6 months follow-up in using two Nit-Occlude coils and Amplatzer duct occluder devices were preferable than Gianturco and Flipper coils (7), and confirmed that the trans catheter Amplatzer for PDA occlusion have a long-term safety and efficacy compared with surgery. In comparison of these methods, Amplatzer occlusion had lower invasive, a few

residual shunt and complications. They also showed that Amplatzer has high effect in returning of pulmonary hypertension and left ventricular dilation to the normal status (8). Between two surgical closure and indomethacin therapy to treat PDA no significant differences observed in hospital mortality, chronic lung disease, necrotizing enterocolitis, sepsis, creatinine level and intraventricular hemorrhage. But the incidences of pneumothorax and retinopathy of prematurity were higher in the surgical group, but in general there is not enough evidences to induce which one is better. From Noori et al. study resulted that an increase in the mortality of premature infants' is associated with lack of closing the duct after treatment. These associations, become stronger in low birth weight (9).

For more confirmation the results of a study showed that Amplatzer had no complication compared with other methods in children less than 12 kg (10). It also is expressed that the treating PDA with medical method not responding after two courses of treatment with Ibuprofen, then the surgery was preferred because of low incidence for various morbidities (11). Surgical ligation produces complete ductus arteriosus closure; however, it is associated with its own set of morbidities: thoracotomy, pneumothorax, chylothorax, post-operative hypotension, vocal cord paralysis, infection, and scoliosis (12-15).

In addition, several studies suggest that early surgical ligation may produce detrimental effects on lung function and growth and may even contribute to the development of bronchopulmonary dysplasia so that this raise of the possibility of ductus ligation may create problems that counteract with any of the benefits derived from ductus closure (16, 17). Accordance with several reported evidences delay in ligation is useful because of having association with

decreasing in several morbidities such as hypotension, vocal cord paralysis and bronchopulmonary dysplasia. Therefore, conservative approach is associated with decrease in the rate of ductus ligation and lower rates of necrotizing enterocolitis (NEC) (18). With considering what above mentioned we aimed to evaluate the clinical course of patent ductus arteriosus after discharge and comparing in therapies technique.

## 2- MATERIALS AND METHODS

### 2.1. Study design

This descriptive analytical study performed on children with PDA within 10 years period from 2005 to 2015. The sampling method was census because of low prevalence. The places of the study were Ali Asghar and Aliebne Abitaleb hospitals located in the capital city of the Sistan and Baluchestan province, (Zahedan) Iran.

### 2-2. Criteria

Accordance with exclusion and inclusion criteria, these children followed for at least one year after treatment and discharge from the hospitals. If we missed a patient in the follow up, the patients excluded from the study. Error and mistake in medical record information of patients was an exclusion criterion. Patients with any kinds of heart diseases except PDA also excluded from the study.

### 2-3. Samples and methods

By considering all these limitations for patients in entering study our sample size reached to 144 children who had PDA. PDA diagnosis was accordance with performing echocardiography by pediatric cardiologist with using Mylab 60 and challenge 7000 made of Italy. Video-assisted thoracoscopic surgery (VATS) and Amplatzer performed in centers with enough facilities in the other cities of Iran, but the two other methods, surgery and

medical treatment performed in our centers. VATS technique included of "an electrocautery hook, titanium clips (Ligaclip LT 400; Ethicon Endosurgery, Cincinnati, Ohio), a clip applier, lung retractor, trocar, suction device, and a videoscope (Karl Storz Endoskope GmbH, Tuttlingen, Germany)"(19).

Amplatzer Ductal Occluder II (ADO) is a "self-expanding Nitinol device with a central waist and two symmetrical retention discs. The central waist is designed to fill the defect and the two retention discs are designed to be deployed on the aortic and pulmonary side defect. It is like a multifold and multi segmented design that creating 6 potential planes of occlusion with no central fabric (20).

Surgical interruption of patent ductus arteriosus (PDA) using a left posterolateral thoracotomy was the only available technique until 1971 when Porstmann and colleagues applied it for the first time (21). Prostaglandin inhibitors (NSAIDs) such as indomethacin and ibuprofen are used to treat patent ductus arteriosus (PDA) in the premature and term neonate in which named as medical treatment for PDA. Many studied revealed that oral ibuprofen is the best drug for this treatment (22, 23).

Medical therapy is a good method and initial treatment in PDA closure. Indomethacin and ibuprofen are used mostly with more benefits and are preferable medicines because of low side effects (11). Patients with age less than 28 days treated with oral ibuprofen in medical approach in two courses in every 3 days. Patients discharged from the hospital after taking telephone number and full address. Within one year or more follow-up they were asked to refer to the heart clinic for echocardiography after one month and after one year. The purposes of echocardiography were measuring residual shunts in PDA level and the left atrium-to-aorta (LA/Ao) ratio. For this study all complications after hospital discharge

considered and necessary information recorded in a researcher made data sheet.

## 2.4 Analysis

The data were analyzed using SPSS for Windows, Version 15.0 (Chicago, SPSS Inc. USA). Data were summarized as percent, means  $\pm$  standard deviation (SD). The normal distribution of cases is analyzed by Shapiro-Wilk test. The comparison of categorical data set was performed with Chi-square test. In not normally distributed data Mann-Whitney U-test was utilized for comparison. In comparison of more than two groups Kruskal-Wallis test was used. In normally distributed data, two groups were compared with Student's t-test and analysis of variance was used for the comparison of more than two groups. In the analysis of variance, Bonferroni test was used for post-hoc analysis. The significant level considered with 0.05 errors.

## 3- RESULTS

Patient's age ranged from 11 days to 192 months with mean of  $36 \pm 39.16$  months. Of 144 patients 51 (35 %) were boys with mean weight of  $12 \pm 6.85$  kg and 93 (65 %) were girls with mean weight of  $10.49 \pm 6.10$  kg. Mean height of boys was  $87.92 \pm 21.81$  cm and was  $81.22 \pm 22.10$  cm for girls.

Patients were under different methods of treatment with the frequencies of 42, 45, 17 and 40 with VATS, Amplatzer, medical and surgery, respectively, so that patients who were under treatment with medical method were younger ( $7.59 \pm 7.64$  months), and patients who were treated with surgery were older ( $52.29 \pm 43.38$  months). Mean ages of patients under the Amplatzer and VATS treatment were  $30.12 \pm 34.24$  and  $36.70 \pm 40.30$  months, respectively.

Weight and height means of patients were compared based on the various treatment types of PDA and observed significant difference among methods ( $F= 5.92$ ,

$P=0.001$ ) and ( $F=9.4$ ,  $P<0.001$ ), respectively. The results also showed that in the paired comparisons methods only medical treatment made this difference in height and in the weight along with a difference of amplatzer with surgery (**Tables.1 and 2**).

Of 144 patients, 82 (56.9%) were with normal PAP and 62 (43.1%) were in the increasing pattern of PAP. Of patients with normal PAP, 21 (25.6%), 26 (31.7%), 17 (20.7%) and 18 (22%), and of patients with increasing PAP 21(33.9%), 19(30.6%), 0(0%) and 22(35.5%), were under treatment of VATS, amplatzer, medical and surgery methods respectively. Chi-square test analysis showed a significant relationship between residual shunt and types of PDA treatment (Chi-Square=9.976,  $P= 0.019$ ). VATS method had not any residual shunt one month after treatment. This trend followed by Amplatzer (86.6%), surgery (80%) and medical (76.4%), respectively in descending ranking (**Table.3**).

ANOVA test was applied to evaluate LA/Ao ratio after one month and after one year among types of PDA treatment. For the ratio of LA/Ao size after one month the table showed that Amplatzer had the highest mean size ( $1.42 \pm 0.29$ ) of LA/Ao ratio and followed by surgery ( $1.39 \pm 0.23$ ). The medical treatment had the lowest mean ( $0.97 \pm 0.14$ ).

The critical value of variance was  $F=16.83$  with the P- value  $<0.001$  which showed the significant differences. After one year the differences of LA/Ao ratio in four types of treatments had significant difference ( $F=19.19$  and  $P<0.001$ ). The mean of LA/Ao for VATS, Amplatzer, and medical surgery were  $1.11 \pm 0.08$ ,  $1.15 \pm 0.11$ ,  $0.94 \pm 0.08$  and  $1.13 \pm 0.09$ , respectively. As the table showed the mean of LA./Ao ratio from one month to one year in follow up, the different of mean for LA/Ao between one month and one year, showed a significant different

( $F= 11.194$  and  $P<0.001$ ). The follow-up Tukey test applied to find those significant differences that were due to which type of treatments (**Table.5**).

One month, one year after treatment and in the time between, the value sizes of the LA/Ao ratio was different significantly in medical compared with VATS, Amplatzer

and surgery. The results of paired t-test showed that the difference of means for VATS, Amplatzer, medical and surgery were  $0.22\pm0.19$ ,  $0.275\pm0.195$ ,  $0.031\pm0.099$  and  $0.285\pm0.153$ , respectively. These decreased values were significant for all except medical method of treatment ( $P<0.001$ ) (**Table.6**).

**Table-1:** Mean weight and height in different types of PDA treatment

Variables	Types of treatment (number)	Mean± SD	Min	Max	F	P-value
Weight	VATS (42)	6.12±11.51	4.5	28	5.92	0.001
	Amplatzer (45)	5.98±10.94	5	35		
	Medical (17)	2.49±5.96	2.7	10		
	Surgery (40)	7.20±13.38	4	40		
	Total (144)	6.42±11.20	2.7	40		
Height	VATS (42)	20.85±84.61	58	135	9.4	0.001
	Amplatzer (45)	19.48±81.44	60	137		
	Medical (17)	11.04±62.23	48	85		
	Surgery (40)	23.60±93.25	58	155		
	Total (144)	22.11±83.38	48	155		

SD: Standard deviation.

**Table-2:** Results of follow-up test for weight and height in different types of PDA treatment

Variables	Types of treatment	Types of treatment	Mean differences	P-value
Weight	VATS	Amplatzer	1.31±0.57	0.971
		Medical	1.75±5.55	0.01
		Surgery	-1.35±1.86	0.513
	Amplatzer	Medical	1.74±2.97	0.025
		Surgery	-1.33±2.44	0.259
	Medical	Surgery	-1.77±7.42	<0.001
Height	VATS	Amplatzer	4.37±3.17	0.887
		Medical	5.86±22.38	0.001
		Surgery	-4.50±8.63	0.226
	Amplatzer	Medical	5.80±19.20	0.006
		Surgery	-4.43±11.80	0.042
	Medical	Surgery	-5.90±31.01	<0.001

**Table-3:** Relationship between residual shunt and types of treatment in PDA

Residual		Treatment				Chi- square test	P-value
		VATS	Amplatzer	Medical	Surgery		
No	N	42	39	13	32	9.976	0.019
	(%)	100%	86.60%	76.40%	80%		
Yes	N	0	6	4	8		
	(%)	0%	13.30%	23.5%	20%		
Total	N	42	45	17	40	144	
	(%)	29.20%	31.20%	11.80%	27.80%	100%	

**Table-4:** Means of LA/Ao ratio after one month, after one year and between these two times due to PDA treatment methods

Variables	Type of treatment	Mean± SD	F	P-value
LA/Ao ratio after 1 month	VATS	1.33±0.17	16.83	<0.001
	Amplatzer	1.42±0.29		
	Medical	0.97±0.14		
	Surgery	1.39±0.23		
	Total	1.33±0.26		
LA/Ao ratio after 1 year	VATS	1.11±0.08	19.19	<0.001
	Amplatzer	1.15±0.11		
	Medical	0.94±0.08		
	Surgery	1.13±0.09		
	Total	1.11±0.11		
Differences	VATS	0.22±0.11	11.194	<0.001
	Amplatzer	0.27±0.19		
	Medical	0.031±0.09		
	Surgery	0.25±0.15		
	Total	0.22±0.16		

SD: Standard deviation.

**Table-5:** Means of LA/Ao ratios after one month, after one year and between these two times due to PDA treatment methods

Variables	Type of treatment	Type of treatment	Mean± SD	P-value
LA/Ao ratio after 1 month	VATS	Amplatzer	-0.08±0.05	0.31
		Medical	0.36±0.06	0.001
		Surgery	-0.05±0.05	0.726
	Amplatzer	Medical	0.45±0.06	0.001
		Surgery	0.03±0.05	0.914
	Medical	Surgery	-0.4±0.06	0.001

LA/Ao ratio after 1 year	VATS	Amplatzer	-0.03±0.02	0.461
		Medical	0.12±0.02	<0.001
		Surgery	-0.01±0.02	0.895
	Amplatzer	Medical	0.2±0.02	<0.001
		Surgery	0.01±0.02	0.885
	Medical	Surgery	-0.19±0.02	<0.001
Different means	VATS	Amplatzer	-0.05±0.03	0.347
		Medical	0.17±0.02	<0.001
		Surgery	-0.03±0.03	0.683
	Amplatzer	Medical	0.24±0.04	<0.001
		Surgery	0.01±0.03	0.956
	Medical	Surgery	-0.22±0.04	<0.001

SD: Standard deviation.

**Table-6:** Reduction of LA / AO in the periods of one month and one year after treatment

Treatments	Time duration	Mean± SD	Different means	Paired t-test	P-value
VATS	After one month	1.33±0.170	0.22±0.19	12.06	<0.001
	After one year	1.11±0.087			
Amplatzer	After one month	1.42±0.297	0.257±0.195	9.44	<0.001
	After one year	1.15±0.118			
Medical	After one month	0.97±0.145	0.031±0.099	1.34	0.198
	After one year	0.94±0.089			
Surgery	After one month	1.39±0.236	0.258±0.153	10.628	<0.001

#### 4- DISCUSSION

The results of the present study were accounted lower frequency, higher mean of weight and height in boys compared the girls. Our patient's age ranged from 0.36 to 192 months with mean of  $36 \pm 39.16$  months. The frequency of patient's was accounted the highest in Amplatzer and the lowest in medical. PDA patients who treated with medical had lower weight and height compared to other methods.

The majority of our patients had PDA with normal PAP. Vast method had not any residual shunt after one month treatment. This trend followed by Amplatzer in the second rank. To evaluate LA/Ao ratio among types of PDA treatment Amplatzer had the highest mean and followed by surgery after one month

and after one year. The decreased size of LA/Ao ratio mean was the highest for Amplatzer. Surgery took the second rank in this term. Since, PA pressure required 2-6 weeks to receive to the normal status in neonate after birth, and because these patients were under medical treatment until 28 days, therefore, significant shunt not observed between Aorta and Pulmonary artery.

The study found that in using VATS to treat patients not observed any residuals during one month after discharge and the rate of residuals started to increase from Amplatzer with the lowest rate to medical with the highest rate. Therapies comparison with regard the size of LA / AO ratio had significant reduction by time in VATS, Amplatzer and Surgery.

According to our study, one death occurred in Amplatzer method that was due to underlying disease (Niemann-Pick). From 40 patients who treated with surgery method 8 had residual shunt so that, three of them were treated by medical and remained were under surgical treatment. The question here come in mind that why these patients had double surgical treatment? Why that, the PDA closure with ligation were used for the first time and in the second time the surgery method was used by division and ligation. In the patients who were treated by Amplatzer echocardiography did not show any residual after one year follow up. In the medical treatment for PDA closure the four patients who had not respond to treatment referred to the other methods.

Nezafati et al., reported that Video-assisted thoracoscopic surgery is the best, safe and effective method with low complication and high success rates. In the study the complete closure occurred completely with very low complications, so that there were 4 late residuals shunt that was a very low percent and transient laryngeal nerve dysfunction observed in 14 patients. In the present study did not observe any patients with laryngeal nerve dysfunction and residuals that is similar with Nezafati results (21).

Ghasemi et al., conducted a study on PDA closure by devices of Coil Gianturco, Flipper Coil, Amplatzer and Nit- Occlude Coil in children. From this study resulted that 7.2% patients had residual shunt. The Nit- Occlude Coil, Amplatzer, Flipper Coil and Coil Gianturco groups had residual shunts in increased ranking respectively, so that 2.1% where the lowest for Nit-Occlude Coil and 15.6% were the highest for Gianturco at six-month follow (7). It is necessary to report that in this study 3.3% of patients had residual shunt after PDA closure by Amplatzer in six months follow up. When in the present study the residual was 8.8% after one month so that we did

not have any residual after a year follow up. According to a conducted study by Chen et al., on long-term comparison and clinical course between Amplatzer and surgery on isolated patients with PDA, confirmed a long term efficiency of Amplatzer. This method had lower invasive, fewer complications and a few residual shunts. Amplatzer method also had high effective on pulmonary hypertension regression and dilation on left ventricle to the normal status. Amplatzer method in our study was associated with good results. In our study, one patient died after closing PDA with Amplatzer that was due to the underlying disease (Niemann-Pick) (8).

Accordance with a study conducted by Noori et al. on preterm neonates who their PDA were closed spontaneous or due to pharmacologic treatment, failure in PDA treatment had 8 folds more mortality compared with patients who respond to the treatment (24). In our study the frequency of patients who treated by medical method were 17, so that 4 of them did not respond to medical treatment. It is needed to express that our patients were term neonates with higher age range compared to very low birth weight patients in the Noori's study.

Lee et al., performed a study to evaluate PDA ligation on premature neonates. Surgery method was a suitable technique, because of having high percentages of survival with considerable delay in death, but with high rate of illness. In our study the patients were not faced with death after hospital discharge within one year follow because of their higher age, dividing and ligation of PDA. They also showed that there were not significant effects on duration of oxygen dependency and mortality between the groups of infants who did not receive any prostaglandin synthetize inhibitors prior to ligation compared with those who received. In our study none of our patients did not received



prostaglandin synthetize inhibitors prior of surgery that would strongly be comparable with their results (25). In our study two patients who had residual shunt in PDA level after ligation, responded to the medical treatment (Oral Ibuprofen). Muhammad Younas and Ahsan Beg studied on the early results of device occlusion complication in PDA closure in young children less than 12kg weight and resulted, a successful procedure without any major complication and deaths. They observed only minor complication such as loss of arterial pulse which resolved within first 24 hours by heparin infusion, protrusion of aortic end of device without aortic obstruction, partial left pulmonary artery occlusion and residual PDA (10). Similar results received by Butera et al., on children with age of 6 to 36 months and weight less than 16kg (22).

Behjati-Ardakani et al., also performed a study on the long term results of trans catheter closure of PDA using Amplatzer. They showed that PDA closure with Amplatzer was an effective and safe method for PDA closure with low complications (26). In the present study we did not observed any complications except residual shunt and one death due to underlying diseases within three months after discharge (Niemann-Pick).

Vida et al., answered to a question about the optimal timing for surgical ligation of PDA in preterm infants; and was answered that PDA must be ligated anytime that patients did not respond to the medical treatment or contraindicated due to renal failure, NEC and thrombocytopenia. They also reported that the proper time for surgical PDA ligation is better to be after initial medical treatment or soon after the second unsuccessful cycle of ibuprofen or indomethacin. In the present study the medical treatment performed on term infants and other methods were applied on children with higher age (11). Jahaveri et al., evaluated the effects of a conservative

approaches on PDAs that failed to close after indomethacin treatment compared to early surgical. They reported that both conservative approach and early surgical had same complication such as sepsis, intracranial hemorrhage, neurologic injury, bronchopulmonary dysplasia, retinopathy of prematurity and death, but a significant difference in necrotizing enterocolitis with much higher value in early surgery compared to conservative approach (18). Noori et al., reported that in PDA closure by oral ibuprofen seems to be valuable without complications in term neonates (27). In our study patients with residual shunt, were more in medical treatment compared to surgery.

Adrouche-Amrani et al., conducted a study on medical treatment with no responding to close a PDA, and resulted that it could be a risk factor for developing chronic lung disease in early low birth weight. The results of the present study with this study supported that medical treatment can make high risk of some morbidities such as chronic lung diseases and retinopathy of prematurity when failed to close PDA and suggested that would be better to change the approach in surgery method (28).

Chorne et al., also reported same results that the majority of predictive effects to close a PDA on immature gestation were chronic lung diseases and independent of immature gestation in surgical ligation (17). In our study on term neonates, we resulted that the response to the treatment of PDA were lower in surgery compared in medical. Carmen et al., conducted a study to determine the effect of a long course indomethacin on the failure of medical treatment without side-effects; after reviewing 5 studies reported that the major side effect of indomethacin was included of renal dysfunction, decreased platelet aggregation and necrotizing enterocolitis (29). Tashiro et al., reported that PDA ligation is the best type of treatment for having lower mortality rate in very low

birth weight and premature neonates compared with their methods. In our study surgery was performed on infants and younger children to close PDA after discharge from hospital free of death. The lack of success in surgery was ligation for PDA closure (30). The possible role of echocardiographic markers is uncertain to predict the type of treatment for PDA closure. Flood and Guthrie conducted a study in this term and received to the similar conclusion in premature neonates. They resulted that the sensitivity and specificity of left atrium-to-aorta, PDA/Left pulmonary artery, and patent foramen ovale diameter were not high enough to predict PDAs that there were significantly in hemodynamically, and surgical intervention was needed, but for older neonates they resulted that LA/Ao was useful marker to predict PDA significantly (31). But in another study Guthrie et al., attempted to predict hemodynamically PDA by combination of some individual markers and resulted that the sensitivity of LA/Ao with cutoff of 1.5 as a positive test for the presence of PDA was high; when its specificity was low.

At the same time, the sensitivity was lower for age group of 0-3 days when the specificity was higher. We evaluated the size of LA/AO after PDA treatment after one year. We measured the LA/Ao after one month and after one year. We observed that the size of LA/Ao decreased in about 57% patients from 1.33 (34.7% of patients) to 1.11 (91% of patients). Therefore, LA/Ao could be an accepted marker in evaluation of left heart chambers returning to the normal state. With a deep review in our study would be recognized that the present study had different methodology compared with above studies with similarities in results (32).

#### **4-1. Limitations of the study**

Limitation of the present study was related to lack of corporation by some of parents in the follow up.

## **5- CONCLUSION**

This study was the first study in this specific area about measuring of LA / Ao after one month and after one year to evaluate the clinical course of patent ductus arteriosus after discharge from hospital due to this fact that LA/Ao regression to the normal status needs times. In the methods of VATS, Amplatzer and Surgery have been shown that a closed PDA needs to the time for left chamber normality by changes in LA/Ao, but in the medical method, did not resulted for different of LA/Ao in the time between one month and one year. Not observed any residual due to VATS method after discharge from hospital and in the methods of surgery and Amplatzer the rate was very low, so that 90% of the residuals will be closed by one year.

In the medical method, the patients were neonates and were under two course oral treatments by ibuprofen; Majority of the patients had positive response to the treatment. The patients, who did not respond to the treatment, were under other types of treatment.

## **6- CONFLICT OF INTEREST**

The authors would like to declare any conflict of interest.

## **7- ACKNOWLEDGEMENT**

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