Original Article

Comparison of Effect of Combined Intravenous Amiodarone and Surgical Closure of OS ASD in Adults with Surgical Closure alone on Sinus Conversion of Concomitant Atrial Fibrillation — A Retrospective Case Series Analysis

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Closure of Atrial Septal Defect has been proposed to increase conversion of concomitant Atrial Fibrillation (AF) to Normal Sinus Rhythm (NSR). Amiodarone is known to convert AF to NSR. Our findings support the use of single intraoperative dose of intravenous Amiodarone for increased conversion of pre-operative AF to NSR in OS ASD patients undergoing closure on CPB, although the effect was short lasting. [*J Indian Med Assoc* 2022; **120(6):** 40-3]

Key words **: ASD Surgery, Amiodarone, Sinus Conversion.**

Amongst the Congenital Cardiac Disorders presenting in adulthood, ASD is the commonest, a prevalence of 0.2 to 0.7 per thousand[1]. with late presentation due to functional limitation, either because of development of arrhythmia or progression of pulmonary hypertension[1]. Atrial Fibrillation (AF) is the most common arrhythmia in adult ASD patients[2] and incidence increases with age being as high as 52% in patients aged > 60 years[3]. Hence, a significant number of adult patients have AF when they come for ASD correction. The ensuing tachycardia, impaired ventricular filling, decreased cardiac output with development of Atrial Fibrillation, renders the patient symptomatic[2], together with increased risk of developing thromboembolic complications in 17-18% of patients[4,5]. Several previous investigators who have studied the effect of ASD closure on concomitant AF in adult patients, have found mixed results[2,6-10]. Conversion to sinus rhythm is better seen with ASD closure in younger patients <25 years[11], in those with paroxysmal AF[2] or in older patients undergoing concomitant Maze[12] or radiofrequency ablation[13].

Among all anti arrythmic drugs evaluated for AF, amiodarone has shown the most promising results with successful conversion and maintenance of Normal Sinus Rhythm (NSR) in 50-70% patients[14-16]. Pre treatment with oral amiodarone and cardioversion resulted in NSR restoration in approx 80.6% non-surgical patients with persistent AF[17]. In the 2009 prospective, randomized case controlled study by Selvaraj *et al,* in rheumatic AF patients undergoing Elective Valve Replacement Surgery under CPB, a single intraoperative dose of IV amiodarone increased the conversion rate of AF to NSR in 73.5% patients after release of Aortic Cross Clamp (ACC), compared to 58.5% in control group[18].

Editor's Comment :

- In adult patients >40 years age with ostium secundum atrial septal defect (ASD) and concomitant atrial fibrillation, undergoing surgical closure of ASD under cardiopulmonary bypass, a single intraoperative Intravenous bolus dose of amiodarone probably increases rate of sinus conversion after aortic cross clamp removal.
- However, the effect is short lasting. For sinus conversion and long term maintenance, probably concomitant Maze or radiofrequency ablation may prove to be effective.

In our clinical practice, we found that using single intraoperative IV bolus dose of Amiodarone before CPB, in adult OS ASD patients with AF for rate control, not very infrequently, resulted in conversion to NSR, immediately after release of ACC.

Therefore, in this retrospective case series analysis, comprising adult OS ASD patients >40 years age with concomitant AF, undergoing ASD closure under CPB, we attempted to analyze the rate of sinus conversion and course of pre-operative AF after single intraoperative bolus dose of IV amiodarone, compared to those who did not receive such dose.

Material and Method

Twenty three adult patients, aged >40 years, with Ostium Secundum Atrial Septal Defect (OS ASD) with left to right shunt, who underwent surgical closure on Cardiopulmonary Bypass (CPB), between January, 2019 and 31st March, 2022 in Cardiothoracic OT of

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IPGME&R Kolkata, were reviewed for presence of concomitant Atrial Fibrillation prior to surgery. Eleven such patients with no features of Heart Failure pre-operatively, and uneventful postoperative recovery, were shortlisted and recruited in our retrospective case series analysis. Amongst them, 6 patients who had received intraoperative, pre-pump intravenous single bolus dose of Amiodarone at 3mg/kg were grouped into Group A (n=6) and 5 patients who had not received such a dose of IV Amiodarone were enlisted in Group B (n=5) or control group. Institutional Ethics Committee approval was taken.

All these patients had a pre-operative controlled ventricular rate <100 beats per minute (bpm) with the use of some oral rate control medication, digoxin, beta blocker (metoprolol) or a combination of both. Oral anticoagulation was managed prior to surgery as per institutional protocol.

On the day of surgery, in the Operation Theatre (OT), General Anaesthesia was induced in all patients with intravenous midazolam 0.05mg/kg, fentanyl 3µg/kg, propofol 2-3 mg/kg and intubation using rocuronium 1mg/kg, under continuous monitoring of ECG, Pulse Oximetry, Invasive Blood Pressure, BIS. Following institutional protocol, invasive arterial line was done under Local Anaesthesia prior to induction and central venous line post induction. Temperature probe, urinary catheter and Transesophageal Echocardiography (TEE) probe were inserted post induction. Pre-induction ventricular rate (baseline) was noted in all patients. Post induction TEE parameters were noted. There was no left atrial thrombi in any of the patients. Anaesthesia was maintained with 0.5 MAC isoflurane in O_2 and N_2O with intermittent vecuronium 0.01 mg/kg and fentanyl 0.5µg/kg , as and when needed, to maintain a BIS between 40-60. Heart rate prior to going on CPB was noted in all patients. Surgical repair was performed with the support of CPB. Aortic Cross Clamp (ACC) time and CPB time were noted. Most of the patients required minimal dose inotropes, dobutamine and/or adrenaline while weaning from CPB. The emerging rhythm together with heart rate after ACC removal, was noted in all patients. DC shock (20-30J), using internal cardiac paddles, was instituted on table, if ventricular rate was found to be >100bpm causing unstable haemodynamics. Rhythm at end of surgery was noted. Following institutional protocol, all patients were shifted to postoperative cardiac surgical ICU on ventilator, monitored and managed in the ICU for the next 24 hours. Following uneventful recovery, all patients were extubated within 24 hours following institutional protocol. Oral rate control medication the patient was on pre-operatively, was started in patients with Atrial Fibrillation and ventricular rate >100 bpm, orally or through ryles tube, as applicable. Since all the patients with AF were haemodynamically stable postoperatively in ICU, none received DC shock in the first 24 hours. The following recorded parameters were compared between the two groups:

Pre-operative patient related variables: age, sex distribution, body weight, presence of comorbidities (Hypertension, Diabetes, Previous Stroke), TEE parameters like Qp/Qs (pulmonary *versus* systemic blood flow ratio), ASD size, Left Atrial (LA) size, Left Ventricular Ejection Fraction (LVEF), Left Ventricular End Diastolic Diameter (LVEDD), Left Ventricular End Systolic Diameter (LVESD), Right Ventricular Systolic Pressure (RVSP).

Intraoperative Variables : pre-induction (baseline) ventricular rate, ventricular rate prior to going on CPB, ACC time, CPB time, inotrope requirement, need for blood transfusion and number of units transfused.

Primary Outcome Variables : rhythm after release of ACC (sinus, AF or other rhythm), number of patients requiring DC shock post CPB in OT, number of patients with AF at end of surgery, number of patients with AF at end of 24 hours in ICU.

Statistical analysis :

The above data were summarized by routine descriptive statistics, namely mean and standard deviation for numerical variables and counts and percentages for categorical variables. Numerical variables were compared between groups by Student's 't' test. Categorical variables were compared between groups by Fischer's exact test. A P value $\leq$0.05 was considered to be statistically significant.

Observations

Amongst the 23 adult patients aged >40 years with OS ASD, who underwent surgical closure on CPB, between January, 2019 to 31st March, 2022, reviewed for our study, we found 11 patients (47.82%) with concomitant Atrial Fibrillation as baseline rhythm. These 11 patients who met our inclusion and exclusion criteria, were recruited and randomized into two groups. Group A (n=6) and control group Group B (n=5). Table 1 summarizes pre-operative patient related variables. Mean age was found to be 51.6 years in Group A and 50.4 years in Group B (P>0.05). Sex distribution was equal in Group A while in Group B 60% were male (P>0.05). Remaining variables including body weight, associated comorbidities, Qp/Qs, other echo parameters and intake of rate control drugs, were found to be comparable between the two groups (P>0.05). Compared to no patient of Group B, one patient in Group A had a prior h/o stroke (P<0.05).

Table 2 summarizes the comparison of intra-operative variables between the two groups. Mean CPB time,

Basal Heart Rate, use of inotropes while weaning from CPB, blood transfusion and number of units transfused, were found to be comparable between the groups (P>0.05). However, the mean ventricular rate just before going on CPB was found to be significantly lower in Group A compared to Group B (P=0.05).

A comparison of primary outcome variables between the two groups are summarized in Table 3. With regards to rhythm after release of Aortic Cross Clamp, 5 out of 6 (83.33%) patients in Group A presented in sinus rhythm versus no patient in Group B (P<0.05). Atrial fibrillation was the emerging rhythm in all 5 patients (100%) of Group B versus in only one patient of Group A (16.67%) (P>0.05). DC shock was required in 2 out of 5 (40%) patients of Group B with atrial fibrillation due to a higher ventricular rate and unstable haemodynamics, resulting in sinus conversion in one of them and a lower ventricular rate with improved haemodynamics in the other. In comparison, none of the patients in Group A required DC shock (P>0.05). Amongst the five in Group A who had initial sinus rhythm after Aortic Cross Clamp release, two of them reverted to Atrial Fibrillation by the end of Surgery, resulting in 3 out of 6 (50%) patients in Group A with AF at the end of surgery. In comparison, in Group B, except for one patient who converted to sinus rhythm after receiving DC shock, all other ie, 4 out of 5 (80%) patients had rhythm AF by the end of surgery (P>0.05). At the end of 24 hours after shift to ICU, 5 out of 6 (83.33%) patients in Group A regained AF, with maintenance of sinus rhythm in 1 out of 6 (16.67%) patient. In comparison in Group B, all the 5 (100%) patients had AF by the end of 24 hours in ICU (P>0.05).

Discussion

About 13-52% patients older than 40 years with ASD have a concomitant Atrial Fibrillation[1]. In our retrospective case series analysis, we found an incidence of 47.82% of concomitant pre-operative AF in OS ASD patients >40 years age who underwent surgical closure under CPB.

The two groups of patients in our analysis, were found to be comparable (P>0.05) with respect to preoperative patient characteristics, echo parameters, intraoperative variables except for aortic Cross Clamp time, which was significantly longer in control group B (P<0.05). After [a]miodarone IV bolus dose infusion, ventricular rate before going on CPB, was lower in Group A compared to control Group B patients with the difference being just at the level of significance (P=0.05). Conversion to NSR immediately after release of ACC was found in 83.33% patients in Group A, who received IV Amiodarone vs in no patient in control group B (P> 0.05). Atrial fibrillation was the emerging rhythm in 100% patients of control Group B vs in only one patient (16.67%) in group A. DC shock

Table 1 — *Pre-operative patient related variables*

	Group A (n=6)	Group B (n=5)	P value
Age in years (Mean±SD)	51.6±5.32	50.4±3.049	0.667
Sex (M/F)	2/4	3/2	0.7
Body weight (Mean±SD)	66.8±7.85	67±10.67	0.978
Comorbidities (no of pts)	6 out of 6 (100%)	3 out of 5 (60%)	0.182
Hypertension	2 out 6 (33.33%)	2 out of 5 (60%)	0.709
Diabetes	3 out of 6 (50%)	1 out of 5 (20%)	0.361
Previous stroke	1 out of 6 (16.67%)	0 out of 5 (0%)	0.014
Echo parameters			
Qp/Qs (Mean±SD)	2.92±0.277	2.98±0.443	0.775
ASD size in mm (Mean±SD)	21.82±1.267	21.38±1.118	0.228
LA size in mm (Mean±SD)	43.94±0.99	44.46±0.76	0.43
LVEF% (Mean±SD)	61.6±3.05	60.4±4.21	0.72
LVEDD in mm (Mean±SD)	42.64±1.02	41.86±1.05	0.077
LVESD in mm (Mean±SD)	26.34±0.517	26.44±0.591	0.806
RVSP mm Hg (Mean±SD)	44.76±0.702	44.86±0.709	0.777
Rate control drugs (no of patients) :			
Digoxin	2 out of 6 (33.33%)	2 out of 5 (40%)	0.136
B blocker	2 out of 6 (33.33%)	2 out of 5 (40%)	0.136
Both	2 out of 6 (33.33%)	1 out of 5 (20%)	0.576

Qp/Qs : Ratio of Pulmonary Blood Flow to Systemic Blood Flow; ASD : Atrial Septal Defect; LA : Left Atrium; LVEF : Left Ventricular Ejection Fraction; LVEDD: Left Ventricular End Diastolic Diameter; LVESD : Left Ventricular End Systolic Diameter; RVSP : Right Ventricular Systolic Pressure.

Table 2 — *Intraoperative variables*

	Group A (n=6)	**Group B (n=5)**	**P value**
CPB time in mins (Mean±SD)	75.5±0.791	76.26±2.040	0.488
ACC time (Mean±SD)	60±2.598	62.7±1.204	0.044
Basal HR in bpm (Mean±SD)	89.8±6.87	88.4±7.76	0.754
HR prior to CPB in bpm (Mean±SD)	79.4±6.107	89±3	0.05
Inotrope use (no of patients)	6 out of 6 (100%)	4 out of 5 (80%)	1.0
Blood transfusion (no of pts)	3 out of 6 (50%)	3 out of 5(60%)	0.7
No of transfused blood units (Mean±SD)	0.667±0.816	0.5±0.547	0.741

CPB : cardiopulmonary bypass; ACC : aortic cross clamp;
Basal HR : preinduction ventricular rate.

Table 3 — *Primary outcome variables*

	Group A (n=6)	Group B (n=5)	P value
Rhythm at release of ACC (no of patients) :			
Sinus rhythm	5 out of 6 (83.33%)	0 out of 5 (0%)	0.0152
Atrial fibrillation	1 out of 6 (16.67%)	5 out of 5 (100%)	0.304
No of patients requiring cardioversion	0 out of 6 (0%)	2 out of 5 (40%)	0.461
No of patients with AF at end of surgery	3 out of 6 (50%)	4 out of 5 (80%)	0.545
No of patients with AF within 24 hours	4 out of 6 (66.67%)	5 out of 5 (100%)	0.454

ACC : Aortic Cross Clamp; AF : Atrial Fibrillation

for rate control had to be instituted in 40% patients of control Group B and in no patient of Group A. About 50% patients in Group A had reverted to AF by end of surgery compared to 80% patients in control Group B (P>0.05). At the end of 24 hours in ICU, 66.67% patients regained AF in Group A in comparison to 100% patients in control Group B (P>0.05).

In the 2013 retrospective study by Wi J *et al*[2], the investigators examined the clinical course of pre-operative AF after correction of ASD and/or after concurrent Maze operation in 40 patients who underwent ASD repair by surgical or transcatheter device closure. In patients with Parosxysmal AF (PAF), isolated ASD closure resulted in conversion to maintenance of sinus rhythm in 88% patients and continuation of AF in 12% patients. While in patients with Persistent AF (PeAF), isolated ASD closure resulted in sinus conversion and maintenance in 18% patients and continuation of AF in 82% patients. In PAF patients who underwent surgical closure with concomitant Maze procedure, 100% patients reverted to and maintained sinus rhythm, while in PeAF patients, surgery with Maze resulted in sinus conversion and maintenance in 75% patients and persistence of AF in 25% patients. All patients were on pre-operative oral anti-arrythmics. The investigators concluded that, most of the ASD patients with pre-operative Paroxysmal AF, maintained SR after correction of ASD, rationalizing this finding by the potential anti arrythmic effect of ASD correction resulting from haemodynamic correction and subsequent structural and electrophysiological reverse remodelling[19,20]. Haemodynamic correction was not found to be totally effective in reversing AF in patients with pre-operative Persistent AF. However, a concurrent Maze procedure was found to be very effective in maintaining SR in these patients. Therefore, a concurrent Maze procedure or transcatheter ablation before ASD closure, needs to be considered in patients with pre-operative persistent AF.

From our analysis, we can conclude that although single intraoperative bolus IV dose of Amiodarone may result in increased conversion to sinus rhythm, but the effect is short lasting. Therefore, probably concurrent Maze or transcatheter ablation before/after ASD closure needs to be considered for maintenance of NSR.

Limitations :

Firstly, a retrospective analysis of a small sample size makes the results of our analyzed data not accurate enough to be extrapolated on actual population, necessitating the need for larger prospective trials. Secondly, we did not have complete information on the type of concomitant AF ie, whether paroxysmal or persistent, because the data was collected retrospectively. Thirdly, a longer study period beyond first 24 hours is probably required for better analysis of the course of AF.

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