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COMPARISON OF PROPHYLACTIC USE OF INTRAVENOUS N ACETYLCYSTEINE V/S AMIODARONE IN PREVENTING POST OPERATIVE ARTRIAL FIBRILLATION AFTER CORONARY ARTERY BYPASS GRAFT

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ABSTRACT… Objectives: compare the effectiveness of intravenous N-acetylcysteine and amiodarone in prevention of pos operative atrial fibrillation. **Study Design:** Randomized control trial **Place and duration:** study was conducted cardiac surgery department of Choudhary Pervaiz Elahi Institute of Cardiology, Multan from December 2017 to December 2018 in one year duration. **Methodology:** study was conducted on 130 patients. Patients were divided into two equal groups by lottery method. Study was started after permission from academic affairs committee written informed consent from the patients. Non probability consecutive sampling was used Study variables are age, gender, duration of ICU stay and mortality. An outcome variable was post operative atrial fibrillation. Data was computed on software SPSS version 23 and analyzed for all possible variables. P value ≤0.05 was taken as significant. **Results:** POAF of amiodarone and NAC group was noted as 26.2% and 13.8%, respectively. The difference was statistically insignificant (0.079). Mortality of amiodarone and NAC groups was occurred as 7.7% and 4.6%, respectively. The difference was statistically insignificant (0.465). **Conclusion:** intravenous N-acetylcysteine is more effective in prevention of post operative atrial fibrillation as compared to intravenous amiodarone but post operative stay is prolonged in patients of NAC.

Keywords: Amiodarone, N-acetylcysteine, atrial fibrillation, coronary artery bypass graft, Mortality.

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INTRODUCTION

Among the post operative complications of cardiac surgery atrial fibrillation is most common with incidence of 10% to 65% varying with the type of surgery method of monitoring para operative characters and definition of artrial fibrillation. In many previous studies it was reported that artrial fibrillation is responsible for prolonged hospital stay mortality and risk of stroke. Lot of research has been completed to understand the mechanism of POAF and it's method of prevention.

Current guidelines on this topic recommends that use of beta blockers and amiodarone redud the risk of POAF. But the use of this drug is precautionary due to their potential of side effects. Previous clinical studies reported a higher oxidative damage and inflammatory cytokynes level in patients of POAF as compared to those patients who did not underwent

Another anti inflammatory and anti oxidant agent is N acetyl cistine (NAC) that have the capability of reducing the cellular damage due to oxidative stress and systemic inflammation during cardiac surgeries. Previous Meta analysis concluded that a supplimentation of NAC is very effective for the reduction of POAF incidence. Another anti arrrhythmic drug with multiple channels of ion blocking characteristics is amiodarone. Amiodarone also has anti adrenergic effect due to which very effective in reducing the incidence of POAF up to 51%.

It was also reported in literature that amiodarone reduce the mortality and hospital stay of patients by reducing the bad incidence of POAF. Aim of our study is to evaluate the effectiveness of NAC on the prevention of POAF in comparison with role of amiodarone and prevention of POAF.

METHODOLOGY

This randomized controlled trial was conducted in the department of cardiac surgery in Ch Pervaiz Elahi institute of cardiology Multan. Study was started after permission from academic affairs committee written informed consent from the patients. Non probability consecutive sampling was used. The study was conducted in the supervision of senior professor of department to senior colleagues of department.

Total number of patients was divided into two groups, group N and group A. Patients in group N were given post operative intravenous N acetylcysteine and group A patients were given amiodarone infusion 5mg/kg loading dose and first hour after surgery and then 10mg/kg for the first 24 hours. Patients with chronic artrial fibrillation paceaker dependents second or third degree heartblock thyroid disease , valvular disease , previously taken the treatment of amiodarone and N acetyl cistine chronic liver or renal disfunctions and associated cardiac surgeries were excluded from the study.

All patients were given diazepam as a pre medication before shifting In the operation theater. General anaesthesia was induced with midazolam and fentanyl and vecuronium bromide and maintained with propofol. Systemic hypothermia was achieved at 28degree centigrade and cardiac arrest was achieved with cold blood cardioplegia. After completion of the surgery patients were shifted to the ICU where mechanical ventilation was waned off and extubation was done. After monitoring the central venous catheter was removed after confirmation of no evidence of cardiac disfunction and no furth er need for catecholoamian infusion. Patients were discharged from the ICU and shifted to the ward when their respiratory and haemodynamic condition was stable. Study drugs were started within one hour or shifting in ICU. This study drugs were prepared in opaque syringes by a person who is the study drugs administration patients were monitored with holter meter ECG recording. After 12 hours an additional 12 leads ECG was obtained. During the prophylaxis once artrial fibrillation was occurred treatment considered as failed.

Data was computed and analyzed with SPSS version 23. Mean and standard deviation were calculated for quantitative data like age, clamp time CPB time frequency and percentages were calculated for qualitative data like gender and efficacy. Student t test and chi square were applied to see the association among variables. P value $\leq$ 0.05 was considered as significant.

RESULTS

One hundred and thirty patients were included in this study. The patients were divided into two groups as amiodarone n=65 and NAC n=65. DM hypertension and CAD of amiodarone group was noted as n=15 (23.1%), n=33 (50.8%) and n=28 (43.1%), respectively. While, DM, hypertension and CAD of NAC groups was noted as n=13 (20%), n=31 (47.7%) and n=25 (38.5%), respectively. The differences were statistically insignificant. (Table. I).

The mean duration of ICU of amiodarone and NAC group was 117.56±2.79 hours and 125.18±2.38 hours, respectively. Significant difference was noted as (p=0.000). POAF of amiodarone and NAC group was noted as n=17 (26.2%) and n=9 (13.8%), respectively. The difference was statistically insignificant (0.079). While, mortality of amiodarone and NAC groups was occurred as n=5 (7.7%) and n=3 (4.6%), respectively. The difference was statistically insignificant (0.465). (Table. II).

Table-I

CHARACTERISTICS OF BOTH GROUPS

Variable	Amiodarone n=65	NAC n=65	P-value
DM	n=15 (23.1%)	n=13 (20%)	0.670
Hypertension	n=33 (50.8%)	n=31 (47.7%)	0.726
CAD	n=28 (43.1%)	n=25 (38.5%)	0.592

Table-II

OUTCOMES OF BOTH STUDY GROUPS

Variable	Amiodarone n=65	NAC n=65	P-value
Duration of ICU (hours)	117.56±2.79	125.18±2.38	0.000
POAF	n=17 (26.2%)	n=9 (13.8%)	0.079
Mortality	n=5 (7.7%)	n=3 (4.6%)	0.465

DISCUSSION

In our study N-acetylcysteine has less atrial fibrillation in post operative period; in comparison amiodarone has double incidence of atrial fibrillation (26.2%). Similarly mortality rate is also less in group of NAC treatment as compared to amiodarone, but this diference is not statistically significant. In contrast to literature available before duration of ICU stay is much higher in NAC group with statistically significant difference between both groups. In a study conducted by Onk OA et al11 compared amiodarone with metoprolol and reported that aiodarone is an effective drug for the treatment of post operative AF but in comparison with metoprolol both drugs are equally effective. Similarly in terms of ICU stay and hospital stay both drugs are again equally effective. In his study he used oral amiodarone but in our study we used intravenous. In another study Guarnieri T et al12 compared amiodarone with placebo and reported 35% reduction in POAF after amiodarone in open surgery as compared to placebo that reduced incidence of POAF 47% in post operative period. Liu XH et al13 conducted a study on role of NAC in prevention of POAF an reported that NAC reduced the incidence of POAF to a significant range and reduced the in hospital mortality rate. Like our study he also reported prolonged ICU stay in NAC group as compared to control group. He also recommended more studies regarding efficacy of NAC in prevention of POAF. Ozaydin M et al14 reported in 2008 that NAC is very effective in prevention of POAF. In his study he compared NAC with placebo and observed POAF in 5.2% of patients and 21.1% in placebo group. Both these studies are in favor of our study. Gu WJ et al15 conducted a study on comparison of intravenous and oral NAC and concluded that prophylactic intravenous NAC reduce the incidence of POAF to a significant range but oral NAC have poor results. Another study was conducted by White CM et al16 in 2003 on comparison of intravenous and oral amiodarone in control of POAF and concluded that both oral and intravenous amiodarone are effective. He also reported that use of amiodarone with pacing is more effective. Mitchell LB et al17 conducted a study on amiodarone prophylaxis for prevention of atrial fibrillation after cardiac surgery. He used 300 mg amidarone and concluded that lower doses of amiodarone are not effective, so in randomized trials lower doses should never be used for better results of study and exact conclusion. Wang G et al18 conducted a study on perioperative use of NAC and reported that use of NAC in perioperative period have no effects in patients of cardiac surgery. Alqahtani AA19 and Daoud EG et al20 also reported good results of amiodarone on control of POAF.

CONCLUSION

Results of our study reveal that intravenous N-acetylcysteine is more effective in prevention of post operative atrial fibrillation as compared intravenous amiodarone but post operative stay is prolonged in patients of NAC.

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