

Pre-operative N-Acetyl Cysteine for Prevention of Atrial Fibrillation After CABG Surgery in Pakistan

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ABSTRACT

Objective: To determine the effect of NAC in prevention of post-operative atrial fibrillation in patients undergoing CABG.

Study Design: Quasi experimental study.

Place and Duration of Study: Adult Cardiac Intensive Care Unit, Armed Forces Institute of Cardiology & National Institute of Heart Diseases (AFIC&NIHD) Rawalpindi during 6 months.

Methodology: 146 patients of both gender undergoing elective CABG were included in the study, having age between 30-70 years. However, any patient with history of arrhythmia including AF, thyroid dysfunction, ejection fraction less than 25%, any valvular lesion, dilated left atrium, dilated left ventricle, dilated right atrium, dilated right ventricle or having right atrial tear during surgery were excluded from the study. By using non-probability consecutive sampling, patients were divided into two groups by using envelope method. One group was given standard treatment (control group) while other group was named as NAC group (experimental group). Data analysis was performed using SPSS version-23. Descriptive statistics were reported as Mean±SD. Categorical variables were reported as frequency and percentage. Chi square test and T-test was used to determine association between different variables.

Results: A total of 146 patients with mean age 55.27±7.3 yrs. 127(87%) were male and 19(13%) were females. 28(19.2%) patients had atrial fibrillation while 11(7.5%) patients had ventricular premature contractions (VPC). There was no statistically significant difference between ages ($p=0.784$), gender ($p=0.461$), AF ($p=0.207$) and VPC ($p=0.347$). Out of 73 (50%) patients from each group; the mean age of NAC group was 55.41±7.3 yrs and of control group was 55.08±7.1 yrs ($p=0.784$). Gender wise distribution of NAC group had 8(11%) females and 65(89%) males while in control group 11(15%) females and 62(85%) were males. AF was found to be 11(15%) and 17(23.3%) in NAC and control group respectively. In NAC group, VPC was 4 (5.5%) and in control group it was 66 (90.4%).

Conclusion: This study shows that NAC decreases the frequency of post-operative atrial fibrillation and ventricular premature contractions, but the decrease is statistically insignificant in Pakistani population. However, keeping in view other beneficial effects of NAC, we would recommend more studies on this subject in Pakistani population.

Keywords: Atrial Fibrillation (AF), N-Acetyl cysteine (NAC), ventricular premature contractions (VPC).

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INTRODUCTION

Atrial fibrillation (AF) is Rapid, irregular rhythm associated with absence of p wave on ECG. AF has a higher frequency after cardiac surgery with a range of 10-65%.¹ Studies carried out in Pakistan have reported frequency of 15%.² It depends on different factors including surgery type, perioperative management, monitoring methods etc.³ AF increases the hospital stay of patients and mortality. Different studies have therefore, focused on methods to decrease frequency of atrial fibrillation so as to reduce the complications arising from post operative AF (POAF).⁴ Currently beta blockers and amiodarone are used for this purpose.⁵ However, side effects associated with these

require careful monitoring. Studies have demonstrated high levels of inflammatory cytokines and oxidative stress to be responsible for POAF.⁶

N-acetylcysteine (NAC) has antioxidant and anti-inflammatory properties, and can counter oxidative stress and inflammatory response in cardiac surgery.⁷ Studies have focused on use of NAC for prevention of POAF.⁸ Even it has been used to treat POAF.⁹ Most of other studies have focused on its intravenous use. NAC also results in decreasing frequency of post cardiac surgery reperfusion injury,¹⁰ hence adding to its benefits.

METHODOLOGY

It was a quasi-experimental study, conducted at Adult Intensive Care Unit (ITC) of Armed Forces Institute of Cardiology over a period of 06 months

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after receiving approval from Institutional Ethical review board.(IERB# 18/5/R&D/2021/106)

Sample Size: A total of 146 patients were included in this study with prevalence of 10.56% Sample size was calculated keeping confidence level at 90% and power at 80%.⁸

Inclusion Criteria: All patients, male and female, undergoing elective CABG were included in the study, having age between 30 to 70 years.

Exclusion Criteria: However, any patient with history of arrhythmia including AF, Thyroid dysfunction, ejection fraction less than 25%, any valvular lesion, dilated left atrium, dilated left ventricle, dilated right atrium, dilated right ventricle or having right atrial tear during surgery were excluded from the study.

The recruitment of patients was done using Non-Probability consecutive sampling. After inclusion of the patients in study, informed consent was obtained from them. Patients were equally divided into two groups by using envelope method. One group was given standard treatment (control group) while other group was named as NAC group (experimental group). 1.2 grams of NAC was started in divided doses, three times a day, 48 hours before surgery in NAC group. All patients received medication as recommended by hospital guidelines. Bed side monitor with 3 lead ECG continuous monitoring was used once these patients were received from operation theatre. Post operatively, medication was given using nasogastric tube.

Medication was continued for 72 hours after procedure, and monitoring was in place till that time. Serum Potassium was maintained between 4.5 and 5 mEq/L, PaO2 greater than 80 mm Hg, and PaCO2 less than 40 mm Hg in all patients. Any episode of AF was noted by Nurse in charge of patient, and Doctor in charge of ICU was notified immediately.

Statistical Analysis: Descriptive statistics were calculated with the help of SPSS-21. Descriptive stats were reported as Mean±SD. Categorical variables were reported as frequency and percentage. Chi square test was used to determine association between different variables.

RESULTS

A total of 146 patients included in the study through non probability consecutive sampling having mean age 55.27±7.3 yrs. Majority of the study population was male i.e., 127(87%) and 19(13%) were females (Figure-1).

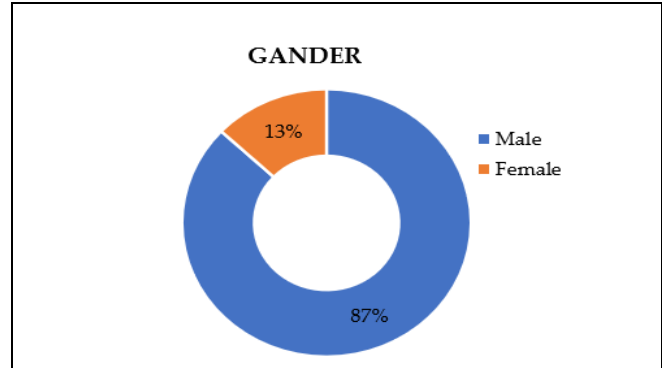


Figure-1: Genderwise Distribution of Study Participants

Patients were divided into two groups; Group-I was NAC group and Group-II was a control group by having 73(50%) patients in each group. Patients were equally divided into two groups. 28(19.2%) patients had atrial fibrillation while 11 (7.5%) patients had ventricular premature contractions (VPC) as shown in Table-I.

Table-I: Descriptive Statistics of Study Population (n=146)

Variables		Frequency	Percentages %
Gender	Female	19	13%
	Male	127	87%
Group	NAC	73	50%
	Control	73	50%
AF	Yes	28	19.2%
	No	118	80.8%
VPC	Yes	11	7.5%
	No	135	92.5%

Pearson’s chi-square test was applied to compared the both groups, there was no statistically significant difference between ages ($p=0.784$), gender ($p=0.461$), frequency of atrial fibrillation ($p=0.207$) and ventricular premature contractions (VPC) ($p=0.347$) with both of the groups as depicted in Table-II.

Table-II: Comparison of Both Groups with AF, Gender, VPC and Age

Variables		Group (n=146)		p-value
		Nac (n=73)	Control (n=73)	
AF	Yes	11(15.1%)	17(23.3%)	0.207
	No	62(84.9%)	56(76.7%)	
Gender	Female	8(11%)	11(15.1%)	0.461
	Male	65 (89%)	62(85%)	
VPC	Yes	4(5.5%)	7(9.6%)	0.347
	No	69(94.5%)	66(90.4%)	
Age in Yrs (Mean±SD)		55.41±7.3	55.08±7.1	0.784

Out of 73(50%) patients from each group; the mean age of NAC group was 55.41±7.3 yrs and of

control group was 55.08 ± 7.1 yrs ($p=0.784$). Genderwise distribution of NAC group was 8(11%) females and 65(89%) males while in control group 11(15%) females and 62(85%) were males. AF was found to be 11(15%) and 17(23.3%) in NAC and control group respectively. In NAC group, VPC was 4(5.5%) and in control group it was 66(90.4%) as shown in Figure-2 & Table-II.

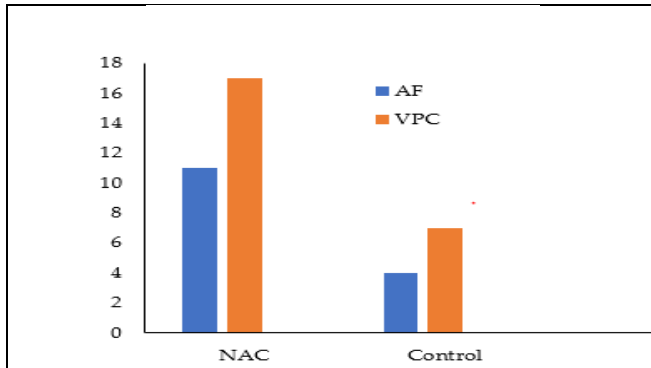


Figure-2: Comparison of AF and VPC in Both Groups

DISCUSSION

NAC has been studied for reduction of POAF a lot in other countries. Studies about its efficacy are contradictory in nature. The drug has demonstrated antioxidant and anti-inflammatory effects, which caught the attention of researchers. Orhan G,¹¹ studied the effect of NAC for myocardial ischemia-reperfusion injury and found that Tumor necrosis factor-alpha levels and creatinine kinase-MB levels were significantly less in NAC group as compared to control. Shafiei *et al.* also studied the role of NAC in reducing early post operative reperfusion injury after CABG, and concluded that it has significant effect.¹² Systematic review and meta-analysis by Sher Ali Khan and his colleagues demonstrated the potential NAC carries in reduction of reperfusion injury after CABG.¹³ Apart from these effects, NAC has shown improvement in systemic oxygenation and decreasing the frequency of acute lung injury after CABG surgery.^{14,15} Some researchers have also stated that NAC decreases the frequency of mechanical ventilation in Covid-19 patients.¹⁶ Others have pointed to the protective effects of NAC against acute kidney injury following CABG surgery.¹⁷

Regarding AF, Ozaydin and his colleagues studied the role of NAC for conversion of Post operative AF after CABG to sinus rhythm and recommended using it.⁹

However, our study differs from this study as we have studied the preventive role of NAC in Post

operative AF after CABG. We included 146 patients, and divided them into equal groups of 73. 11 patients in NAC group had POAF, whereas 17 patients in control group had POAF. Statistically speaking, the difference is insignificant. Another observation was that patients in NAC group had lower frequency of ventricular premature contractions (VPC). 4 patients in NAC group developed VPCs, whereas 7 patients in control group developed VPCs. The difference between the two groups is statistically insignificant.

Kazemi and his colleagues,¹⁸ used 1.2 G of oral NAC in 240 patients. They started giving medicine 48 hours prior to CABG and continued it for 72 hours after surgery. Though frequency of POAF was less in NAC group, the difference was not statistically significant. Also, they reported that length of stay, morbidity and mortality were similar between placebo and NAC group. Regarding the groups characteristics, Kazemi and colleagues reported that NAC group had more age, acute coronary syndrome (ACS) and hypercholesterolemia. Certain studies have shown that risk of atrial fibrillation is high in ACS and hypercholesterolemia.^{19,20} This raises the possibility that these factors may also have played their role.

El-Hamamsy and his colleagues,²¹ conducted a randomized controlled trial to study the effect of NAC in regards to different factors including 30 day mortality, MI, Low cardiac output syndrome, Supraventricular arrhythmia, ventricular arrhythmia and AF. They concluded that prophylactic NAC did not prove beneficial in regards to these factors which were studied. However, the frequency of AF was actually less in NAC group as 7 out of 50 patients developed AF, in contrast to 12 out of 50 patients in control group.

Keeping these studies in mind, meta analysis of Khan and his colleagues highlight the importance of NAC for its preventive role during coronary artery reperfusion. There was reduction in cardiac troponin, POAF, length of stay in ICU and improvement in EF.²²

LIMITATIONS OF STUDY

Small sample size was the main study restriction that can have an impact on the findings. Additionally, the lack of randomization limits the study's capacity to establish a causal relationship between an intervention and its effects.

CONCLUSION

This study shows that NAC decreases the frequency of Post-operative atrial fibrillation and ventricular premature contractions, but the decrease is statistically insignificant in Pakistani population. However, keeping in view other beneficial effects of NAC, we would recommend more studies on this subject in Pakistani population

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Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

SARAS: Manuscript writing, Concept, review, manuscript writing

SMHK: Intellectual contribution, idea, intellectual contribution

SAH: Intellectual contribution, data analysis, review

HK: Data analysis, interpretation, editing

SSN: Formatting, data management, review of articles

SKZK: Intellectual contribution, data analysis, review of articles

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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