INTRODUCTION

Cardiovascular disorders (CVD) are leading cause of morbidity and mortality. It has been predicted that CVD deaths will reach 25 million per year by 2020 globally. Aspirin has acquired the pivotal place in the primary and secondary prevention of ischemic heart disease. This study was carried out to analyze the effect of smoking on aspirin efficacy in coronary heart disease patients. Methods: In this cross sectional analytical study, 384 ischemic heart disease patients were enrolled. Light transmission Aggregometry (LTA) with arachidonic acid was utilized to assess the platelet function. Data was analyzed using SPSS-23. Chi-square test Odds Ratio were utilized to find out association of smoking with aspirin response status. Results: The study contained 272 (70.8%) male and 112 (29.2%) females with the mean age of 48.22±11.87 years. There were 199 smokers (51.82%) and 185 non-smokers (48.18%). Frequency of aspirin resistant among smokers was 41 (20.60%) whereas the frequency in non-smokers was 12 (6.50) and the difference was significant (p<0.001). The adjusted Odds Ratio was 4.44 with 95% confidence interval of 2.07–8.90. Frequency comparison of aspirin responders between males and females was non-significant both in, smokers and non-smokers (p=0.14 and 0.92 respectively). Conclusion: Cigarette smoking adversely affects the antiplatelet efficacy of aspirin irrespective of gender.

Keywords: Aspirin resistance, smoking, platelet aggregation


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antiplatelet efficacy of aspirin in ischemic heart disease patients.

MATERIAL AND METHODS

This cross-sectional analytical study was conducted from Oct 2015 to December 2016 at Pharmacology Department, Army Medical College, National University of Medical Sciences, Rawalpindi, in collaboration with Hematology Department, Armed Forces Institute of Pathology, and Armed Forces Institute of Cardiology?National Institute of Heart Diseases, Rawalpindi. The study protocol was approved by Ethical Review Committee of Centre for Research in Experimental and Applied Medicine (CREAM), Army Medical College as well as Institutional Ethical Review Board of Armed Forces Institute of Cardiology, Rawalpindi.

Sample size was calculated using WHO sample size calculator. Considering the values of alpha as 0.05, beta as 0.1, proportion of AR in smokers as 0.22 and in non-smokers as 0.13, a sample size of 373 was calculated. However, we included 384 patients in the current study. Patients from both the genders taking aspirin 75–100 mg/day for at least last 7 days, aged between 18 to 70 years, attending outpatient department or admitted were recruited by convenient sampling after written informed consent. The aspirin compliance was established on individual interview of patient. They were subsequently alienated into smoker and non-smoker groups depending upon their smoking habits, according to WHO’s 10th revision of international statistical classification of diseases and related health problems criteria of harmful use. The smoker was defined as having 5–15 pack years history of smoking (1 pack year=20 cigarette per day for 1 year). The patients concurrently using other antiplatelet or anticoagulant drugs, having any bleeding disorder or platelet count <150×10³/µl to 350×10³/µl by utilizing PPP. Platelet aggregation studies were performed on Chrono-Log Aggregometer (Chrono-log, Havertown, Pa., USA) by using Arachidonic acid (0.5 mM) as an agonist. Results were obtained in the form of graph. Platelet aggregation studies were completed within three hours of sampling.

The results were analyzed using SPSS-23. Categorical variables were presented as frequency and percentage whereas numerical variables as mean and standard deviation. Chi-square test was used to find out the association between aspirin resistance and smoking. Strength of association was measured by calculating odds ratio. Binary logistic regression was used to determine the adjusted odds ratio after controlling the effect of confounders, and p≤0.05 was considered significant.

RESULTS

Our sample population contained 272 (70.8%) males and 112 (29.2%) females with mean age of 48.22±11.87 years. There were 199 (51.82%) smokers and 185 (48.18%) non-smokers. Out of these smokers, 177 (88.94%) were male and 22 (11.05%) were female. Among non-smokers, 95 (51.35%) were male and 90 (48.64%) were female.

Table-1 is a cross tabulation between aspirin response and smoking status showing frequency of smokers and non-smokers for each category of aspirin response status. The table also shows crude and adjusted odds ratios.

Table-2 shows association of gender with aspirin response status in smokers and non-smokers separately. In both cases aspirin response is not associated with gender (p=0.14 and 0.92 respectively). This illustrates that smoking affects aspirin response independent of gender.

DISCUSSION

The outcomes of current study suggest that tobacco smoking, irrespective of gender, adversely affects the antiplatelet efficacy of aspirin and smokers are particularly at higher risk of development of aspirin non-responsiveness. Our results have reiterated the
significance of termination of smoking especially in IHD patients. Such patients may be vigilantly reviewed as aspirin may not be effectively reducing the platelets in these individuals.

Various studies have advocated that tobacco smoking enhances the platelet stimulation and aggregation. Mirkhel and colleague utilized ‘verify now’ assay and indicated the firm involvement of cigarette smoking with antiplatelet therapy resistance on the basis of multivariate analysis. Pamukcu et al also concluded that aspirin could not successfully inhibit the platelet activation caused by smoking in IHD patients. Platelet Function Analyzer (PFA) with collagen was utilized to assess platelet function in this study. The instigation and progression of cardiovascular disease is significantly influenced by cigarette smoking due to variety of its actions including enhanced oxidation of pro-atherogenic cholesterol, endothelial injury and stimulation of platelet activation and aggregation leading to procoagulant state in body.

However, some studies have concluded that there is no difference in hemostasis and platelet aggregation in smokers as well as in non-smokers. For instance, a study concluded almost similar platelet competency for hemostasis and their ability to respond to stimulating factors in regular smokers as well as in non-smokers. In the same way, another study probed the impact of smoking on platelet function and failed to show any adverse consequence of consistent smoking on platelet function among healthy volunteers.

The possible rationalization of contentious results obtained in various trials with comparable patient variables is the utilization of dissimilar method to ascertain the function of platelet. The current study may be considered superior in many aspects, most importantly the number of patients we enrolled was reasonably high and we utilized light transmission aggregometry with arachidonic acid for assessment of platelet function which is considered the gold standard method worldwide.

The most efficient way to avoid smoking induced ischemic cardiovascular events is to quit tobacco inhalation. Presently, IHD patients on antiplatelet treatment are not assessed for platelet function but selected individuals who are at greater risk of adverse ischemic attack, for instance, active smokers with recent history of stent thrombosis may be the possible contestant for platelet function assay. It has been indicated in a trial done in near past that aspirin in low doses may not effectively halt the platelet aggregation in smokers with IHD but combination of high dose aspirin (300 mg/day) and clopidogrel can efficiently inhibit platelet activity. In a research conducted on coronary heart disease patients, who were prescribed aspirin for thrombotic prophylaxis indicated a well-defined alliance between platelet over activity and tobacco inhalation. The antiplatelet efficacy of aspirin was improved either by increasing the dose from 81 mg/day to 325 mg/day or by adding up clopidogrel in the treatment. Yet another study performed on 259 elective coronary angioplasty patients revealed that clopidogrel successfully inhibited platelet aggregation in current smokers as compared to nonsmokers, these findings were contrary to the poor effects of low dose aspirin on platelet activity in smokers with coronary heart disease.

**CONCLUSION**

Cigarette smoking adversely affects the antiplatelet efficacy of aspirin irrespective of gender. Low dose aspirin, commonly used for primary and secondary prevention of IHD, may not be effective in smokers with IHD and thus explicates, to some extent, the comparatively higher mortality and morbidity in such patients. It is thus essential for IHD patients to refrain from smoking and those who do not give up, may be kept on higher aspirin dose to achieve efficient antiplatelet effects.

**REFERENCES**