



EFFECT OF ASPIRIN AND ATORVASTATIN COMBINATION FOR PRIMARY PREVENTION OF ACUTE CORONARY SYNDROME IN ELDERLY DIABETIC PATIENTS IN A TERTIARY CARE HOSPITAL WITH TRIBAL BASED POPULATION

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ABSTRACT

Aspirin is an anti Thrombotic agent that inhibits Platelets by irreversibly acetylating the serine residue of cyclooxygenase 1 in platelets with subsequently reduced level of Prothrombotic Thromboxane A2. In patient with known cardiovascular disease the potential for Aspirin to reduce further cardiovascular events. Significantly out weight the risk of major bleeding and thus Aspirin has become a mainstay in secondary prevention of CVD. However in primary prevention it's role was dubious. This is due to an unclear balance between the risk and benefit in Aspirin treated patients without a diagnosed atherosclerotic disease. Previously published meta analysis have indicated that Aspirin significantly reduces myocardial infarction and major adverse cardiovascular events without impact on stroke and CV mortality. Moreover an increased risk of major bleeding events with Aspirin strongly out weight the benefits of Aspirin Treatment in primary prevention. As a result current consensus ECG guideline does not recommend routine Aspirin Treatment without high CV risk. Similarly use of pharmacological lipid lowering intervention in individual with hypercholesterolemia and known cardiovascular disease is well established. Currently European society of cardiology guidelines recommended immediate initiation of drugs in adjunct to lifestyle intervention in these patients with high cardiovascular risk. In these clinical setting Statins are generally chosen as the first choice drug intervention in consideration of the robust evidence showing a reduction in all causes of mortality and major adverse cardiac events. In contrast primary prevention with only statin even in subset of patients with high risk of cardiovascular events are not well established. In our study we uses combination of low dose Aspirin and Atorvastatin in primary prevention of cardiovascular risk in diabetic patients in a Tribal based population.

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INTRODUCTION

Aspirin is an anti Thrombotic agent that inhibits Platelets by irreversibly acetylating the serine residue of cyclooxygenase 1 in platelets with subsequently reduced level of Prothrombotic Thromboxane A2. In patient with known cardiovascular disease the potential for Aspirin to reduce further cardiovascular events. Significantly out weight the risk of major bleeding and thus Aspirin has become a mainstay in secondary prevention of CVD. However in primary prevention it's role was dubious. This is due to an unclear balance between the risk and benefit in Aspirin treated patients without a diagnosed atherosclerotic disease. Previously published meta analysis have indicated that Aspirin significantly reduces myocardial infarction and major adverse cardiovascular events without impact on stroke and CV mortality.

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MATERIALS AND METHODS

In our study we selected elderly diabetic population (age>60 yrs) admitted in our hospital with 1st ACS events. Control population was selected from elderly diabetics without acute coronary syndrome attending at our OPD at BSMC cardiology department. The study was conducted for 20 months. For sample size calculation it was assumed that the exposure rate (ie Aspirin and statin use) in controls would be 25% with this assumption it was estimated 186 subjects (distributed as 62 cases, 124 controls) would be required to achieved 80% power at 95% confidence level for defecting a minimum odd ratio 2.5 as significant. Sample size was designed as cross sectional observational study. Following group of population were excluded from study.

1. Patients with previous history of ACS.
2. Patients with Type 1 Diabetes mellitus.
3. Patients with end stage renal disease.
4. Patients with unstable cardiovascular status, cardiogenic shock, aerodynamically significant cardiac arrhythmia.
5. Contraindication to Aspirin use.

RESULT AND ANALYSIS

60 to 80 years aged population was selected for study. Out of total 186 population group 62 was case and 124 was selected as control. Among the population 163 was in 60 to 70 years age. 23 patient population was between 70 to 80 years age. considering the use of oral hypoglycemic taking into account control group 109 population uses oral hypoglycemic agent for their control of diabetes. 15 patient population in control group did not uses OHA. In case group the figure was 50 and 12 respectively. 9% in case group and 9 patient in case group and Nineteen in control group uses insulin. In comparison total 158 patient population did not uses insulin, 53 in case and 105 in control group. out of total 186 population 63 was female and 123 was male. Ninety six patient was smoker, 90 was not smoker. When considering hypertension 177 population was hypertensive nine was non hypertensive. Out of 186 patient population 141 was dyslipidemic 44 was eulipidemic and one was non assessor. 120 patient population had history of statin use and 66 of them did not use state in for ever. 117 patient population had history of Aspirin use and 69 had not history of Aspirin use.

DISCUSSION

Categorical variables ware observed as number of patients and percentage of patients. Comparison across group was performed using Pearson's chi square Test for interdependence of attributes.

Continuous variables were evaluated as mean standard deviation. Comparison across groups was performed using unpaired t test. All the analysis was done using statistical software SPSS version 16.

An Alpha level of 5% has been taken hence P value less than 0.05 has been considered to be significant. The study was carried out with 62 type 2 DM patients suffering from 1st

attack of acute coronary syndrome and 124 T2 DM patients who did not suffer from ACS when taken as control prior exposure i/e H/O. taking Aspirin and statin was taken from both cases and control. Out of 62 patients having a ACS, 3 patients only uses Aspirin and 3 patients only statin. Out of 124 controls 6 gave history of not taking both Aspirin and statin, 4 patients only statin and 7 only Aspirin. Thus prior exposure of Aspirin and statin is statistically significant in occurrence of first exposure of a ACS. Out of 62 cases 48 patients were smoker and 14 was non-smoker. 55 patients gave history of hypertension and taking anty hypertensive. Thus smoking and hypertension are statistically significant risk factor for ACS.

As described in in earlier studies in our study we found that chest pain was the the commonest presenting symptoms of ACS.

Out of 62 cases 61 patient presented with chest pain. However other symptoms like dyspnoea, diaphoresis, loss of consciousness occurred less frequently.

Of the 62 patients who had ACS, 49 had STEMI, 4 had NSTEMI, 9 had UA.

Available data from major clinical studies suggest that there may not be a net clinical benefit in favour of routine Aspirin for the prevention of major vascular events in T2 DM patients but studies are still ongoing for determine the benefit of Aspirin and statin therapy in Diabetic patients with risk factors. Current guidelines encourages consideration of Aspirin for primary prevention of first vascular events in high-risk men and women with T2 DM.

Specifically aspirin is appropriate in Diabetic men aged more than 50 years yes and women aged more than 60 years with atleast one additional CVD risk factor who are at low for Major bleeding(I.e no history of Prior GI bleeding, peptic ulcer digit or concurrent uses of other medicine that increases bleeding risk such as Warfarin).

This criteria for the description of high risk Patients with T2 DM and therefore it is recommended that appropriately selected patients at low risk for bleeding be treated with low dose aspirin and statin for primary prevention of of events in T2 DM patients.

SUMMARY AND CONCLUSION

The study was conducted in 186 patient distributed as 62 cases and 124 control. Symptoms like chest pain, dyspnoea, diaphoresis, loss of consciousness are are associated with ACS, history e of taking aspirin and atorvastatin was taken from both cases and control. It was found that in T2 DM Patient there was a statistically significant relation between consumption of Aspirin and statin and occurrence of 1st episode of ACS.

We conclude that early treatment with Aspirin and statin in T2 DM patients provides an important benefit by bi preventing fast episode of ACS. This is in conformity with an analysis of medical treatment of conclusive patients with acute coronary syndrome of MITRA PLUS REGISTRY showed that 28% of patients with coronary artery disease risk equivalent such as diabetes received statin therapy. Data from several large registries support the disappointing implementation. Treatment guidelines in actual clinical practice, showing that we are far

away from over treatment of patients with cardiovascular disease risk. Aspirin and statins are drugs with strong evidence of their beneficial effects with a significant reduction of cardiovascular events and low rate of side effects. Therefore we conclude that a broad use of Aspirin and statin treatment in T2 DM patients is recommended to prevent 1st episode of ACS. Based on this evidence for the benefit of Aspirin as well as of Statin in primary and secondary prevention in diabetic patients and degreasing compliance with an increasing number of medications, it might be time again to discuss the concept of polypill, starting with a simple composition of drugs with standard doses. Especially in the setting of diabetes.

References

1. ETDRS Investigators. Aspirin effects on mortality and morbidity in patients with diabetes mellitus. Early Treatment Diabetic Retinopathy Study report 14. *JAMA* 1992; 268:1292–1300. [PubMed] [Google Scholar]
2. Ogawa H, Nakayama M, Morimoto T, et al Low-dose aspirin for primary prevention of atherosclerotic events in patients with type 2 diabetes: a randomized controlled trial. *JAMA* 2008; 300: 2134–2141. [PubMed] [Google Scholar]
3. Belch J, MacCuish A, Campbell I, et al The prevention of progression of arterial disease and diabetes (POPADAd) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. *BMJ* 2008; 337: a1840. [PMC free article] [PubMed] [Google Scholar]
4. Kunutsor SK, Seidu S, Khunti K. Aspirin for primary prevention of cardiovascular and all-cause mortality events in diabetes: updated meta-analysis of randomized controlled trials. *Diabet Med* 2017; 34: 316–327. [PubMed] [Google Scholar]
5. The ASCEND Study Collaborative Group. Effects of aspirin for primary prevention in persons with diabetes mellitus. *N Engl J Med* 2018; 379: 1529–1539. [PubMed] [Google Scholar]
6. McNeil JJ, Wolfe R, Woods RL, et al Effect of aspirin on cardiovascular events and bleeding in the healthy elderly. *N Engl J Med* 2018; 379: 1509–1518. [PMC free article] [PubMed] [Google Scholar]
7. Bibbins-Domingo K, U.S. Preventive Services Task Force. Aspirin use for the primary prevention of cardiovascular disease and colorectal cancer: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med* 2016; 164:836–845 [PubMed] [Google Scholar]
8. American Diabetes Association. Cardiovascular disease and risk management: standards of medical care in diabetes 2018. *Diabetes Care* 2018; 41(Suppl 1): S86–S104. [PubMed] [Google Scholar] 1. King H, Aubert RE,
9. Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. *Diabetes Care*. 1998; 21:1414–1431. doi: 10.2337/diacare.21.9.1414. [PubMed] [CrossRef] [Google Scholar] W.H. Organization. Global report on diabetes. Geneva: World Health Organization; 2016. [Google Scholar]
10. Massing MW, Foley KA, Sueta CA, Chowdhury M, Biggs DP, Alexander CM, Simpson RJ. Trends in lipid management among patients with coronary artery disease: has diabetes received the attention it deserves? *Diabetes Care*. 2003; 26:991–997. doi: 10.2337/diacare.26.4.991. [PubMed] [CrossRef] [Google Scholar]
11. Naeem F, McKay G, Fisher M. Cardiovascular outcomes trials with statins in diabetes. *Br J Diabetes*. 2018;18:7–13. doi: 10.15277/bjd.2018.161. [CrossRef] [Google Scholar]
12. Svensson E, Nielsen RB, Hasvold P, Aarskog P, Thomsen RW. Statin prescription patterns, adherence, and attainment of cholesterol treatment goals in routine clinical care: a Danish population-based study. *Clin Epidemiol*. 2015; 7:213. doi: 10.2147/CLEP.S78145. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
13. Tomkin GH. Targets for intervention in dyslipidemia in diabetes. *Diabetes Care*. 2008; 31:S241–S248. doi: 10.2337/dc08-s260. [PubMed] [CrossRef] [Google Scholar]
14. Lee VW, Ho IC, Chan WS, Tam KY, Lee KK. Statin utilization patterns for the primary prevention of cardiovascular events: a retrospective study in patients with diabetes mellitus in Hong Kong. *Am J Cardiovasc Drugs*. 2008;8:199–205. doi: 10.2165/00129784-200808030-00006. [PubMed] [CrossRef] [Google Scholar]
15. Ramos R, Comas-Cufí M, Martí-Lluch R, Balló E, Ponjoan A, Alves-Cabreros L, Blanch J, Marrugat J, Elosua R, Grau M. Statins for primary prevention of cardiovascular events and mortality in old and very old adults with and without type 2 diabetes: retrospective cohort study. *BMJ*. 2018;362:k3359. doi: 10.1136/bmj.k3359. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
16. IDF, International Diabetes Federation. Clinical practice recommendations for managing type 2 diabetes in primary care. Brussels: IDF; 2017. ISBN: 978-972-930229-930285-930220.
17. Berthold HK, Gouni-Berthold I, Böhm M, Krone W, Bestehorn KP. Patterns and predictors of statin Prescription in patients with type 2 diabetes. *Cardiovasc Diabetol*. 2009;8:25. doi: 10.1186/1475-2840-8-25. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
18. American Diabetes Association Standards of medical care in diabetes—2019. *ADA Diabetes Care J Clin Appl Res Educ*. 2019;42(Suppl 1):S90–S102. doi: 10.2337/dc19-S009. [PubMed] [CrossRef] [Google Scholar]
19. 12. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Himmelfarb CD, DePalma SM, Gidding S, Jamerson KA, Jones DW. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASP/C/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018;71:e127–e248. doi: 10.1016/j.

- jacc.2017.11.006. [PubMed] [CrossRef] [Google Scholar]
20. Lin Y-C, Yang C-C, Chen Y-J, Peng W-C, Li C-Y, Hwu C-M. Utilization of statins and aspirin among patients with diabetes and hyperlipidemia: Taiwan, 1998–2006. *J Chin Med Assoc.* 2012;75:567–572 doi: 10.1016/j.jcma. 2012.08.020. [PubMed] [CrossRef] [Google Scholar]
21. Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HAW, Livingstone SJ, Thomason MJ, Mackness MI, Charlton-Menys V, Fuller JH. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet.* 2004; 364:685–696. doi: 10. 1016/ S0140-6736(04)16895-5. [PubMed] [CrossRef] [Google Scholar]
22. Ginsberg HN. Efficacy and mechanisms of action of statins in the treatment of diabetic dyslipidemia. *J Clin Endocrinol Metab.* 2006; 91:383–392. doi: 10.1210/jc.2005-2084. [PubMed] [CrossRef] [Google Scholar]
23. Costa J, Borges M, David C, Carneiro AV. Efficacy of lipid lowering drug treatment for diabetic and non-diabetic patients: metaanalysis of randomised controlled trials. *BMJ.* 2006; 332:1115–1124. doi: 10.1136/bmj.38793.468449.AE. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

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