Use of antiplatelets and lipid lowering therapy in patients with peripheral vascular disease

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ABSTRACT

Objectives: To investigate the use of antiplatelet and lipid lowering therapy among patients undergoing peripheral vascular surgery, and to compare their use with that reported among a similar population of patients in Canada.

Methods: Chart review of a cohort of 52 patients undergoing peripheral vascular surgery. The study was carried out at King Fahad National Guard Hospital, Kingdom of Saudi Arabia in May 2000.

Results: On discharge, less than 50% of the patients received any antiplatelet or antithrombotic medication. Only 13% of the patients received lipid-lowering therapy. Those findings parallel those of Canadian publications.

Conclusion: Current literature supports the use of antiplatelet and lipid-lowering therapy among patients with peripheral vascular disease. In King Fahad Hospital, National Guard, Kingdom of Saudi Arabia, the use of those beneficial interventions is likely sub-optimal. Factors other than randomized clinical trial derived evidence likely influence practice and behavior. Whether dissemination of evidence may change such a pattern of behavior requires further study.

Keywords: Peripheral vascular disease, prevention, antiplatelet, lipid lowering therapy.

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In 1999 Anand et al.1 published a study looking at the rates of preventative practices in patients with peripheral vascular disease (PVD). We evaluated the therapy of 195 patients with a diagnosis of PVD who were hospitalized in a tertiary care hospital in Ontario, Canada between 1996 and 1998. The main reason for the admission of the patients was peripheral artery bypass surgery (88% of patients). Analysis of discharge orders for those patients revealed that 49% were discharged on any antiplatelet or antithrombotic therapy and 20% patients were treated with beta-blocker or cholesterol lowering medication 16%. Anand1 concluded that in Canada, in this population, the use of beneficial medications is sub-optimal. We will present similar data that was obtained recently in the Kingdom of Saudi Arabia (KSA), especially in the light of recent evidence of the effectiveness of antiplatelet and lipid lowering therapy, and the contemporary guidelines of practice concerning this population.

Background. Atherosclerosis is the cause of vast majority of cases of chronic PVD of lower extremities and leads to intermittent claudication, leg ulceration and gangrene. More importantly, symptomatic PVD signifies that widespread...
Atherosclerosis is likely present. Current treatment of PVD may involve medical, surgical therapies or both. A medical treatment of PVD was published in New England Journal of Medicine (NEJM) and we summarize its relevant parts: To start the author reinforced the information that patients with peripheral arterial disease, even in the absence of a history of myocardial infarction or ischemic stroke, have approximately the same relative risk of death from cardiovascular causes as do patients with a history of coronary or cerebrovascular disease, and that, the severity of peripheral arterial disease is closely associated with the risk of myocardial infarction, ischemic stroke, and death from vascular causes. The available strategies of managing such patients concentrate on risk factor modification, exercise training, rehabilitation, and pharmacologic therapy. The modified risk factors for the development of PVD include cigarette smoking, diabetes mellitus (DM), hypertension, and hyperlipidemia. Summarizing the evidence concerning lipid-lowering therapy, the current recommendation for patients with peripheral arterial disease is to achieve a serum low density lipoprotein (LDL) cholesterol concentration of less than 100mg per deciliter (2.6mmol per liter) and a serum triglyceride concentration of less than 150mg per deciliter (1.7mmol per liter). These conclusions, correspond to those of the Cochrane collaboration review, which considered 7 good quality randomized controlled trials involving a total of 698 participants. The follow-up period varied from 4 months to 3 years. Lipid-lowering therapy produced a marked although non-significant (likely due to sample size) reduction in mortality (odds ratio 0.21, 95% confidence interval (CI) 0.03 to 1.17). In 2 trials there were a significant overall reduction in the disease progression on angiogram (odds ratio 0.47, 95% CI 0.29 to 0.77). Reviewing the use of antiplatelet-drug therapy, it is known that in patients with cardiovascular disease, antiplatelet drugs reduce the risks of non fatal myocardial infarction, ischemic stroke, and death from vascular causes. These conclusions are based primarily on meta-analyses of studies of antiplatelet-drug therapy (primarily aspirin) conducted by the Antiplatelet Trialists’ Collaboration (ATC), which included 102,459 patients who had clinical evidence of cardiovascular disease (acute or prior myocardial infarction, ischemic stroke, or other vascular diseases, including peripheral arterial disease). The principal conclusion was that antiplatelet-drug therapy reduced the risk of fatal or nonfatal cardiovascular events from 11.9% in the control group to 9.5% in the treatment group. Thus, aspirin is recommended for secondary disease prevention in patients with cardiovascular disease. The analysis by the ATC included a subgroup of 3295 patients with claudication. In these patients, the risk of myocardial infarction, stroke, or death from vascular causes after a mean of 27 months of follow-up was 9.7% in patients who received antiplatelet therapy, as compared with 11.8% in control patients - a reduction of 18% (not statistically significant). In addition, aspirin may favorably affect the peripheral circulation by decreasing the need for peripheral arterial surgery (primary prevention) and by improving vascular-graft patency in patients with peripheral arterial disease who were treated with bypass surgery (with a saphenous-vein or prosthetic graft) or peripheral angioplasty. In this latter situation, there was a 43% reduction in the rate of vascular-graft occlusion: 25% in the control group as compared with 16% in the aspirin group. It appears that ticlopidine and clopidogrel are reasonable alternatives to aspirin. The data on the use of clopidogrel is derived mostly from the Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial. This trial compared 75mg of clopidogrel per day with 325mg of aspirin per day in more than 19,000 patients with recent myocardial infarction, recent ischemic stroke, or peripheral arterial disease (6452 patients). In this trial, clopidogrel was associated with an overall reduction of 8.7% in the primary end point of fatal or non fatal ischemic stroke, fatal or non fatal myocardial infarction, or death from other vascular causes (P=0.04). In the subgroup of patients with peripheral arterial disease, the primary end point of fatal or non fatal myocardial infarction, fatal or non fatal stroke, or death from other vascular causes occurred at an annual rate of 4.9% in patients taking aspirin and 3.7% in patients taking clopidogrel, and a reduction of 23.8%. This result led to Food and Drug Administration (FDA) approval of clopidogrel for the secondary prevention of atherosclerotic events in patients with atherosclerosis, including those with peripheral arterial disease. The recommendation for the uses of ticlopidine are influenced by the substantial risk of thrombocytopenia, neutropenia (which occurs in 2.3% of treated patients), and thrombotic thrombocytopenic purpura (which occurs in one in 2000 to 4000 patients), for which extensive hematologic monitoring is required.

In summary, after reviewing available evidence experts agree, that antiplatelet agents (aspirin, aspirin+dipyridamole, clopidogrel) are warranted in all patients with claudication. The Sixth ACCP Consensus Conference recommended that aspirin alone (81 to 325 mg/day) or in combination with dipyridamole should be given indefinitely since it can modify the natural history of intermittent claudication and since the patients are at high risk for future cardiovascular events. The guidelines suggest that clopidogrel may be superior to aspirin and should be considered an alternative treatment. As indicated above, it is also accepted that lipid lowering is clearly beneficial in patients with peripheral vascular disease. Taking into account the above
recommendations for the use of antiplatelet and lipid lowering therapies, we set up to investigate the pattern of drugs use in this clinical situation among patients admitted for PVD surgery in KSA. Although, the evidence supporting the routine use of beta-blocks in this population is less compelling, we investigated it to complete the comparison with the Canadian data. Our assumptions were that beta-one selective blockers do not appear to adversely effect claudication symptoms or peripheral circulation, and that coronary artery disease (CAD) is the main cause of mortality and morbidity of such patients.

Methods. The charts of 52 consecutive patients who were discharged with a diagnosis of vascular bypass of lower limb and aorta-femoral bypass between January 1998 and April 2000 from a tertiary care hospital in Riyadh, KSA, were reviewed. A standardized data collection form (age, sex, history of DM, hypertension, or cardiovascular disease, history of smoking, using beta-blocker or cholesterol lowering agent, presence of antithrombotic or antiplatelet therapy, its onset, and type of the operation), was developed and a single reviewer abstracted all the data. When applicable, we manually analyzed the data.

Results. Demographic profile and risk factors. The mean age of all patients admitted to the hospital was 53.2 years (standard deviation [SD] 13.1), and 25% (13 of 52) of patients were women. Forty percent of patients (21 of 52, 95% CI 27% to 53%) had clinically apparent coronary or cerebrovascular disease. The majority of the patients, 87% (45 of 52, 95% CI 78% to 96%) had at least one major cardiovascular disease (CVD) risk factor (diabetes, hypertension, elevated cholesterol or history of smoking). Specifically, 58% (30 of 52) were current or former cigarette smokers, 50% (26 of 52) were hypertensive-requiring treatment and 62% (32 of 52) were diabetic. Only 13% (7 of 52) of patients with peripheral vascular disease admitted for vascular bypass had neither a history of established CVD or a CVD risk factor.

Procedures in hospital. The majority of patients had either aortofemoral bypass, 54% (28 of 52) or femoropopliteal bypass 38% (20 of 52). Four other procedures were performed for each patient, axillaryfemoral bypass, iliopopliteal bypass, femorarteribial bypass, and thrombectomy. Out of 52 patients, 51 received a prosthetic graft, and one received a venous graft.

Patterns of drug use. Out of the 52 patients (46%, 95% CI 33% to 49%), 24 were discharged on antithrombotic or antiplatelet therapy and 15 out of the 52 (29%, 95% CI 17% to 41%) were on anti-platelet therapy. Of those 15 patients 6 were started on treatment on the 2nd postoperative day, 9 of 15 patients started therapy on discharge. An additional 9 patients (17%, 95% CI 7% to 27%) received warfarin. The 3 discharged patients were prescribed with aspirin and warfarin. Overall, 54% of the patients did not receiving either antiplatelet drug nor warfarin (which would in most situations invalidate the use of acetylsalicylic acid [ASA]). Among 52 patients, beta-blockers were prescribed for 10 patients (19%, 95% CI 9% to 29%) and cholesterol lowering medication for 7 patients (13%, 95% CI 4% to 22%). Those observations are similar to that obtained during the Canadian study: antiplatelet or antithrombotic treatment was used in KSA at the rate of 46%, beta-blockers at the rate of 19%, lipid lowering therapy at the rate of 13% and in Canada, antiplatelet or antithrombotic treatment was used at the rate of 49%, beta-blockers at the rate of 20%, lipid lowering therapy at the rate of 16%.

Discussion. Our data indicates a low rate of use of preventive strategies in patients with PVD, even though they are at very high risk of suffering from cardio-vascular and cerebro-vascular disorders (75% of patients with lower extremity arterial disease die of coronary or cerebrovascular event over a 15-year period). The magnitude of this risk and possibility of risk reduction through a variety of preventative strategies dictates, that this patient group, more than most, requires a comprehensive management approach, which includes both surgical revascularization where necessary and intensive CVD risk factor modification, with lifestyle changes (for example, smoking cessation, regular physical activity) and medications to, among others, control blood pressure, lower cholesterol, and provide antiplatelet action. Those should be promoted by primary care physicians and specialists alike. It is worth noticing that the pattern of use of the above interventions in our institution parallels the pattern of use in a major Canadian center producing guidelines for practice in a variety of cardio-vascular conditions. It is therefore likely that factors other than randomized clinical trial derived evidence that influence practice and behavior. Whether dissemination of evidence may change such pattern of behavior requires further study.

Study limitations. This data is based on review of charts of PVD patients hospitalized in one tertiary care hospital and are, therefore, not necessarily generalizable. Given the retrospective nature of the data collection, missing or unrecorded information in the charts could not be included. Missing data predominately affected the accuracy of the risk factor prevalence - the proportion of unrecorded data ranged from 0% for smoking history to 36% for angina history. It is also possible, that the reported frequency of medication use on discharge is an underestimate of the real use of proven medical
therapies given that some patients may only restart these medications after a certain postoperative delay (despite the lack of evidence supporting such an approach). Lastly, it is not impossible that the use of considered medications was limited by patient-specific contraindications. Our observations did not deal with other aspects of the management of the patients with PVD, including tight control of glucose among diabetics, and the use of angiotensin converting enzyme inhibitors (HOPE trial).

In conclusion, the current literature supports the use of antiplatelet and lipid-lowering therapy among patients with peripheral vascular disease. Beta-blockers are not contraindicated and, taking into account high prevalence and high future risk of CVD in this population may be in fact of major benefit. In our institution, the use of those beneficial interventions is likely sub-optimal. Health professionals need to be aware of the high risk nature of this population and develop strategies to ensure that care is optimal.

References