A STUDY ON THE EFFECT OF CLINICAL PHARMACIST PROVIDED PATIENT COUNSELLING ON THE GLYCEMIC CONTROL OF PATIENTS UNDERTAKING CORONARY ARTERY BYPASS GRAFT SURGERY OR PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY.

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ABSTRACT

Introduction:- Diabetes Mellitus is an established risk factor for coronary artery disease which leads the patient to undertake a Coronary Artery Bypass Graft Surgery or Percutaneous Transluminal Coronary Angioplasty. The patients who have DM have higher chance of re-occlusion. Controlling the glycemic levels lessen the chance of re-occlusion. A counselling programme provided by a clinical pharmacist could have greater impact in controlling the glycemic levels of post-operative patients. Materials And Methods:- 90 patients were recruited to the study. 60 belongs to the intervention and 30 belongs to the control group. The Fasting Blood Sugar values of the patients were recorded. The values before and after intervention were compared and analysed with control group. Results:- the patients included in the intervention group was found to have statistically significant glycemic control than the patients included in the control group.

KEYWORDS: Coronary Artery Bypass Grafting, Percutaneous Trans-luminal Coronary Angioplasty, Diabetes Mellitus, Patient Counselling, Ischemic Heart Disease, re-occlusion.
INTRODUCTION

Coronary Artery Bypass Graft (CABG) and Percutaneous Trans-luminal Coronary Angioplasty (PTCA) are coronary revascularising methods. The decision of CABG or PTCA for revascularization is based on the extent of Ischaemic Heart Disease (IHD) and ventricular functions of the heart. PTCA involves the insertion of a guide wire and inflatable balloon into the affected coronary artery and enlarging the lumen of the artery by stretching the vessel wall. CABG involves the bypass replacement of coronary arteries with saphenous artery or mammary artery. Diabetes Mellitus has been associated with development of cardiovascular diseases. From the Bypass Angioplasty Revascularisation Investigation (BARI) study, the incidence of diabetes ranges from 12-38% in CABG patients and is a strong predictor of risk of death and mediastinitis. Renal failure and Peripheral Vascular Disease (PVD) which are diabetic co-morbidities have also been associated with increased short term morbidity and mortality with CABG surgery and also have a significant impact on both the annual incidence of death and long term survival. Survival among diabetic subjects was significantly worse than among non-diabetic subjects. Annual incidence of death among diabetic subject was 5.5 deaths per 100 persons.\textsuperscript{[1]}

Weintraub et al. demonstrated that diabetic patients with multi-vessel coronary artery disease treated with angioplasty have a markedly worse clinical outcome than non-diabetic patients.\textsuperscript{[2]} There are a number of mechanisms able to explain the higher restenosis and occlusion rate in diabetic patients. Diabetics have a number of hematological abnormalities that can predispose them for an enhanced risk of vascular thrombosis. Spontaneous and induced platelet aggregation is increased, platelet synthesis of thromboxane A2 is enhanced and platelet activation (platelet factor 4 and b-thromboglobulin) can be elevated.\textsuperscript{[3,4]} In addition, a relatively greater coagulation activity may be present in diabetic patients.\textsuperscript{[5]} Pro-coagulant factors, (fibrinogen, factor VII, and von Willebrand factor) may be increased in diabetics. Mechanisms involved in reducing intravascular clotting may also be impaired. Synthesis of prostacyclin is reduced, and fibrinolysis may be attenuated because of increases in plasminogen activator inhibitor type 1.\textsuperscript{[4,6]} In addition, a number of functional abnormalities of the vascular endothelium are associated with diabetes mellitus that may further pronounce the propensity to vasospasm and coronary thrombosis. Hyperglycemia directly causes endothelial dysfunction by decreasing the production of endothelium-derived relaxing factor, increasing oxidative stress by vascular protein glycation and free radical formation, and decreasing prostacyclin production.\textsuperscript{[7,10]} Also, lipoprotein abnormalities may impair
endothelium-dependent relaxation; moreover, a greater growth factor stimulation occurs in diabetics.\cite{8,11-13} All these mechanisms may also lead to a pronounced intimal hyperplasia, the main mechanism of restenosis in diabetic patients.\cite{14}

Clinical pharmacy is the practice of pharmacy as part of a multidisciplinary healthcare team directed at achieving quality use of medicines. One of the integral roles of a clinical pharmacist is patient counselling. It refers to the process of providing information, advice and assistance to help patients use their medications appropriately. The information and advice is given by the pharmacist directly to the patient or the patient representative. It may also include information about the patient’s illness or recommended life style changes. The information is usually given verbally but may be supplemented with written materials. During counselling, the pharmacist should assess the patient’s understanding about his or her illness and its treatment and provide individualized advice.

In this study we are analyzing the effect of patient counselling provided by a clinical pharmacist in glycemic level of patients, who underwent coronary revascularising procedures.

**MATERIALS AND METHODS**

A prospective, well controlled interventional study was conducted in cardiology department of 500 bedded in a tertiary care teaching hospital. The study was carried out after getting approval from Institutional Ethical Committee (IEC). The patients who were admitted in the hospital for elective CABG or PTCA were selected and from those patients who satisfy inclusion as well as exclusion criteria were recruited after explaining the study and obtained signed consent form. The inclusion criteria were such that the patients must be above 18 years of age who is going to undertake elective CABG or PTCA with Diabetes Mellitus (DM) as co-morbid condition. For the study 90 patients were enrolled. The 90 patients were kept in two groups by stratified randomization techniques i.e. 60 in interventional group and 30 in control group. The control and intervention patient’s demographical details, past medical and medication history, social habits, family history, laboratory investigations, medication order review were collected. The intervention group patients were counselled for the management of their diabetes on various aspects like lifestyle modification, diet and their management. The counselling points which were included in the programme are given in Table 1. They were also asked to come for the follow up after one week of the surgery. After one week (first follow up) the Fasting Blood Sugar (FBS) value of patient were
collected. The intervention group was counselled and also provided with patient information leaflet. After one month (second follow up) their second review was taken and review medicines were noted. Intervention was made after obtaining FBS values. The obtained data was recorded and subjected for suitable statistical analysis.

Two–tailed statistical analysis were done using graph pad prism version 6, software package. For comparing control and interventional group we used unpaired t-test and for comparing before and after by paired t-test. Descriptive statistics are given as means and standard deviation.

**Table 1:** Counselling points which were included in the counselling session.

<table>
<thead>
<tr>
<th>Counselling points</th>
<th>Procedure complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG &amp; PTCA</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>regarding the disease</td>
</tr>
<tr>
<td>Hypoglycemia &amp; hyperglycemia</td>
<td>signs &amp; symptoms how to tackle</td>
</tr>
<tr>
<td>Insulin &amp; OHA</td>
<td>dosage and frequency administration techniques.</td>
</tr>
</tbody>
</table>

**RESULTS AND DISCUSSION**

**Evaluation of Glycemic Control**

**Table no: 2 The Mean Fasting Blood Sugar (FBS) Values of Diabetic Patients.**

<table>
<thead>
<tr>
<th>FBS values</th>
<th>Base line (mg/dL)</th>
<th>1st follow-up (mg/dL)</th>
<th>2nd follow-up (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>158.03±35.24</td>
<td>156.40±29.33</td>
<td>171.40±32.56</td>
</tr>
<tr>
<td>Intervention</td>
<td>156.50±42.50</td>
<td>145.53±39.56</td>
<td>126.97±32.06</td>
</tr>
<tr>
<td>P-value</td>
<td>0.1865</td>
<td>0.1866</td>
<td>&lt;0.0001 (significant)</td>
</tr>
</tbody>
</table>

The comparison of the FBS values of the intervention group between various follow ups are given below:

- **Base line vs. 1st follow-up:** $p<0.0001$ significant.
- **Base line vs. 2nd follow up:** $p<0.0001$ significant.
- **1st follow-up vs. 2nd follow-up:** $p<0.0056$ significant.

There is a significant difference in the glycemic control values of the patients in intervention and control group when compared using un-paired t-test. Also there is significant
improvement in intervention group after each follow-up when their mean FBS values were compared using paired t-test.

DM is an established risk factor for the development of coronary artery disease. Epidemiologic data from the Framingham study have shown that diabetes is a major independent risk factor for cardiovascular disease even after adjusting for other confounding risk factors such as age, HTN, hypercholesterolemia, and tobacco abuse.\cite{15} Compared with patients without diabetes, diabetes patients have increased predisposition for accelerated atherosclerosis. Diabetic patients have a higher incidence of two- and three-vessel disease and a lower incidence of one-vessel disease than do non-diabetic patients. Therefore, diabetic patients constitute an important segment of the population undergoing surgical coronary revascularisation. Due to hyperglycemia, insulin resistance and oxidative stress, inflammatory processes commences; leading to an atherosclerotic thrombus formation which evolves as a coronary artery disease.

In our study there were 90 patients who were suffering from DM of which 60 patients belonged to the intervention group and 30 patients belonged to the control group. From the study, after the patient counselling provided by the pharmacist the patients who were in the intervention group have statistically significant glycemic control than those patients in the control group. The glycemic control is essential to maintain the bypass graft as well as the stent intact after the intervention procedure. The increased sugar level in the blood could cause increased viscosity of the blood thus affecting the blood rheology, by increasing the viscosity, leading to the re-occlusion after the coronary intervention procedures.\cite{16} It has effect in a short term as well as long term basis. In studies, it has seen that if the proper glycemic control is not maintained the anti-platelet effects of Aspirin and Clopidogrel could not give its desired effect which also points out the importance of maintaining proper glycemic control.\cite{17}

Clinically, dyslipidemia is highly correlated with atherosclerosis and up to 97\% of patients with diabetes are dyslipidemic with a pattern of increased triglycerides and decreased HDL cholesterol in the plasma. In our study 44.44\% of the patients were dyslipidemic. In diabetes, the predominant form of lipid is LDL, which is more atherogenic because they can more easily penetrate and form stronger attachments to the arterial wall, and they are more susceptible to oxidation. Oxidized LDL is pro-atherogenic because once the particles become oxidized they acquire new properties that are recognized by the immune system as “foreign”.
Thus, oxidized LDL produces several abnormal biological responses such as attracting leukocytes to the intima of the vessel, improving the ability of the leukocytes to ingest lipids and differentiate into foam cells and stimulating the proliferation of leukocytes, endothelial cells and smooth muscle cells, all of which are steps in the formation of atherosclerotic plaque.

In patients with diabetes, LDL particles can also become glycated, in a process similar to the glycation of the protein hemoglobin (measured in the hemoglobin A1c [A1C] assay). Glycation of LDL lengthens its half-life and therefore increases the ability of the LDL to promote atherogenesis. Paradoxically, however, glycation of HDL shortens its half-life and renders it less protective against atherosclerosis.\[18,30\]

Besides DLP, endothelial dysfunction also often contributes. Healthy endothelium regulates blood vessel tone, platelet activation, leukocyte adhesion, thrombogenesis, and inflammation. The net effect of healthy endothelium is vasodilatory, anti-atherogenic and anti-inflammatory. When these mechanisms are defective, the process of atherosclerosis is accelerated. Therefore, both insulin deficiency and insulin resistance promote dyslipidemia accompanied by increased oxidation, glycosylation and triglyceride enrichment of lipoproteins. Plasma levels of oxidation free radicals are higher in subjects with type 2 diabetes compared to non-diabetic subjects and these levels are inversely correlated with the degree of glycemic control. In addition, endothelial dysfunction is present and all of these factors contribute to the increase in atherogenicity and thus macrovascular disease, found in patients with diabetes.\[31,34\]

In addition to the above, patients with diabetes have been found to have decreased bioavailability of NO, a potent vasodilator, as well as increased secretion of the vasoconstrictor endothelin-1. This resulting state of vasoconstriction has been found in subjects with the metabolic syndrome as well as those with diabetes. In this situation, the vasculature is in a hyper-constricted state. Not only do hypertension and its concomitant complications result from vasoconstriction, but blood flow is limited to respective tissues. Diabetes decreases NO bioavailability because of either insulin deficiency or defective insulin signaling (insulin resistance) in endothelial cells. Hyperglycemia also acutely inhibits the production of NO in arterial endothelial cells.\[35\]
Diabetes is also related to a hypercoagulable state. The coagulability of the blood is crucially important in ischemic cardiovascular events because the majority of Myocardial Infarction (MI) and stroke events are caused by the rupture of atherosclerotic plaque and the resulting occlusion of a major artery by a blood clot (thrombus). Up to 80% of patients with diabetes die a thrombotic death. Seventy-five percent of these deaths are the result of an MI and the remainder is the result of cerebro-vascular events and complications related to PVD. The first defense against a thrombotic event is the vascular endothelium. Diabetes contributes to widespread endothelial dysfunction. The endothelium and the components of the blood are intricately linked, such that clotting signals initiated in the endothelial cell can activate platelets and other blood components and vice versa. Patients with diabetes exhibit enhanced activation of platelets and clotting factors in the blood. Coagulation activation markers such as prothrombin activation fragment 1+2 and thrombin–anti-thrombin complexes are also elevated in diabetes. In addition, patients with diabetes have elevated levels of many clotting factors including fibrinogen, factor VII, factor VIII, factor XI, factor XII, kallikrein and von Willebrand factor. Conversely, anticoagulant mechanisms are diminished in diabetes. The fibrinolytic system, the primary means of removing clots, is relatively inhibited in diabetes because of abnormal clot structures that are more resistant to degradation and also because of an increase in PAI-1. Clinicians attempt to reverse this hypercoagulable state with aspirin therapy, widely recommended for use as primary prevention against thrombotic events in patients with diabetes. However, numerous studies have suggested that aspirin in recommended doses does not adequately inhibit platelet activity in patients with diabetes causing an “aspirin resistance”.[36,37]

The pharmacist oriented patient counselling motivated the patients to regulate their glycemic levels through pharmacological and non-pharmacological methods. Thus the patients who underwent the counselling session had a greater glycemic control than other.

CONCLUSION
The present study was performed to get a comprehensive overview of the impact of pharmacist in improving the glycemic control of CABG and PTCA patients. Managing the diabetes reduces the chances of re-occlusion thereby the quality of life can be improved. Improvement in patients QOL, level of care and management of diabetes justify the need for active collaboration between clinical pharmacist and physicians in the management of CAD patients who underwent coronary revascularising procedures such as CABG and PTCA.
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BIBLIOGRAPHY


24. (cross reference) Rosenson RS: Clinical role of LDL and HDL subclasses and


