Clinical outcomes

7. Clinical Outcomes

Clinical outcomes can be identified as, Major adverse cardiac event (MACE) – includes, death from any cause – either cardiac or non cardiac, non fatal MI, Coronary Artery Bypass Grafting (CABG), target vessel revascularization (TVR), stent thrombosis, stroke and intracranial bleeding.

7.1 Major adverse cardiac events

In the present study, Death from cardiac problem was observed in one patient in Intervention Group (IG) and two patients in Control Group (CG). One patient underwent CABG in IG due to progression into triple vessel disease and one patient in CG underwent CABG due to in-stent Re-stenosis. One Patient in each group had chest pain due to in stent re-stenosis and advised PCI. Hospital readmissions due to non cardiac problems are – Inguinal hernia was documented in IG and weakness and fatigability, Iron deficiency anemia, and road traffic accident was documented in CG.

A study comprising of 1000 consecutive patients who underwent PCI procedure and followed up to 10 years, a total of 67 (6.7%) patients died, 60 patients (6%) had MI, 8% of patients underwent CABG and 171 (17%) had repeat angioplasty. Non-diabetic patients had better survival rates (95%) in five years was reported (1).

ASCERT registry found higher mortality rate with PCI patients aged above 65 years and advantages scores over in CABG group of patients (2).

In the ERACI III registry, increased incidence of death and MI was reported with DES group, when compared with BMS or CABG group and these difference were significant even at 5 years of follow up (3). SYNTAX trial data highlights the similar incidence of death, MI and composite of death/MI and CVA between PCI and CABG at 1 year of follow up. At fourth year, MACE has higher incidences in PCI group of patients (4).
The researchers had concluded that, Men had higher risks of cardiac death (3.7% v/s 1.6%) and MACE (8.4% v/s 4.7%) at five years when they compared with women. It was also noted that, non fatal MI and TLR were similar between Men and Women (5).

Part and co-workers conducted the study, which evaluated the long term outcomes of PCI and CABG in diabetic and non diabetic patient pool. After the 2 years of follow up, death by either cardiac or non cardiac reason is 12.6% and 16.5%, composite outcome as 14.9% and 19.9% and repeat revascularization was 19% and 4.6% in PCI and CABG group respectively, in Diabetic population. Whereas, in non diabetic population, death-8.1% and 10.4%, composite outcome – 10.1% and 13.6% and repeat revascularization was 16.6% and 5.4% in PCI and CABG group respectively (6).

In a 5 year follow up study (7), multicenter registry of 4338 CAD patients has concluded that, MACEs of PCI group (41.8%) and CABG group (29.2%) which is significant(p<0.001). The odds ratio for mortality comparing CABG to PCI was 0.69, whereas odds ratio for any MACE was 0.58 (p<0.001).

In a study conducted at Poland, researchers evaluated the BMS and DES in STEMI patients for their clinical outcomes. Mortality rate in DES group (8.9%) was observed v/s BMS group (15.5%). Lower incidences of both death and MI were observed in PCI group (9.5% v/s 16%). Combined endpoint of death, MI and TVR (19.3% v/s 31.3%, p<0.001) was recorded in favour of DES (8).

In the recently published New England Journal of Medicine, Armstrong and his co-workers (9) evaluated the clinical outcomes in STEMI patients after fibrinolysis or primary PCI. Composite of death from any cause, shock, congestive heart failure or MI are occurred in 12.4% patients in fibrinolysis group (relative risk 0.86;95% confidence interval, p=0.21) and 14.3% in primary PCI group. More intracranial haemorrhages occurred in fibrinolysis group (1%) compared with PCI group (0.2%).
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The study presented the data from Zwolle-6 trial emphasized the co-morbid condition of diabetes mellitus and compared the results between PCI v/s Balloon angioplasty. After One year of the follow up, Death occurs in 10.7% patients of stent group, whereas, 9.2% patients in balloon angioplasty group. Death and or repeat MI was 14.3% and 11.8% for stent and balloon angioplasty group respectively. 21.4% and 18.4% patients had TVR in stenting and balloon angioplasty group respectively (10).

7.2 Lipid profile

NCEP adult treatment plan III guidelines (11) suggests that, LDL values should not be more than 130 mg/dl, Total cholesterol values are less than 200 mg/dl and HDL values are between 40 to 60 mg/dl.

We have evaluated lipid profile of the participants at baseline and at 12 months of follow up and represented in table 14 and 15. Total Cholesterol at baseline in CG was 200.31±39.36 mg/dl which was reduced to 183.35 ± 38.66 mg/dl with the paired mean difference of 16.95 mg/dl (p<0.001). Similarly, HDL values were 36.46 ± 8.55 mg/dl at baseline and was improved to 41.09 ± 8.49 mg/dl with the paired mean difference of -4.62 mg/dl(p<0.001). LDL values were reduced from 135.07 ± 33.97 mg/dl to 121.07 ± 34.93 mg/dl with the paired mean difference of 14 mg/dl (p<0.001). However, Triglycerides values are lowered from 142.78 ± 57.92 mg/dl to 139.70 ± 47.40 mg/dl with the paired mean difference of 3.08 mg/dl, which is not significant (p=0.48).

Lipid profile values in IG showed prominent changes in all the parameters. Total Cholesterol values at baseline were 213.42 ± 53.08 mg/dl, which declined into 176.49 ± 39.93 mg/dl with the paired mean difference of 36.93 mg/dl (p<0.001). Similarly, HDL values at baseline were, 36.78 ± 8.78 mg/dl improved to 42.85 ± 6.43 mg/dl with the paired mean difference of -6.14 mg/dl (p<0.001). LDL values at baseline were 143.08 ± 47.47 mg/dl were decreased to 118.65 ± 38.08 mg/dl with the paired mean difference of
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24.43 mg/dl (p<0.001). Triglycerides values at baseline was, 160.05 ± 57.82 mg/dl declined to 138.60 ± 47.23 mg/dl with the paired mean difference of 21.46 mg/dl (p<0.001).

The point of interest in the lipid profile analysis of both the groups is, Change in mean differences of both the groups. Mean difference of Total Cholesterol in IG, 36.93 is higher than 16.95 of CG. Mean differences of HDL value in IG and CG are -6.14 and -4.62 respectively. Paired mean differences of LDL value in IG and CG are 24.43 and 14 respectively. Paired mean differences of Triglycerides values in IG and CG are 21.46 and 3.08 respectively.

Hence, we can conclude that, even the changes were occurred at CG which is due to drugs, which the participants were consumed. However, the changes were more prominent in IG, which is due to along with drugs; pharmaceutical care was provided by RP.

In a RCT (12), where pharmaceutical care was provided to IG for the patients of dyslipidemia patients, the change in total cholesterol values (17.7 mg/dl) are significant when compared to CG (7.4 mg/dl) and change in LDL values in IG (23.4 mg/dl) was significantly higher compared to CG (12.8 mg/dl). This emphasizes the role of pharmaceutical care in dyslipidemia patients.

In a study similar to our study, where 30 patients were provided the pharmaceutical care after cardiac surgery found that, lipid profile results were achieved the significant (p<0.05) at 2 years of follow up (13).

In a study conducted by Lee and co-workers found that, PC for the elderly patients had no significant changes in LDL values between IG and CG (14).

In a RCT involving dyslipidemia patients of Hong Kong (15), where clinical pharmacist services were provided to IG showed that, 58.7% patients the goals of LDL values as per
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the ATP III guidelines compared to 45.3% patients in CG. Reduction in the LDL, Total Cholesterol and Triglyceride values were significant compared to CG (p<0.05%). In another study done at Hong Kong (16), LDL values (2.80 mmol/L v/s 3.24 mmol/L) were reduced significantly in IG compared to CG; Total cholesterol values (4.75 mmol/L v/s 5.18 mmol/L) were also reduced significantly (p=0.0015).

In a meta analysis, which analyzed the pharmaceutical care in the management of CVD risk factors emphasize that, pharmaceutical care was responsible for reduction in the Total Cholesterol values by 17.4 mg/dL, LDL reduction by 13.4 mg/dL when compared to usual care group (17).

In a systematic review done by Charrois et al., which evaluated the pharmaceutical care of dyslipidemia patients in 21 studies reveals that, mean LDL levels were 10.7 mg/dl lower when compared to standard care group and mean TC levels are significantly lower than usual standard care groups (18).

Our present study also shows that, in IG - mean Total Cholesterol values were 19.98 mg/dl lesser than CG, mean HDL values were 1.52 mg/dl greater than CG and mean LDL values were 10.43 mg/dl lesser than CG. This signifies that, our study yielded the similar results in the management of dyslipidemia across the globe.

7.3 Fasting blood sugar

We have evaluated the Fasting Blood Sugar (FBS) values of the Diabetes Mellitus patients in both the groups. In the CG, mean FBS values are 187.09 ± 54.61 mg/dl and 154.51 ± 38.73 mg/dl at baseline and at 12 months respectively with the paired mean differences of 32.57 mg/dl (p<0.05). In the IG, mean FBS values are 175.64 ± 49.41 mg/dl and 132.80 ± 20.28 mg/dl at baseline and at 12 months respectively with the paired mean difference of 42.83 mg/dl (p<0.001).
In the IG, where pharmaceutical care was provided for the participants, had shown the significant amount of reduction 10.26 mg/dl in the FBS values were observed compared to CG. These results were tabulated in table 17 and represented graphically in figure 18.

In a RCT involving diabetes patients in Jordan (19), Pharmaceutical care provided to the patients in IG had achieved the better fasting blood glucose levels (-2.3 millimoles/L) comparatively to CG patients (+0.9 millimoles/L), who received the standard care.

In a study conducted at UK (20), IG patients provided with pharmaceutical care compared with standard care in CG had revealed that, significant reductions were observed in FBS values from 8.80 to 6.88 millimoles/L in IG, where as it was reduced from 9.53 to 9.04 millimoles/L in CG. BMI of the participants in IG reduced from 30.84 to 26.98 kg/m², compared to 29.82 to 28.73 kg/m² in CG. A significant reduction was seen in lipid profile was also evident for the participants in IG.

A positive result was obtained in the study conducted at UAE (21), mean FBS values are decreased from 10.8 to 7.8 millimoles/liter in IG, where as it decreased from 10.3 to 9.5 millimoles/liter in CG.

7.4 Drug related problems

RP identified and resolved drug related problems in the intervention group of patients. 135 drug related problems were identified which were of drug–drug interactions (104) major category. Clopidogrel and Pantaprazole were given in discharge prescription, which was resolved by counselling the patient to take pantaprazole in the early morning in empty stomach and to take Clopidogrel after breakfast with a time gap of 2 hours.

Other discrepancies like, dose adjustments (15) were done with the consultation with cardiologist. During the discharge prescription- missing of adding diabetic drug (9), beta blocker (4) and ACE inhibitor (3).
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RP identified 12 cases of Amlodipine induced pedal edema in the IG patients and reported to cardiologist, prompted to change into Cilindipine which is successfully reduces the edema. This initiation by RP has led to research on this parameter and resulted in a publication in North American Journal of Medical Sciences.

7.5 Body mass index

We calculated Body Mass Index (BMI) of the participants at baseline and at 12 months for both the groups. These results were tabulated in table 18 and represented graphically in figure 19. In the CG, mean BMI was 23.69 ± 3.87 kg/m² at Baseline and 24.17 ± 3.87kg/m² at 12 months follow up was recorded with the paired mean difference of -0.486 kg/m². This indicates that, BMI has increased in the CG. In the IG, mean BMI was 24.94 ± 3.63 kg/m² at baseline and 22.84 kg/m² at 12 months with the paired mean difference of 2.10 kg/m². It signifies that, pharmaceutical care provided by RP has shown reduction in the BMI which is very much essential parameter of the clinical outcome.

7.6 Pill count score

We calculated the pill count score at first follow up and also at 2nd, 3rd and 4th follow ups i.e. at 12 months. Pill count score > 80% of their prescribed dose was considered as adherent to the therapy. The results were tabulated in table 16 and depicted in the figure 17. At first follow up, mean pill count score for CG was 72.08 ± 6.28% and 89.04 ± 7.20% in IG. It is quite interesting to know that, at 2nd follow up- there is a increasing trend of medication adherence in-terms of pill count score in CG , where as there is a decline in the pill count score in the IG. However, this trend is not observed during further follow up. It was worthy to observe that, after 6 months of the therapy, medication adherence is almost stabilized which is evident by pill count score. At the end of study period, mean pill count scores were 73.03 ± 5.32% and 85.09 ± 4.75% for CG and IG respectively. At the end of study period, 6 participants (6.25% of CG population)
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were adherent to medications in CG compared to 95 participants (93% of IG population) in IG. Upon performing chi square test; it was found statistically significant (p<0.001). On performing repeated measures ANOVA test, we found that there is a significant difference between the IG and CG favouring the participants in IG are more adherent to the therapy (p<0.001) throughout the study period.

In a RCT conducted by Lee (14) and colleagues, pharmaceutical care program had improved medication adherence increased to 96% population in the IG compared to 69% in CG, which is highly significant(p<0.001) and is associated with significant reductions in the systolic BP.

In a RCT conducted at Denmark involving the elderly patients with poly pharmacy, PC was provided to IG at home compared to standard care as CG. Patients were similarly non adherent at 11% and 10% for IG and CG respectively (22).

In a non blinded RCT study conducted by Silveiera (23) et al, 79.8% patients were adherent in IG group compared to 73.8% in CG resulting in 50.3% had undetectable plasma viral load compared to 49.8% in IG and CG patients respectively. This study concluded that, Pharmaceutical care was not associated with the medication adherence to anti retroviral drugs in Brazil. In a similar study, 89% of the IG patients were adherent to medicines compared to 81% of CG (p=0.003). Clinical outcomes measured by CD4+ cell count statistically confirm the impact of PC (24).

In a study conducted at Belgium, where older patients with chronic diseases were provided pharmaceutical care by community pharmacists. Medication adherence was very high (98.1%) which is signifying the effect of PC (25).

In a study involving diabetes patients of Iran, non-adherence to metformin and glyburide were 39.7% and 35.3% for IG and CG respectively. It was concluded that, as medication adherence improves, lower glycated haemoglobin values were observed in the study.
population (26). In a similar study, pill count was improved (+6.8 % v/s -2.8%) in the IG and resulting in the reduction of total cholesterol and LDL values (p<0.001) emphasizing the impact of pharmaceutical care (27).

In a systematic review of RCT concludes that, simplifying the dosage regimen increases the adherence rates from 8% to 19.6% across the studies of interest. Complex interventions like pharmaceutical care increased the adherence rates up to 41% in the study population (28).

**7.7 Conclusion**

In the present study, as the medication adherence increases in the IG, it also decreases the Total cholesterol level, LDL level and Triglyceride levels and increases the HDL level. Fasting blood sugar levels are reduced in the study population. Body mass Index also decreased significantly (p<0.001) in the IG study population compared to CG. Major adverse cardiac events and hospital re-admission rates were similar in both the groups which are not significant between the groups.

Hence, we can conclude that, pharmaceutical care provides the holistic approach to manage the lipid profile, fasting blood sugar and body mass index which is highly significant in the patients who underwent angioplasty procedure.
7.8 References:


4. Serruys PW. The Syntax Trial at 4 years. 2011 Annual EACTS Meeting; Lisbon, Portugal


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