

Drug-Drug Eluting Stents Interactions (DDESI) after Percutaneous Coronary Intervention (PCI) in Coronary Artery Disease (CAD) Patients: A Multicenter Cross-Sectional Observational Study

ABSTRACT

Aims: This study was aimed to evaluate the interactions of commonly used drug eluting stents (DES) along with prescribed medications in coronary artery disease (CAD) patients those underwent percutaneous coronary intervention (PCI).

Study design: Retro-prospective, Multicenter, Cross-sectional Observational study.

Methodology: A total of 127 CAD patients those successfully underwent percutaneous coronary intervention with different DES were enrolled in this study. The study population were divided into 3 groups; i) Patients intervened with Sirolimus DES (n=52), ii) Everolimus DES (n=46) and iii) Zotarolimus DES (n=29) respectively. The patients case report and drug chart were reviewed periodically up to one year regular follow-up period and retro-prospectively analysed. Results were statistically analysed using Graph Pad Prism software version 7.01 to determine the statistical difference between each study groups. $P < 0.05$ was considered as significant. Baseline clinical characteristics, angiographic and procedural characteristics, mostly prescribed medications and the new medical terminology Drug-Drug Eluting Stents Interactions abbreviated as DDESI or DDES Interactions were compared.

Results: Out of 127 total populations, patients intervened with Sirolimus DES reported less (0.85%) DDES interactions compared to Everolimus DES (2.54%) and Zotarolimus DES (1.69%) DDESI. Drugs such as Aspirin, Atorvastatin and Clopidogrel were found to be mostly prescribed drugs to maximize benefits and minimize the complications in patients those underwent percutaneous coronary intervention with different DES.

Conclusion: According to the obtained patients data it is concluded that Sirolimus DES was found to be more suitable and safe when compared to Everolimus DES and Zotarolimus DES after the one year regular follow-up period in the South-Indian CAD patients after PCI.

Keywords: Coronary artery disease; Drug eluting stents; Sirolimus; Everolimus; Zotarolimus; Percutaneous coronary intervention; Drug interactions; DDES interactions; DDESI.

1. INTRODUCTION

Coronary artery disease (CAD) has been remaining the first killer and the major cause of public health problems in the world [1]. Coronary artery disease also called as coronary heart disease (CHD), coronary atherosclerosis or Ischemic heart disease (IHD), which is a branch of coronary vascular disease and a common form of heart disease. And, it is considered as insidious and dangerous disease in the world [2]. Coronary artery disease is the narrowing or blockage of the coronary arteries, usually caused by atherosclerosis. Cardiovascular diseases (CVDs) are the number one cause of death globally, more people

die annually from CVDs than from any other cause. An estimated 17.9 million people died from CVDs in 2016, representing 31% of all global deaths. Of these deaths, 85% are due to heart attack and stroke [3]. According to a WHO report in 2014, the age-adjusted cardiovascular disease mortality rates in India were 349 and 265 per 100 000 in men and women, respectively. These rates are more than two to three times higher than in USA (170 and 108 per 100 000 in men and women, respectively) [4]. It may affect individuals at any age but becomes dramatically more common at progressively older ages, with approximately a tripling with each decade of life. Males are affected more often than females [5]. Treatment goals may include lowering the risk of blood clots forming, preventing complications of coronary heart disease, Relieving symptoms and widening or bypassing clogged arteries. Therefore treatments for coronary heart disease include heart-healthy lifestyle changes, medicines, medical procedures and surgery includes coronary interventions as angioplasty and coronary stent, coronary artery bypass grafting (CABG) and cardiac rehabilitation [6].

Drug eluting stents (DESs) have been widely used for the coronary artery disease since Food and Drug Administration approved use of first DES in April 2003 [7]. DESs have been dominant for the treatment of CAD in the interventional cardiology world owing to their efficacy in significantly reducing restenosis. Drug eluting stent (DES) is a peripheral or coronary stent (a scaffold) placed into narrowed, diseased peripheral or coronary arteries in the heart that slowly release a drug to block cell proliferation [8], but may be associated with the hazard of late stent thrombosis. Antineoplastic, anti-inflammatory and immune modulators are the major agents used in drug eluting stents. Local delivery of drugs using DES provides both biological and mechanical solution and has emerged as a very promising approach effective in management of in-stent restenosis (ISR). For local drug delivery to be successful, challenges to be addressed include decision on the most appropriate agent to be used [9, 10], determination of the proportion of the systemic dose needed locally [11] and identification of a biocompatible vehicle that can deliver drug for the required therapeutic window [12, 13]. Four classes of drugs (anti-inflammatory, antithrombogenic, antiproliferative and immunosuppressive) are candidate drugs to be used in DESs, these drugs inhibit one or more biochemical pathways leading to restenosis. A drug-drug interaction may either increase or decrease the effects of one or both drugs, clinically significant interactions are often predictable and usually undesired [14].

Drug interactions are one of the most common causes of side effects in poly-pharmacy [15]. Drug interactions are usually divided into four groups: antagonism, synergism, potentiation, and interaction with metabolism [16]. Since altered drug metabolism is considered as major mechanism underlying many important drug interactions [17]. Drug-drug interactions (DDIs) are the major causal factor in disease rates and death and they increase the length of hospital stays and admission rates. DDIs happen when one drug's effect on the body is altered when taken in combination with another drug. This interaction can change how the drugs work and are processed in the body. It is established that the way drugs are broken down in the body vary between population subgroups and even among people of the same race and ethnicity, because of genetic differences in the cytochrome P450 enzymes which break down the drugs [18]. Nowadays the drug-drug interactions was found to be one of the major problems in pharmacotherapy worldwide, focus on identifying, resolving and preventing drug therapy problems are the important role of the pharmacy care practitioner. It is observed that several researchers established many drug-drug interactions between prescribed medications but no one established the interactions between drug eluting stents (DESs) like scaffolds and prescribed drugs after PCI, this makes me impress to design this basic observational study as a first attempt to invent and evaluate the term Drug-drug eluting stents interactions first time in the world. Researchers, physicians particularly cardiologists like to use or invent abbreviations and acronyms, the use of abbreviations or acronyms is

necessary to simplify and facilitate modern communication in our highly technical world [19]. Therefore the term Drug-Drug Eluting Stents interactions hereafter will be abbreviated as DDESI or DDES Interactions and may be included in medical terminology, acronym and dictionary of the modern medical world.

2. METHODOLOGY

2.1 Study Design

The present Retro-prospective, Multicenter cross-sectional observational study included coronary artery disease patients treated with different DESs within some selected hospitals (Apollo Multi Speciality Hospital, Trichy, Vivekanandha Medical Care Hospital, Tiruchengode, Sri Gokulam Hospital, Salem) of the three different parts in South India from the beginning of 2016 -2017, the basic features of the selected DES are shown in Table 1.

Table 1. Basic features of the drug eluting stents (DES) studied

Eluting Drug	Brand name	Scaffold material	Nominal Size (Length x Diameter)	Strut thickness (µm)	Polymer material	Polymer thickness (µm)	Drug elution kinetics
Sirolimus	Cypher (Raptor & Raptorail)	Stainless steel	18 x 3mm	140	PEVA, PBMA	12.6	80% within the first 4 weeks
Everolimus	Xience (V, Prime, Xpedition, & Alpine)	Cobalt-chromium	18 x 3mm	81	PBMA, PVDF-HFP	7.6	80% within the first 4 weeks
Zotarolimus	Resolute Onyx & Endeavor	Cobalt-alloy	18 x 3mm	91	PBMA, PHMA, PVP	5.6	85% within the first 8 weeks

PEVA: Poly-ethylene-co-vinyl acetate; PBMA: Poly-n-butyl methacrylate; PVP: Polyvinylpyrrolidone; PHMA: Poly-hexyl methacrylate; PVDF-HFP: Copolymer of vinylidene fluoride and hexafluoro-propylene.

2.2 Ethical approval

Ethical approval was gained through the main centre's Institutional Ethics Committee (IEC) with the approval number SVCP/IEC/JAN/2016/10 dated 27/01/2016. Hence it is a patients data analysis based study it was exempt from obtaining individual informed consent from each patients according to the Helsinki Declaration of 1964 revised in 2000 [20], but the objective of the present study was explained to all participants.

2.3 Study population

Totally N=127 (88 Male + 39 Female) CAD patients those successfully intervened with different DESs were included in this individual data based observational study. The study population were classified in to three groups i) Patients intervened with Sirolimus drug eluting stents N=52 (38 Male + 14 Female), ii) Patients intervened with Everolimus drug eluting stents N=46 (31 Male + 15 Female), and iii) Patients intervened with Zotarolimus drug eluting stents N=29 (19 Male + 10 Female). The selection criteria includes history of unstable angina (UA), chronic stable angina (CSA), myocardial infarction (MI) or the presence of high-risk factors for CAD etc.

2.4 Study protocol

The patient who met the following inclusion criteria was included in this study. A number of variables that play a vital role in stent therapy were analysed. These included baseline patient characteristics, angiographic and procedural characteristics, stent characteristics, mostly prescribed medications and drug-drug eluting stents interactions (DDESI). The patients case reports and drug chart were reviewed in patient who underwent percutaneous coronary intervention and also other details are collected via phone calls whenever required.

2.4.1 Inclusion criteria

Age 30 to 80 years old, both gender male and female, Patients underwent angioplasty using at least one DES, Patients underwent angioplasty with or without hypertension and diabetes mellitus, Patients already prescribed with anti-hypertensive drugs, anti-hyperlipidemic drugs, anti-coagulants, vasodilators and oral hypoglycaemic agents either one or all of the above medications at least one month before they subject to PCI only included in this study.

2.4.2 Exclusion criteria

Patients with age <30 and >80, Pregnancy, Lactation, Critically ill patients, Patients with life style modification alone, patients those received only percutaneous transluminal coronary angioplasty (PTCA) without stent implantation, patients those received bare metal stents (BMS) not DES, patients with complex lesions and who received multiple types of stents concurrently, and patients who were diagnosed with acute MI (NSTEMI) and underwent coronary artery bypass grafting (CABAG) were excluded from this study.

2.5 Statistical analysis

Statistical analysis was done by using Graph Pad Prism software version 7.01 and results were expressed as Mean \pm SEM for numerical variables and as percentage (%) for categorical variables. Column statistics followed by student t test was performed to compare the statistical difference of various groups, $P < 0.05$ was considered as statistically significant.

3. RESULTS

3.1 Baseline patient characteristics

A total of 127 patients were included in the study it is found that 52 patients were treated with Sirolimus DES; 46 patients were treated with Everolimus DES and 29 patients were treated with Zotarolimus DES, several clinical baseline patient characteristics and its significance was determined as shown in Table 2.

Table 2. Baseline Patient Characteristics

Baseline Patient Characteristics	Patients treated with Sirolimus DES (n=52)	Patients treated with Everolimus DES (n=46)	Patients treated with Zotarolimus DES (n=29)	P-value
Age	56.17 \pm 8.79	58 \pm 11.33	58.11 \pm 8.15	-
Male	73.08 %	67.39 %	65.52 %	0.0089
Female	26.92 %	32.61 %	34.48 %	0.0398

History of CAD	21.43 %	07.69 %	11.11 %	0.0832
Smoking	25.00 %	07.69 %	13.88 %	0.0920
Alcoholic	21.43 %	07.69 %	08.34 %	0.1080
Single vessel disease	48.57 %	56.92 %	39.44 %	0.124
Multi vessel disease	51.35 %	43.07 %	60.33 %	0.0109
IWMI	25.00 %	19.23 %	30.55 %	00168
ASMI	30.35 %	15.38 %	16.66 %	0.0468
AWMI	17.86 %	19.23 %	13.88 %	0.088
IPMI	01.79 %	0 %	0 %	0.4226
Stable angina	44.64 %	76.92 %	77.78 %	0.029
Unstable angina	10.71 %	23.08 %	19.44 %	0.0402
Diabetics	23.21 %	42.31 %	36.11 %	0.0265
Hypertension	32.14 %	38.46 %	33.33 %	0.0031
Hypercholesteremia	03.57 %	03.84 %	13.88 %	0.1716
Renal failure	0 %	0 %	02.77 %	0.4226
Heart failure	03.57 %	0 %	02.77 %	0.1899
Arrhythmia	01.79 %	07.69 %	05.55 %	0.1009
Hyperthyroidism	01.79 %	0 %	0 %	0.4226

3.1.1 Gender wise distribution of the study population

In this study, male population was high in patients treated with Sirolimus DES include (73.08%) then Everolimus DES (67.39%) and Zotarolimus DES (65.52%) but female population was found to be high in Zotarolimus DES (34.48%) compared to Everolimus DES (32.61%) and Sirolimus DES (26.92%).

3.1.2 Age wise distribution of the study population

Age is categorized in to six variables and each group is compared with each variable, among 127 populations, the incidence of coronary artery disease was mostly occurred in patients at the age of 51-60.

3.1.3 Coronary artery disease background of the study population

The CAD background of the study population of 127 patients was grouped into patients with the history of CAD and patients without the history of CAD. Among the study population patients without the history of CAD were found to be more in Everolimus DES (92.30%) then Zotarolimus DES (88.88%) and Sirolimus DES (78.47%).

3.1.4 Social habits wise distribution of the study population

Social habits of 127 populations were analysed and categorized to smoker, alcoholic, both and none. All the above four category was found to be high in patients treated with Sirolimus DES; smoker (25%), alcoholic (21.43%), both (14.29%), none (39.28%) then in patients treated with zotarolimus DES; smoker (13.88%), alcoholic (8.34%), both (2.78%) except none (75%). In Everolimus DES group; smoker was (7.69%), alcoholic (7.69%), both (11.54%) and none (73.08%) it is found to be lowest among the all three groups.

3.1.5 Patients with Target vessel diseases (TVD)

CAD was classified into single vessel disease (SVD) and multi vessel disease (MVD). The SVD was found to be high in patients treated with Everolimus DES (56.92%) then in Sirolimus DES (48.57%) and Zotarolimus DES (39.44%) but MVD was found to be high in

patients treated with Zotarolimus DES (60.33%) when compared to Sirolimus DES (51.35%) and Everolimus DES (43.07%).

3.1.6 Patients with Myocardial infarction

Myocardial infarction is categorized into Inferior Wall Myocardial Infarction (IWMI), Anterioseptal Myocardial Infarction (ASMI), Anterior Wall Myocardial Infarction (AWMI) and Infero-posterior Wall Myocardial Infarction (IPWMI or IPMI). IWMI patients are treated more with Zotarolimus DES (30.55%) but ASMI patients are highly treated with Sirolimus DES (30.35%) on the other hand AWMI patients are treated more with Everolimus DES (19.23%) when compared to other two DESs and it is found that only (1.79 %) of IPMI patients treated with Sirolimus DES.

3.1.7 Patients with Angina pectoris

Angina pectoris is categorized into stable angina and unstable angina. Patients treated with Sirolimus DES had (44.64%) of stable angina and (10.71%) of unstable angina but patients received Everolimus DES shows (76.92%) stable angina and (23.08%) unstable angina and Zotarolimus DES treated patients had (77.78%) stable angina and (19.44%) of unstable angina before subject to percutaneous coronary intervention (PCI).

3.1.8 Pattern of Co-morbidities among study population

Out of 127 patients, 99 patients had one or more co-morbid condition and 28 patients did not have any co-morbidity before subject to angioplasty. Out of 99 patients with co morbidities, in patients treated with Sirolimus DES, (23.21%) had diabetics, (32.14%) hypertension, (3.57%) hypercholestremia, (3.57%) Congestive heart failure, (1.79) Arrhythmia and (1.79%) hyperthyroidism but in patients treated with Everolimus DES (42.31%) had diabetics, (38.46%) hypertension, (3.84%) hypercholestremia and (7.69%) arrhythmia. On the other hand in patients with Zotarolimus it is found that (36.11%) had diabetics, (33.33%) hypertension, (13.88%) hypercholestremia, (2.77%) renal insufficiency, (2.77%) congestive heart failure and (5.55%) arrhythmia.

3.2 Angiographic features and procedural characteristics

In this study population, in most of patients it is found that lesions were more often occurred in the left artery descending (LAD) coronary artery and all the lesions were highly treated with Zotarolimus DES (58.33%) when compared to Everolimus DES (46.15%) then Sirolimus DES (44.64%) and the distribution of these lesions was comparable with each other in all the three groups as shown in Table 3.

Table 3. Angiographic and Procedural Characteristics

Angiographic and Procedural characteristics	Patients treated with Sirolimus DES (n=52)	Patients treated with Everolimus DES (n=46)	Patients treated with Zotarolimus DES (n=29)	P-value
<u>ISR location as a unit</u>				
Left anterior descending	44.64 %	46.15 %	58.33 %	0.0075
Left circumflex	33.92 %	07.69 %	33.33 %	0.1154
Right coronary artery	26.78 %	42.30 %	22.22 %	0.0708
Others	0	07.69 %	08.33 %	16.02
<u>No. of Stent as a unit</u>				

Patient with One DES	87.05 %	88.46 %	94.44 %	0.006
Patient with Two DES	12.05 %	11.54 %	05.55 %	0.0453

3.2.1 Route of Stent intervention in the study population

The route by which these stents were introduced was analysed and categorized into two major routes i) through right radial artery route and ii) through right femoral artery route but it is found that right femoral artery route was mostly preferred in all cases in all the three groups.

3.2.2 Patients treated with different number of DES

Patients treated with both one DES and two DES were included in this study, out of 127 cases, (94.44%) of patients intervened with single and (5.55%) of patients intervened with double Zotarolimus DES which is found to be highly significant when compared to patients intervened with (88.46%) single and (11.54%) double Everolimus DES followed by patients intervened with (57.5%) single and (12.5%) double Sirolimus DES.

3.3 CAD patients and medications

3.3.1 Commonly prescribed medications in CAD patients

In the selected study population HMG-CoA reductase inhibitors (86.3%), Aspirin (75.2%), Proton pump inhibitors (60.7%), Platelet P2Y12 Inhibitors (47.6%) and ACE inhibitors (44.8%) are more commonly prescribed medications but GP IIb/IIIa receptor inhibitors (4.9%), Aldosterone antagonists (2.1%) and Morphine sulfate (1.9%) are found to be less commonly prescribed medications in CAD patients before and after they subject to PCI, other commonly prescribed drugs also shown in the Fig. 1.

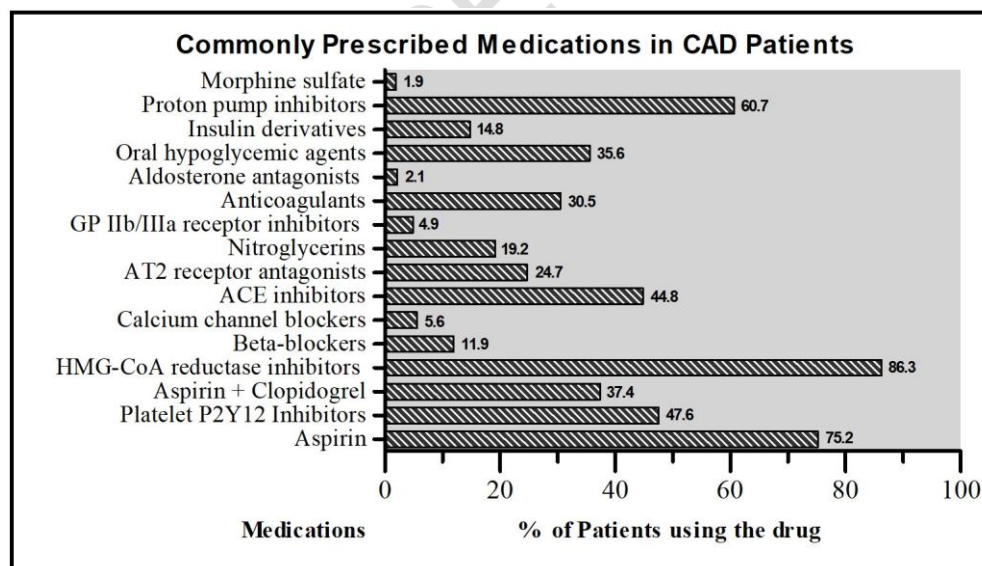


Fig. 1. Commonly Prescribed Medications in CAD Patients

3.3.2 Mostly prescribed drugs in CAD patients before and after PCI

In all the three groups mostly prescribed drugs are Aspirin, Atorvastatin, Clopidogrel, Pantoprazole, Nicorandil, Alprazolam, Ramipril, Telmisartan, Glyceryl trinitrate and Isosorbide dinitrate. Among all drugs it is found that Aspirin is more prevalent in patients with Sirolimus DES (94.64%) and Everolimus DES (80.76%) but in patients treated with Zotarolimus DES Atorvastatin (100%) is more prevalent which is found to be highest then Sirolimus DES (87.50 %) and Everolimus DES (73.07 %) next to that Clopidogrel was highly prescribed, it is found that Aspirin, Atorvastatin and Clopidogrel are the three most commonly prescribed drugs in all the three study groups at least two months before they considered as suitable candidate for PCI, afterwards the patients recommended to continue the same drugs after the completion of PCI procedures with or without little dose adjustments as shown in Table 4.

Table 4. Most prescribed drugs in CAD patients before and after PCI

Drugs	Patients treated with Sirolimus DES (n=52)	Patients treated with Everolimus DES (n=46)	Patients treated with Zotarolimus DES (n=29)	P-value
Aspirin	94.64 %	80.76 %	83.33 %	0.0024
Atorvastatin	87.50 %	73.07 %	100 %	0.0079
Clopidogrel	91.05 %	69.23 %	80.55 %	0.0061

3.4 Drug-Drug Eluting Stents Interactions (DDESI)

Drug-drug eluting stents interactions (DDESI) is the new medical terminology was discovered by the researcher Dr. Vinoth Prabhu Veeramani, Pharmacologist in the year 2007 after he identified mild to moderate interactions between some prescribed drugs and drug eluting stents in coronary artery disease patients after percutaneous coronary intervention during the case studies. Out of 127 patients, (2.54%) of Everolimus DES treated patients and (1.69 %) of Zotarolimus DES treated patients reported less significant DDES interactions after they underwent PCI procedure but Sirolimus DES intervened patients (0.85%) does not reported for any significant DDES interactions as shown in Fig. 2. It is found that the observed drug interactions are mostly occurred in elderly patients particularly those suffering with chronic non-curable illness like hypertension, diabetes mellitus or both, Variations from person to person were also seen this is may be due to several factors like Age, Allergies, Body mass index, Diseases, Drug dosage, Genes, Gender, Physiology and Lifestyle, but serious results of drug interactions and its outcomes like death, disability, permanent impairment of organs, congenital anomaly, life-threatening and hospitalization were not observed in any patients.

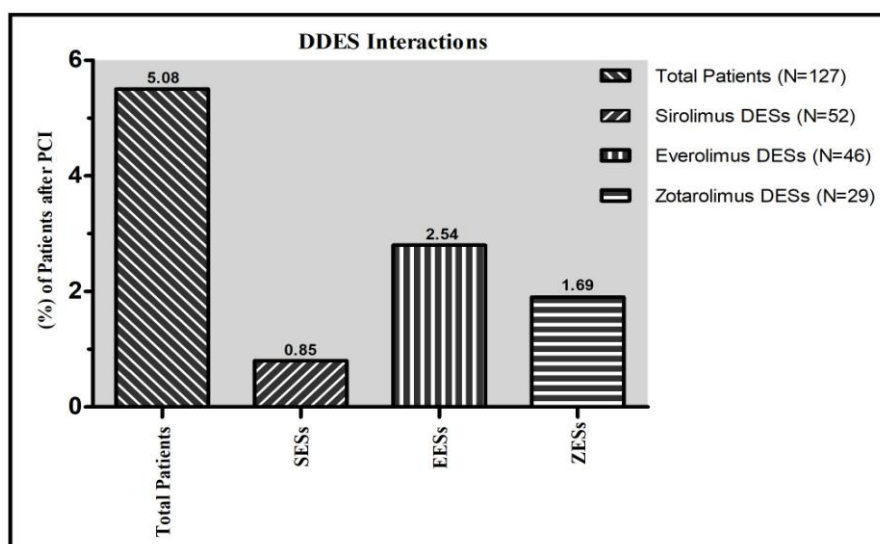


Fig. 2. Drug-drug eluting stents interactions (DDESI)

Due to this evidence of drug-drug eluting stents interactions it may be included in the classification of drug interactions, therefore i am hypothesised the definition for Drug-drug eluting stent interaction (DDESI) and it is defined as “interaction between the drug prescribed and drug which is coated on the stent during elution after percutaneous coronary intervention leads to alternations in pharmacokinetic and/or pharmacodynamic actions of one drug produced by another drug”. The term Drug-drug eluting stent interaction hereafter will be abbreviated as DDESI or DDES Interaction and this acronym may be included in the medical terminology and used in medical dictionary of current advanced medical world, also I well established the different categories of DDES interaction and its directions are given in Table 5.

Table 5. Different Categories of DDES Interactions

DDES Interaction Categories	Directions
Minor	Interaction is Mild or Non-significant (Monitoring may be required)
Major	Potential for Moderate or Significant interaction (Monitoring is required)
Serious	Potential for Severe interaction (Regular monitoring is required or alternate medication may be prescribed)
Contraindicated	High risk for Very severe or Dangerous interaction (Never use this combination of drugs)

4. DISCUSSION

All the three groups are well matched, males are found to be more in all groups, the incidence of CAD are mostly occurs in the age group of 51-60 years old. Among the study population patients without the history of CAD after PCI were found more, Smokers and alcoholics were more prevalent in Sirolimus DES, higher proportion of the patients with Sirolimus DES and Zotarolimus DES had multi vessel coronary disease, and also higher proportion of the patients with Zotarolimus DES had single vessel disease. In this study

population myocardial infarction were categorized into IWMI, ASMI, AWTMI and IPMI. The ASMI had higher prevalence in patients with Sirolimus DES but AWTMI had higher prevalence in patient with Everolimus DES, also IPMI had greater prevalence in patient with Sirolimus DES before they subjects to PCI. Higher proportion of all the three groups had Stable angina, Diabetes mellitus, Hypertension but Arrhythmia were more prevalent only in Everolimus DES.

While comparing angiographic and procedural characteristics few significant differences exist between treatment groups with respect to lesion characteristics. Lesions were mostly located in the left anterior descending, left circumflex or right coronary arteries also lesions were significantly comparable with each other in all the three groups but lesions were found to be more often occurred in the left artery descending (LAD) coronary artery then other arteries. At the same time all the lesions were effectively treated with Sirolimus, Everolimus and Zotarolimus DES respectively. Right femoral route was mostly preferred in all the three groups to introduce DES into the body; single stent was mostly used in all groups then multiple stents.

Among mostly prescribed medications Aspirin, Atorvastatin and Clopidogrel are the three majorly used drugs in patients with DES. Aspirin is more prevalent in patients with Sirolimus DES and Everolimus DES but in case of patients with Zotarolimus DES Atorvastatin was more prevalent. CAD patients with mild to moderate disease severity at initial and considered as not suitable for PCI immediately but prescribed for their major complications with medications such as anti-hypertensive drugs, anti-hyperlipidemic drugs, anti-coagulants, vasodilators and oral hypoglycaemic agents either one or all of the above at least one month before they subject to PCI and not reported for any drug-drug interaction symptoms between the drugs prescribed before PCI with DES and continue the same medications after PCI with or without optimal dose titration is the important inclusion criteria for the selection of the patients for this study, In DES intervened CAD patients all the identified drug interactions originated only after they underwent PCI, therefore the possibility of any drug-drug interactions is less and all the determined drug interactions are considered as DDES interactions.

The DDES interactions were analysed to monitor the effect of drugs in patients intervened with different drug eluting stents. Among all groups, patients treated with Sirolimus DES does not showed any significant interactions with prescribed medications but patients treated with Everolimus and Zotarolimus drug eluting stents reported less significant DDES interactions therefore according to the results obtained Sirolimus drug eluting stents was considered as more superior due to its less affinity towards the commonly co-prescribed medications particularly Aspirin, Atorvastatin and Clopidogrel compared to Everolimus and Zotarolimus drug eluting stents in South Indian CAD patients after they underwent PCI according to the monitoring parameters studied.

5. CONCLUSION

Based on the study carried out, Aspirin, Atorvastatin and Clopidogrel were the mostly prescribed drugs to maximize benefits and reduce the complications in patients those underwent percutaneous coronary intervention. Anti-platelet drugs will reduce the cardiac events without increasing the risk of bleeding, Aspirin is widely used anti-platelet agent in CAD patients; it is effective, safe and inexpensive and is recommended for most of patients undergoing PCI. Aspirin produces beneficial action with intervened DES there by patients will survive more. Clopidogrel has been shown to reduce the rates of cardiac events. Atorvastatin reduces thrombin generation after PCI, these three drugs are considered highly necessary for the maintenance of normal cardiac function after angioplasty, the data derived

from this study as well as total evidence available to date does not support the clinically significant impact of any pharmacokinetic and pharmacodynamics major interactions between these drug eluting stents and prescribed medications such as Aspirin, Atorvastatin and Clopidogrel.

In this study population it is found that drug eluting stents along with prescribed medications does not associated with any major DDES interactions like Bleeding, Increased or decreased blood concentration, Stent thrombosis, Restenosis, Cardiovascular related death and other clinical manifestations. It is observed in this cross sectional observational study Sirolimus DES does not produce any serious DDES interactions with prescribed medications according to the available first one year follow-up records of the patients obtained from the study centres, but few patients those stented with Everolimus and Zotarolimus DES reported chest pain and increased blood flow during the course of medications with optimal dose, therefore it might be a suspected interaction between Atorvastatin and Zotarolimus as well as Everolimus because all statins will increase the level or effect of immunosuppressant by P-glycoprotein (MDR1) efflux transporter mechanism. According to the available resources Everolimus may increase the serum concentration of CYP3A4 substrates which have high risk with inhibitors but advanced screening techniques and molecular level studies are recommended to explore the exact molecular mechanisms behind these DDES interactions.

Although, the observed DDES interactions are considered to be less significant and falls in minor DDESI category, however these DDES interactions can be managed by avoiding combination drug therapy, adjusting the dose of main drug, adjusting the time of intake of two drugs, monitoring the combination therapy or modify the prescription with alternate drug and educating the patient about potential DDES interactions. Therefore it is concluded that Sirolimus drug eluting stents was found to be more suitable and safe when compared to Everolimus and Zotarolimus drug eluting stents in CAD patients those initially considered as not suitable for PCI but prescribed with medications includes Aspirin, Atorvastatin and Clopidogrel to minimize the disease outcomes later recommended for PCI. Further study may be conducted in future internationally with large population size in order to substantiate the observed results.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Author hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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DEFINITIONS, ACRONYMS, ABBREVIATIONS

DDESI: Drug-Drug eluting stent interaction.

Drug-Drug eluting stent interaction: It is defined as “interaction between the drug prescribed and drug which is coated on the stent during elution after percutaneous coronary intervention leads to alternations in pharmacokinetic and/or pharmacodynamic actions of one drug produced by another drug”.