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Effect of Diabetic Medication on Cardiovascular Risk and Microvascular Complication in Diabetic Patients: Retrospective Cohort Study

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ABSTRACT

This study was deliberate to evaluate the effects of diabetic medication on micro vascular and macro vascular complications in diabetic patients. In this retrospective study observational data collected from medical records of type 2 diabetic mellitus (T2DM) patients with index oral hypoglycemic medication over the period of 2009 to 2014, by using the medical record department databases of Vivekananda Medical Care Hospital, Tamil Nadu-25. They were categorised into nine groups based on the treatment received such as metformin alone, sulfonylureas alone, sulfonylureas added to metformin, metformin added to sulfonylureas, metformin with insulin added later, sulfonylureas with metformin, metformin and sulfonylureas with insulin added later, sulfonylureas and metformin with pioglitazone added later, sulfonylureas, metformin and voglibose added later. In Cox regression analyses, we estimated comparative risks for mortality due to cardiovascular problems and cardiovascular hospitalization among study cohorts, with metformin monotherapy as the reference group. The results showed that metformin monotherapy shows less cardiovascular and micro vascular events. Sulfonylurea monotherapy shows significant higher CV risk ratio. Initial sulfonylurea mono therapy with later metformin prescription and initial metformin therapy with later sulfonylureas prescription shows higher CV risk ratio as next to the sulfonylurea monotherapy and increased microvascular complication as compared to the metformin monotherapy. In conclusion the microvascular and macrovascular risks are higher in sulfonylurea alone or in combination with other agents as compared to the metformin monotherapy which has low incidence of cardiovascular risk ratio in type 2 diabetic mellitus.

INTRODUCTION

Diabetes mellitus (DM) is defined as a metabolic syndrome characterized by hyperglycemia which results as of blemish in both secretion and action of insulin. Hyperglycemia is associated with microvascular and macrovascular complications like long-standing dysfunction, damage and failure of various organs, especially the eyes, blood vessels, nerves, heart and kidneys; that considerably increase the morbidity and mortality related to the disease (Funnell, 2010; Underwood, 1992; Morrish, 2001). The reason for this is due to an aging, increasing prevalence of obesity and deskbound lifestyle (Williams, 1998).

The global prevalence of diabetes has nearly increased to two fold since 1980, which is rising from 4.7% to 8.5% in the adults. This shows an increase in associated risk factors such as overweight or obesity. In 2012, 1.5 million mortalities were due to diabetes. Higher than optimal blood glucose caused 2.2 million mortalities, by raising the risks of cardiovascular and other disorders. 43% of these 3.7 million deaths occur before the age of 70 years. World Health Organisation (WHO) says that diabetes will be the 7th foremost cause of death in 2030 (WHO 2016). More than 180 million people worldwide have type 2 diabetes mellitus which is characterized by hyperglycaemia that causes eye, nerve,

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kidney complications and an increased risk for cardiovascular disease. Diabetes is associated with cardiovascular disease doubles the risk of death, (WHO 2008).

To control hyperglycaemia many antidiabetic drugs are available now. The principal endpoint event in most studies on treatment of DM is a reduction of glycated haemoglobin (HbA_{1C}) levels; more increased amounts of HbA_{1C} are strongly linked with microvascular complications such as retinopathy, neuropathy and nephropathy. 1% raises in HbA_{1C} is associated with an 18% increase in the risk of cardiovascular events and 12 to 14% increase in the risk of mortality (Selvin *et al.*, 2004; Gerstein *et al.*, 2005; Stratton *et al.*, 2000). Moreover, previous studies have shown that reduction in HbA_{1C} results in reduced microvascular problems. Existing treatment approaches are therefore, planned to accomplish near-normal levels of HbA_{1C}. Though, decreases of HbA_{1C} have not been found to decrease macrovascular complications (Lancet, 1998; Stolar, 1988).

Reports from previous studies have revealed that recent antidiabetic drugs decrease HbA_{1C} levels but inconsistently increased cardiovascular events or mortality. The choice of antidiabetic agent not only depends on glycemic control, but also on microvascular and macrovascular complications. So this study was intended to evaluate the impacts of diabetic medication on microvascular and macrovascular snags in diabetic patients.

METHODOLOGY

Study Design

In this retrospective inception cohort study was intended to assess the effect of diabetic medication over macrovascular and microvascular risk in diabetic patients by using the Medical record department databases of Vivekananda Medical Care Hospital, Tiruchengode, Tamil Nadu-25. Medical records of type 2 diabetic mellitus (T2DM) patients with index oral hypoglycemic medication were collected over the period of 1 January 2009 to 31 December 2014. This study was approved by Institutional Ethical Committee (SVCP/IEC/JAN/2016/06).

Study Population

These study cohorts comprised of all individuals from 30 years and above aged who were diagnosed with T2DM earlier to December 2014. We then identified all those who were recently treated with Oral hypoglycemic agents (OHAs) during the study period of 1 January 2009 to 31 December 2014. Follow up began on the day after the first prescription of OHAs. Patients with previous records of OHAs treatments in 2008 were not qualified as they were not new OHA user in our study period. We also exclude the patients who were prescribed insulin moreover earlier than or within the 3 months of their first OHA prescription. Selection of study populations were also based on the inclusion and exclusion criteria.

Nine cohorts were included in our study as defined as follows (Fig. 1):

1. Metformin monotherapy: patients treated with metformin alone during the study period, or those treated with metformin with sulfonylureas or other hypoglycemic agents added later (at which point they were censored). Their index date was the date of their original metformin prescription.
2. Sulfonylureas monotherapy: patients treated with sulfonylureas alone during the study period, or those treated with sulfonylureas with metformin or other hypoglycemic agents added later (at which point they were censored). Their index date was the date of their first sulfonylureas prescription.
3. Combination 1: patients treated with metformin with sulfonylureas added later. Their index date was the date of their first sulfonylureas prescription.
4. Combination 2: patients treated with sulfonylureas and metformin added later. Their index date was the date of their first metformin prescription.
5. Combination 3: patients treated with metformin and insulin added later. Their index date was the date of their first insulin prescription.
6. Combination 4: treatment with together sulfonylureas and metformin at same time. Their index date was the date of their first prescription for both.
7. Combination 5: patients treated with metformin and sulfonylureas with insulin added later. Their index date was the date of their first insulin prescription.
8. Combination 6: patients treated with sulfonylureas and metformin with pioglitazone added later. Their index date was the date of their first pioglitazone prescription.
9. Combination 7: patients treated with sulfonylureas, metformin and voglibose added later. Their index date was the date of their first voglibose prescription.

Inclusion criteria

The study population included individuals who generally attended Vivekananda medical care Hospital at periodic intervals. All patients who were newly diagnosed as diabetes, aged between 30–60 years and recently treated with OHAs in the study phase of 1 January 2009 to 31 December 2014 were eligible for inclusion. Patients who had fasting plasma glucose (FPG) > 6 mmol/L on two successive mornings, 1–3 weeks apart and HbA1c >6.5%, were eligible for the study. An FPG of 6 mmol/L and HbA1c >6.5% were included because this was just beyond the greater limit of our normal reference range.

Exclusion criteria

We excluded the patients under the age of 30 years with type 2 DM past to December 2008. This did not comprise the patients had an obligation for insulin within 3 months, and were therefore defined as patients with type 1 diabetes. Diabetic patients on dialysis or who had previous record of coronary artery diseases (CAD) and congestive heart failure (CHF) at baseline were also excluded. Patients with ketonuria > 3 mmol/L, serum creatinine >175 mmol/L, myocardial infarction in the earlier year, current angina or heart failure; more than one major vascular event, retinopathy, neuropathy, nephropathy, malignant hypertension and uncorrected endocrine disorders were excluded. We also excluded those records with multiple or missing data.

Data collection

Data collection includes the baseline medical history such as age, sex, body mass index (BMI), social history (smoking, tobacco chewing, alcohol usage, high salt, high calorie intake and physical inactivity status), systolic and diastolic blood pressure,

HbA1c, Fasting blood glucose level, postprandial glucose (PPBS), Random blood sugar (RBS) and Lipid profile. These study treatment patients were followed from their index data until censoring, primary risk outcome events, mortality or the end of study phase.

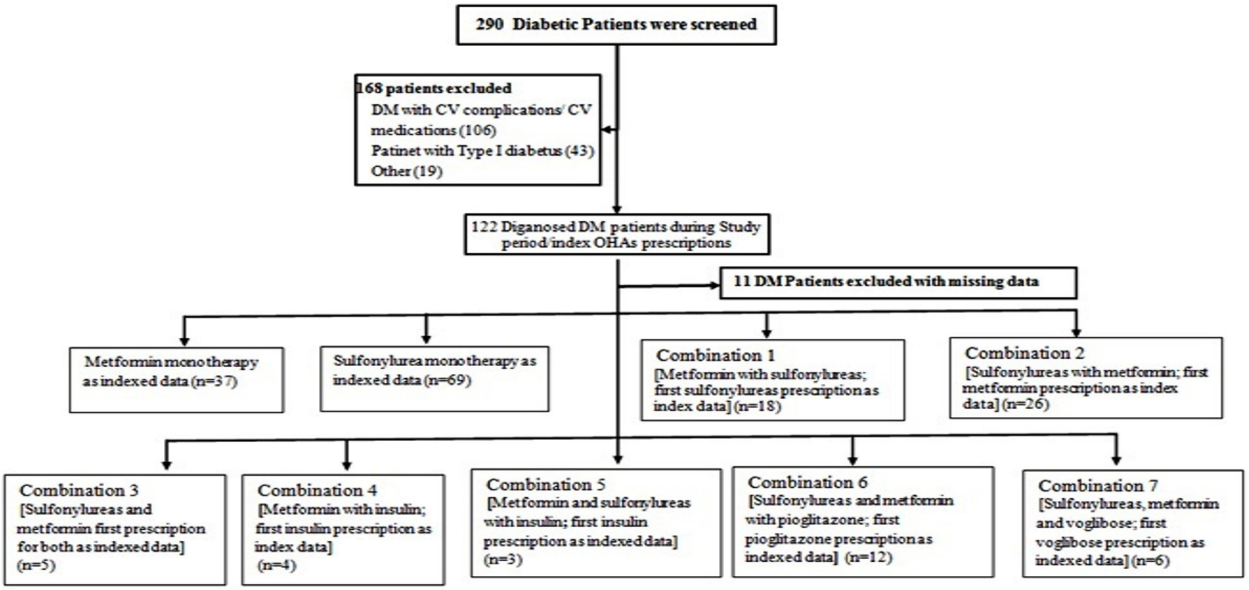

Fig. 1: Trail design.

Primary outcome events

Primary outcome events were the diagnosis and occurrence of call cause of mortality, primary diagnosis of cardiovascular diseases, composite of Myocardial infarction (MI), stroke or cardiovascular death, presence of neuropathy, nephropathy, retinopathy and dementia.

End point events

End point measures were the cardiovascular mortality and all causes of mortality or the end of study period of 31 December 2015.

Statistical analysis

The values were represented as mean ± SD. Results were analyzed statistically by one way ANOVA followed by post hoc Dunnett's test and unpaired t-test by using SPSS V.17 statistical package. The statistical distinction was considered significant when $P < 0.05$. In order to compare patients in each cohorts, we were used a multivariate analysis that allowed us to adjust the variations in baseline characteristics. Multivariate Cox models were used to derive hazard ratios (HR). Survival curves for CAD, CHF, and mortality were estimated with the Kaplan–Meier procedure.

RESULTS

A sum of 290 persons with DM were screened in this study, out of which 168 patients were excluded as they were DM with CV complication/taking CV medication or patients with T_1DM. Out of remaining 122 patients, 111 patients with complete demographic and clinical data were available for analysis. The mean age of the 111 patients receiving oral antidiabetes agents were 55.8 years. The overall sex distribution between treatments group were men 52% and women 48%. Body mass index among the cohorts were ranges from 27.3 kg/m^2 to 31.4 kg/m^2, which was higher in combination7 (Sulfonylurea + Metformin + Voglibose) 31.4 kg/m^2 and least at both Metformin and sulfonylurea treatment cohort. Among this cohorts never smoker, tobacco chewing and alcohol abuse percentage was higher in compare to current and quit patients, as well as social and regular drinkers in alcohol users (Table 1).

There was no significant base line difference in mean HbA_{1c}, FPG and PPG levels. At clinical end point mean HbA_{1c} was significantly ($P < 0.05$) higher in combination 1, 2, 5 and 7 as compare to the metformin cohort. FPG was significantly ($P < 0.05$) higher in combination 1 as compare to the metformin cohort. PPG level was significantly ($P < 0.05$) higher in combination 1 and 2 as compare to the metformin cohort.

There was no significant baseline distinction in mean LDL, HDL, TG and TC levels. At clinical endpoint sulfonylurea monotherapy shows significant ($P < 0.01$) increases in LDL as compare to the metformin monotherapy cohort; metformin monotherapy and combination 5 shows significant ($P < 0.01$) and combination 1 and 4 shows significant ($P < 0.05$) decrease in LDL level as compare to the sulfonylurea monotherapy. There was no significant difference of HDL at clinical end point in treatment groups. Sulfonylurea monotherapy and combination 1 shows significant ($P < 0.001$) and combination 2 and 6 shows significant ($P < 0.01$) increases in TG as compare to the metformin monotherapy cohort; metformin monotherapy shows significant ($P < 0.001$) and combination 4, 5 and 7 shows significant ($P < 0.01$) decrease in TG level as compared to the sulfonylurea monotherapy.

Sulfonylurea monotherapy and combination 1, 2, 7 shows significant ($P < 0.001$) and combination 4 and 6 shows

significant ($P < 0.01$) increases in TC as compare to the metformin monotherapy cohort; metformin monotherapy shows significant ($P < 0.001$) and combination 3 and 5 shows significant ($P < 0.05$) decrease in TC level as compared to the sulfonylurea monotherapy cohort (Table 2).

Frequencies of microvascular events are summarized in Table 3. Microvascular event percentages were higher in order of combination 1, 2, sulfonylurea monotherapy, combination 3 and metformin monotherapy.

Table 1: Baseline Demographic characteristics and cardiovascular risk factors of the patients in treatment groups.

Demographic characteristics	MET	SU	MET + SU (C1)	SU + MET (C2)	MET & SU (C3)	MET + INS (C4)	MET + SU + INS (C5)	SU + MET + PIO (C6)	SU + MET + VOGL (C7)
Total (n = 111)	37	69	18	26	5	4	3	12	6
Mean age (years)	56.3 ± 1.7	54.6 ± 3.2	57.1 ± 1.3	55.7 ± 1.9	55.2 ± 2.8	52.3 ± 4.4	54.0 ± 4.0	58.2 ± 2.2	59.2 ± 2.3
Sex (M/F)	21/16	35/34	8/10	14/12	2/3	1/3	2/1	6/6	2/4
Women%	43.2	49.3	55.6	46.2	60.0	75.0	33.3	50.0	66.7
Mean BMI (kg/m^2)	27.9 ± 1.4	28.3 ± 2.3	30.1 ± 2.8	29.2 ± 3.2	27.3 ± 1.5	29.2 ± 5.3	29.3 ± 4.2	29.6 ± 1.6	31.4 ± 2.8
Smoking (%) Never/Current/Quit	59.5/18.9/13.5	60.9/17.4/8.7	66.7/22.2/11.1	57.7/19.2/15.4	60.0/20.0	75.0/0/25.0	66.7/33.3	66.7/25.0/8.3	66.7/16.7/16.7
Tobacco chewing (%) Never/Current/Quit	64.9/16.2/5.4	58.0/23.2/5.8	61.1/22.2/5.6	57.7/23.1/11.5	60.0/20.0	75.0/0/25.0	66.7/33.3	66.7/16.7/8.3	66.7/16.7
Alcohol (%) Non/Social/Regular	62.2/10.8/24.3	55.1/14.5/17.4	55.6/16.7/22.2	57.7/15.4/23.1	60.0/0/40.0	75.0/25.0	33.3/33.3/33.3	50.0/25.0/16.7	66.7/16.7
High salt/High calorie intake (%)	21.6/27.0	18.8/27.5	22.2/27.8	23.1/30.8	20.0/40.0	25.0/50.0	33.3/66.7	33.3/58.3	33.3/50
Physical activity (%) Sedentary/Moderately active/Active	8.1/37.8/40.5	5.8/31.9/43.5	11.1/33.3/38.9	11.5/26.9/46.2	20.0/40.0/40.0	25.0/50.0/25.0	66.7/33.3	25.0/41.7/16.7	33.3/50.0/16.7

Table 2: The effect of diabetic medication on blood sugar level and lipid profile in treatment groups.

Parameters/Study Cohorts		MET	SU	MET + SU (C1)	SU + MET (C2)	MET & SU (C3)	MET + INS (C4)	MET + SU + INS (C5)	SU + MET + PIO (C6)	SU + MET + VOGL (C7)
Baseline value	HbA_{1c}(%)	8.5 ± 1.1	8.4 ± 1.0	8.9 ± 1.2	8.3 ± 1.0	8.4 ± 1.3	8.8 ± 1.4	9.3 ± 1.2	8.7 ± 1.3	8.7 ± 1.2
	FPG (mmol/L)	12.8 ± 2.1	13.3 ± 3.6	14.1 ± 2.5	13.0 ± 3.2	13.7 ± 3.7	14.7 ± 3.4	13.9 ± 4.2	13.1 ± 3.3	13.3 ± 2.9
	PPG (mmol/L)	13.2 ± 1.2	13.4 ± 1.3	13.8 ± 3.2	13.2 ± 4.2	14.3 ± 5.3	13.5 ± 3.4	13.2 ± 2.4	14.0 ± 3.5	13.8 ± 4.7
	LDL (mg/dl)	132.0 ± 12.5	134.2 ± 23.2	136.3 ± 14.2	135.4 ± 32.2	133.3 ± 21.7	134.4 ± 14.4	140.2 ± 15.5	138.9 ± 22.4	141.2 ± 12.5
	HDL (mg/dl)	42.1 ± 3.4	43.2 ± 5.2	42.6 ± 2.4	45.3 ± 3.6	44.2 ± 4.3	41.3 ± 1.2	41.6 ± 5.3	48.7 ± 4.8	45.1 ± 2.3
	TG (mg/dl	234.7 ± 13.3	231.4 ± 14.9	241.2 ± 45.1	230.2 ± 42.1	231.6 ± 12.2	233.8 ± 14.5	232.4 ± 32.2	228.9 ± 12.4	226.6 ± 20.2
	TC (mg/dl)	222.4 ± 19.2	225.1 ± 12.7	237.2 ± 19.4	228.7 ± 13.4	218.4 ± 19.7	220.7 ± 32.5	219.3 ± 26.3	226.5 ± 15.4	230.2 ± 15.2
End point value	HbA_{1c}(%)	7.3 ± 0.7	7.6 ± 0.7	8.0 ± 0.8*	8.1 ± 0.7*	7.9 ± 0.7	7.9 ± 0.7	8.0 ± 0.2*	7.8 ± 0.6	8.0 ± 0.7*
	FPG (mmol/L)	10.4 ± 1.8	11.9 ± 2.9	12.6 ± 2.0*	11.6 ± 3.2	11.9 ± 3.8	12.2 ± 3.3	11.7 ± 4.1	12.1 ± 3.4	12.2 ± 2.7
	PPG (mmol/L)	11.5 ± 2.3	11.9 ± 2.4	13.5 ± 3.3*	13.6 ± 2.0*	12.3 ± 3.2	12.3 ± 3.2	12.3 ± 1.9	12.3 ± 1.6	13.0 ± 2.4
	LDL (mg/dl)	107.2 ± 12.1^{b**}	121.0 ± 12.4^{a**}	108.9 ± 12.7^{b*}	116.4 ± 10.4	108.9 ± 7.7	107.6 ± 18.9^{b*}	104.2 ± 16.4^{b**}	109.4 ± 12.1	109.7 ± 15.6
	HDL (mg/dl)	43.2 ± 3.2	39.8 ± 2.5	41.3 ± 5.6	43.2 ± 4.2	43.1 ± 3.4	40.2 ± 8.2	41.3 ± 4.8	46.5 ± 2.9	44.8 ± 3.4
	TG (mg/dl)	195.8 ± 13.6^{b***}	223.3 ± 15.4^{a***}	232.1 ± 23.9^{a***}	215.8 ± 11.2^{a**}	207.7 ± 21.4	198.8 ± 9.0^{b**}	199.3 ± 13.1^{b**}	213.7 ± 18.4^{a**}	201.2 ± 11.5^{b**}
	TC (mg/dl)	197.9 ± 12.9^{b***}	221.8 ± 12.8^{a***}	225.8 ± 25.1^{a***}	222.0 ± 15.0^{a***}	201.9 ± 12.1^{b*}	211.9 ± 10.2^{a**}	203.0 ± 6.4^{b*}	215.8 ± 9.4^{a**}	220.5 ± 12.2^{a***}

Values are expressed as mean ± SD.
Comparisons were made between: a- Metformin Vs others; b- Sulfonylureas Vs others,
Symbols represent statistical significance: *** -P < 0.001, **-P < 0.01, *-P < 0.05.

The number of patients in every cohort who had cardiovascular outcomes is represented in Table 4, with unadjusted risk ratios. We found that 5.0% of patients in metformin monotherapy showed cardiovascular death, compared with 17% (3.01 of RR) of patients in sulfonylurea monotherapy, 15% (2.04 of RR) of patients with combination 2, 11% (1.90 of RR) of patients with combination 1. Primary outcome event was 33% (1.5 of RR) of patients with combination 1, 31% (2.3 of RR) of patients with combination 2, 20% (1.2 of RR) of patients with combination 3, 23% (1.6 of RR) of patients with combination 6 and 33% (1.7 of RR) of patients with combination 7 cohort.

DISCUSSION

Our study represents observational data from medical records of type 2 diabetic mellitus (T2DM) patients with index oral hypoglycemic medication were collected over the period of 1 January 2009 to 31 December 2014, by using the medical record department databases of Vivekananda Medical Care Hospital, Tiruchengode, Tamilnadu-25. Observed data in our study from general practice allows evaluation of the essential benefits and hazards of use of diabetic medication at CV risks associated with DM.

Table 3: Frequencies of microvascular and macrovascular events.

Events	MET	SU	MET + SU (C1)	SU + MET (C2)	MET & SU (C3)	MET + INS (C4)	MET + SU + INS (C5)	SU + MET + PIO (C6)	SU + MET + VOGLI (C7)
Neuropathy (%)	3	9	14	12	20	-	-	8	17
Nephropathy (%)	3	7	17	19	-	-	-	17	-
Retinopathy (%)	-	3	5	8	-	-	-	-	-
Dementia (%)	3	3	11	15	-	-	-	17	17
Primary diagnosis CV disorders (%)	8	13	22	23	20	25	33	25	17
Cardiac dysrhythmia (%)	3	4	6	4	-	-	-	8	-
MI (%)	3	3	6	4	-	-	-	8	17
Stroke or Cardiovascular death (%)	5	17	11	15	20	-	-	25	17

Table 4: The unadjusted risk ratio (with 95% CIs) for cardiovascular mortality and cardiovascular admission for the patients in the study cohorts.

Study Cohort	Cardiovascular mortality		Cardiovascular admission	
	RR (95% CI)	Events/total (%)	RR (95% CI)	Events/total (%)
MET	1.00 (referent)	2/37 (5%)	1.00 (referent)	5/37 (14%)
SU	3.01 (2.7–3.3)	12/69 (17)	1.12 (0.8–1.9)	18/69 (26%)
ET + SU(C1)	1.90 (1.4–2.3)	2/18 (11%)	1.50 (0.7–2.1)	6/18 (33%)
SU + MET (C2)	2.04 (1.7–2.5)	4/26 (15%)	2.30 (1.3–2.9)	8/26 (31%)
MET + SU (C3)	1.70 (1.2–2.1)	1/5 (20%)	1.20 (0.7–1.8)	1/5 (20%)
MET + INS (C4)	-	0/4 (0)	-	1/4 (25%)
MET + SU + INS(C5)	-	0/3 (0)	-	1/3 (33%)
SU + MET + PIO (C6)	1.60 (1.5–1.9)	3/12 (25%)	1.60 (0.8–2.1)	5/12 (23%)
SU + MET + VOGL(C7)	1.80 (1.4–2.2)	1/6 (17%)	1.70 (1.2–2.3)	2/6 (33%)

RR-Risk ratios.

Persons with T2DM are at high risk of CV morbidity and mortality. Some of previous studies report that almost 75% of patients with T2DM were died due to macrovascular events, such as MI and stroke. (Bo *et al*., 2006). In this study, persons with T2DM who were recently prescribed with sulfonylureas monotherapy, later metformin prescription; initial metformin therapy with later sulfonylureas prescription; initial sulfonylurea monotherapy with later prescription of metformin and voglibose were at higher risk of cardiovascular mortality and cardiovascular admission when compared to the patients who were newly prescribed with metformin. The unadjusted risk ratio of CV mortality were 3.01 (95% CI 2.7–3.3) at sulfonylurea monotherapy, 2.04 (95% CI 1.7–2.5) at later metformin prescription, 1.90 (95% CI 1.4–2.3) at initial metformin therapy with later sulfonylureas prescription, 1.80 (95% CI 1.4–2.2) at initial sulfonylurea monotherapy with later prescription of metformin and voglibose. It is consisted with previous studies that found patients treated with metformin where at lower cardiovascular risk (Evans *et al*., 2006).

The increased risk of CV morbidity and mortality linked with diabetes has lead to the perception that hyperglycaemia may be one of the risk factor for CVD (Kuusisto *et al*., 1994; Haffner and Cassells, 2003; Takahashi *et al*., 2006). The UK prospective study reported that each 1% (<6% to ≥ 10%) diminution in HbA_{1c} was linked with a reduction in risk of 21% for any diabetic end point death and 14% for MI (Stratton, 2000). In this study the level of HbA_{1c} shows significant increases in initial metformin therapy with later sulfonylureas prescription (C1); initial sulfonylurea monotherapy with later prescription of metformin (C2) and initial sulfonylurea monotherapy with later prescription of metformin and voglibose (C7) cohort as compared to the metformin monotherapy. This may be one of the risk factor which may increases the macrovascular and microvascular risk in those cohorts.

Postprandial glucose control also plays a considerable role in overall glycemic control and became more essential

than fasting plasma glucose when better control is achieved (Monnier *et al*., 2003). In this study PPG and FPG level shows significantincreases in initial metformin therapy with later sulfonylureas prescription (C1) and PPG level was also significantly higher in initial sulfonylurea monotherapy with later prescription of metformin (C2). This may be one of accompanying risk factor for the cardiovascular and microvascular risk in those cohorts.

The mechanism by which enhanced glycemic control reduces cardiovascular risk are not absolutely unstated, but probably related to the betterment of dyslipidemia, endothelial dysfunction, vasomotor dysfunction, and coagulation malfunction all of which are aggravated by hyperglycemia (Avena *et al*., 1998; Mather *et al*., 2001). This study shows that LDL, TG, and TC level was moderately decreased in Metformin monotherapy as compare to the other treatment cohort. This may confirm the cardio protective property of the metformin.

Total cholesterol and triglyceride level in sulfonylurea monotherapy; initial metformin therapy with later sulfonylureas prescription (C1); initial sulfonylurea monotherapy with later prescription of metformin (C2) and initial sulfonylurea monotherapy with later prescription of metformin and pioglitazone cohorts were significantly higher as compared to the metformin monotherapy. This may confirm the cardio toxic property of these combinations.

CONCLUSION

This retrospective cohort study was carried out in 111 patients who were newly diagnosed with DM and their index treatment of Metformin, sulfonylurea or both at the study site of Vivekananda Medical Care Hospital, Tiruchengode, Tamilnadu-25. Metformin monotherapy cohort showed less cardiovascular and micro vascular events when compared to the other cohorts. It may be due to the significant reduction action against blood sugar and lipid profile in T2DM patients. Sulfonylurea monotherapy cohort is the most prescribed medication among this population; it showed significant higher CV risk ratios when compared to the other cohorts. Initial sulfonylurea mono therapy with later metformin prescription (C2) and initial metformin therapy with later sulfonylureas prescription (C1) cohort showed higher CV risk ratio as next to the sulfonylurea monotherapy and higher percentage of microvascular complication as compared to the metformin monotherapy cohort. Combination 3, 4 and 5 cohort included study populations were not showed significant difference in our study so it was difficult to assess macrovascular and microvascular complication in these treatment cohorts. At initial sulfonylurea monotherapy with later prescription of metformin and pioglitazone or voglibose showed milder incidence of macrovascular and microvascular complication when compared to metformin monotherapy.

In conclusion the microvascular and macrovascular risks are higher in sulfonylurea monotherapy or in combination with other agents when compared to the metformin monotherapy, which has low incidence of risk ratio in type 2 diabetic mellitus cohorts.

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