



**ORIGINAL RESEARCH PAPER**

**Pharmacology**

**EFFECT OF SOME INDIRECT VASODILATORS ON BLOOD GLUCOSE IN HYPERTENSIVE DIABETIC PATIENTS WHO ARE ILL CONTROLLED ON ORAL ANTIDIABETIC DRUGS - A PILOT STUDY.**

**KEY WORDS:** Amlodipine, Enalapril, Telmisartan, Concomitant.

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**ABSTRACT**

Indirect vasodilators Amlodipine, Enalapril, Telmisartan are the commonly used medicines for hypertension with diabetes mellitus type 2 wherein regular concomitant use of anti diabetic is advocated. Telmisartan in dose of 40 mg, Enalapril 5 mg, Amlodipine 5 mg doses were selected and administered in hypertensive diabetic patients where blood sugar was more than 150 mg fasting and 180 mg postprandial with Metformin therapy were selected forming three different groups. Enalapril was more effective as cotherapy with Metformin to produce reduction in blood sugar in 8 weeks duration. This concluded that all three may be continued as cotherapies along with Metformin 500 mg.

**Introduction:**

Cardiovascular diseases and Diabetes are the leading cause of mortality and morbidity in developed and developing countries.<sup>1</sup>Type 2 Diabetes mellitus and hypertension may co exists in around 15-25% individuals in industrialised countries.<sup>2</sup> Both these are to be effectively controlled to prevent their respective complications. Insulin insensitive and insulin resistance patients of type 1 are given insulin receptor sensitising agents. So also type 2 Diabetes mellitus non responders to diet modification, exercise followed by sulfonylurea or biguanide member as main drug need to be concomitantly treated by adding insulin receptor sensitising agent - Thiazolidinedione, Glinides, or other group of member.<sup>3</sup> Indirect vasodilators Prazosin, Amlodipine, ACE inhibitors and Telmisartan from ARBs are being shown as not having adverse profile on blood glucose in hypertensive diabetic subjects.<sup>4,5,6,7</sup>

Telmisartan by virtue of its additional PPAR gamma activity is likely to enhance eNOS and suppress iNOS activity in myocytes thereby likely to improve glucose uptake via GLUT4 activity enhancement.<sup>8</sup> Other three indirect vasodilators may be beneficial by improving insulin action through eNOS mediated action mechanism.

**Material and methods:**

We have planned a preliminary pilot study with commonly used indirect vasodilator i.e. Amlodipine, Enalapril and Telmisartan on small number of patients forming three different drug treated groups. The patients young adult patient in the age range of 18 to 65 yrs applying exclusion criteria were included in non interventional, observational study in medicine OPD at GMC Akola hospital in a nonrandomised first come first serve open clinical parallel group study design. The drugs were prescribed by clinicians and patients were included in respective groups. Pretreatment (without indirect vasodilator group) blood sugar of each patient served as individual control. Data was recorded at interval of 2 weeks for 8 weeks duration and changes in blood sugar were analysed by applying paired 't' test for within group comparison and repeated measure ANOVA for intergroup comparison using SPSS Version 16. As patients were ambulant they continued to take their diet without further modification, and also no modification in exercise in the study groups.

**Exclusion criteria:-**

- Young patient < 18 years of age being juvenile DM-underlying cause is insulin synthesis defect.
- Old patients > 70 years age – due to less muscle activity and increase chances of associated illness.
- Pregnant females on ethical ground to avoid exposure to drugs.
- Patients with other cardiovascular diseases.
- Patients on other vasodilator drugs.
- Patients who are already receiving another member of the observational test drug.
- IDDM (Type-1 DM) due to insulin synthesis defect.(receptor level defect less likely)

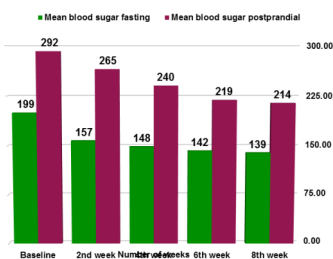
- Patients who are overweight and obese as per BMI guidelines, who have dyslipidemia.
- Patients having liver and kidney dysfunction.
- Data of patients on 20 and 80 mg of Telmisartan was excluded.

**Observation and Results:**

Table 01 and Fig 01 shows that reduction of blood sugar with coadministration of Metformin and Telmisartan caused reduction in fasting blood sugar which is significant (p<0.05) from 2nd week and reduction of postprandial from 4th week onwards. There was no episode of hypoglycaemia was reported by patient.

**Table 01: Comparison of Blood Glucose in Telmisartan treated group**

	Mean blood sugar fasting	Mean blood sugar postprandial	P value Fasting	P value Post prandial
<b>Baseline</b>	199.46 ± 34.09	291.66± 79.17		
<b>2nd week</b>	157.33 ± 38.7	264.86 ± 87.65	<0.001	0.113
<b>4th week</b>	148.3 ± 39.96	240.13 ± 83.57	<0.001	<0.001
<b>6th week</b>	141.86 ± 37.36	218.66 ± 75.64	<0.001	<0.001
<b>8th week</b>	139 ± 34	214.13 ± 71.21	<0.001	<0.001



**Fig 01: Comparison of mean fasting with postprandial blood glucose of Telmisartan group**

Table 02 and Fig 02 shows that reduction of blood sugar with coadministration of Metformin and Enalapril caused reduction in fasting blood sugar and postprandial which is significant (p<0.05) from 2nd week. There was no episode of hypoglycaemia was reported by patient.

**Table 02: Comparison of Blood Glucose in Enalapril treated group**

	Mean blood sugar fasting	Mean blood sugar postprandial	P value Fasting	P value Post prandial
<b>Baseline</b>	191.93 ±42.58	263.4 ± 71.63		

2nd week	156 ± 32.62	226.66 ± 65.25	<0.001	<0.001
4th week	139.13 ± 28.26	195.66 ± 59.17	<0.001	<0.001
6th week	114.93 ± 21.28	170.73 ± 53.06	<0.001	<0.001
8th week	104.13 ± 14.52	163.26 ± 51.18	<0.001	<0.001

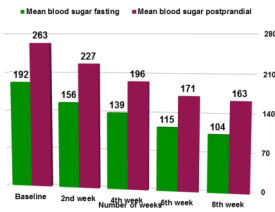


Fig 02: Comparison of mean fasting with postprandial blood glucose of Enalapril group

Table 03 and Fig 03 shows that reduction of blood sugar with coadministration of Metformin and Amlodipine caused reduction in fasting blood sugar and postprandial which is significant (p<0.05) from 2nd week. There was no episode of hypoglycaemia was reported by patient.

Table 03-Comparison of Blood Glucose in Amlodipine treated group

	Mean blood sugar fasting	Mean blood sugar postprandial	P value Fasting	P value Post prandial
Baseline	180.2 ± 35.95	278 ± 68.31		
2nd week	163.93 ± 31.82	253.13 ± 54.61	0.001	0.011
4th week	152.86 ± 33.11	242.26 ± 52.35	0.001	0.002
6th week	145.06 ± 34.89	230 ± 52.60	<0.001	0.001
8th week	144.06 ± 31.43	220.13 ± 50.30	<0.001	<0.001

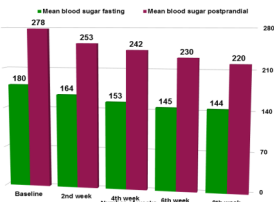
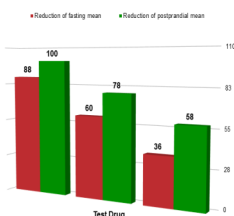


Fig 03 Comparison of mean fasting with postprandial blood glucose of Amlodipine group

Fig.04 shows intergroup comparison of the average change in blood glucose from baseline up to 8<sup>th</sup> week for all three groups. Average reduction in fasting blood glucose in Enalapril group was 87.8 mg/dl Telmisartan 60.46 mg/dl and Amlodipine 36.14 mg/dl respectively. In comparison to the three groups Enalapril group shows more reduction in average blood sugar at 8th week than Telmisartan and Amlodipine group.

Also we found similar findings in average change in post prandial blood sugar from base line to 8th week for Enalapril 100.14 mg/dl, Telmisartan 77.53 mg/dl and Amlodipine 57.87 mg/dl respectively. So there were significant reduction in fasting as well as post prandial blood sugar from base line to eighth week in Enalapril group as compared to Telmisartan and Amlodipine respectively.



**Discussion:**

Previous studies have shown that there is significant reduction in the blood glucose with Metformin + vasodilator drug when used in higher dose i.e. Telmisartan 80 mg - 12 weeks Amlodipine 5-10 mg 12 Weeks<sup>9</sup> and Enalapril 5 mg once daily 12 weeks<sup>10</sup>. Glycosylated haemoglobin estimation was hence not done on the basis of observation of previous studies where none has reported reduction in HbA1C in 8week duration. Telmisartan despite the vasodilator and PPAR gamma agonist stands second to Enalapril.

**Conclusion:**

It is concluded from this limited duration pilot study that concomitant administration of Enalapril/ Telmisartan/ Amlodipine with oral antidiabetics receiving Metformin can help in reducing blood sugar in ill controlled type 2 diabetes mellitus patients with hypertension. This is required to be confirmed in large number of patients for a similar benefit on glycemic control for which the study for 12 weeks and above is required.

**Conflict of interest :** NIL

**Funding:** NIL

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