EFFECT OF SHORT TERM GLP-1 MODIFYING THERAPY ON INTIMA MEDIA THICKNESS

Bengur Taskiran, Eylem Bahadir, Guven Baris Cansu, Ruya Mutluay

Yunus Emre State Hospital

Objectives:

- Atherosclerosis is the major cause of death in type 2 DM.
- Increased intima media thickness (IMT) denotes subclinical atherosclerosis.
- Endothelial cells express GLP-1 receptors.
- We aimed to compare the effect of sitagliptin, vildagliptin, and exenatide on IMT measurement in type 2 DM.

Methods:

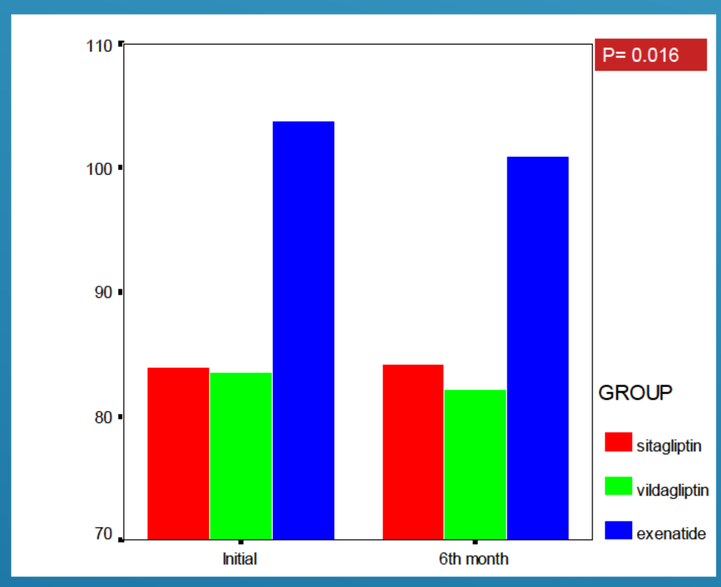
- Common carotid artery IMT was measured and the presence of plaque was evaluated by real time B mode ultrasonography (MyLab 70 XVG, Esaote SpA, Genoa, Italy) using 4.0-13.0 MHz linear probe at the beginning and 6 months of therapy.
- The distance from the media-adventitia interface to lumen-intima of common carotid artery and internal carotid artery was measured on both sides. Measurement was done 10 mm proximal and 10 mm distal to the bifurcation free of plaque respectively.
- Atherosclerotic plaque was defined as intima-media thickening over 1 mm or double that of the adjacent vascular segment.
- Haemoglobin A1c (HbA1c) was studied by HPLC.

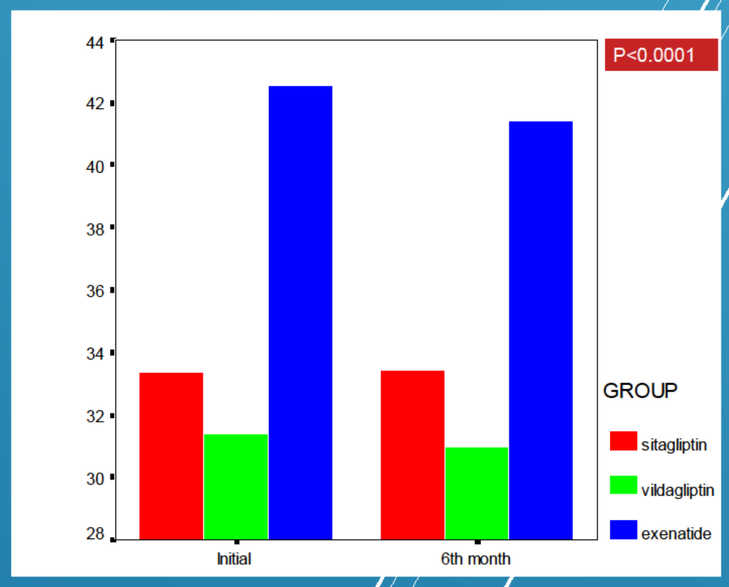
Results:

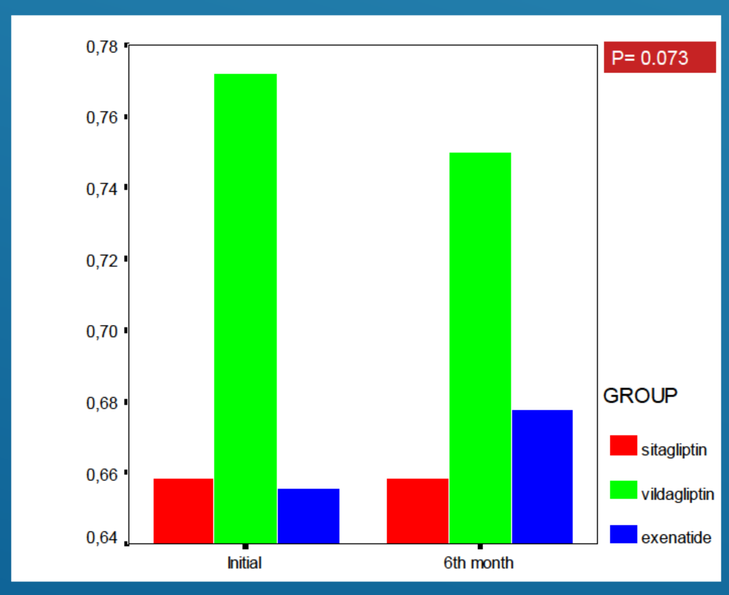
- We enrolled 24 patients (7 male, 17 female, aged 53.5±8.2 years, DM duration 4.63±4.46 years, 15 hypertensive, mean initial hemoglobin A1c %7.66±1.43) with type 2 DM.
- The patients were already using various combinations of oral antidiabetic drugs including metformin, sulphonylurea, or pioglitazone.
- Glucose, hemoglobin A1c, calcium, LDL, HDL, triglyceride, TSH, and IMT values obtained initially and at 6th month of therapy were similar in 3 treatment groups.
- Weight and BMI measured at 6th month of therapy values continued to differ significantly between 3 treatment groups (p=0.011 and p=0.001, respectively). Baseline data and p value is shown in the table.
- Right- and left-side IMT and mean IMT were similar between 3 groups both at baseline and after 6 months of therapy.
- When baseline and 6th month IMT values in each group were analyzed by Wilcoxon test, only right side IMT (lower) differed significantly after 6 months of exenatide therapy (p=0.046).
- Data at two time points were analyzed by general linear model for repeated measures test according to treatment group. Weight and BMI at baseline and 6 months of therapy were signicantly different regarding treatment groups (Figure).

	Sitagliptin (n=6)	**Vildagliptin (n=9)**	**Exenatide (n=9)**
Gender (Female)	3	6	8
Age (yrs)	56 (40-69)	55 (41-67)	55 (39-63)
DM duration (yrs)	4 (1-20)	2 (1-6)	5 (1-10)
Initial			
Weight (kg)*	83.9 (66-101)	87.1 (68.5-98.1)	100.2 (87.1-132.0)
BMI (kg/m^2)*	32.38 (26.83-36.65)	32.46 (29.13-44.7)	40.3 (36.99-51.24)
Glucose (mg/dl)	129 (104-235)	168 (121-304)	145 (9-188)
HbA1c (%)	7.6 (6.7-8.3)	7.1 (6.2-12.5)	7.8 (5.7-9.3)
Corrected calcium (mg/dl)			
LDL (mg/dl)	113.5 (80-178)	117 (60-163)	97 (44-180)
HDL (mg/dl)	40.3 (37-54)	42 (29-64)	48.2 (32-118)
TG (mg/dl)	140 (58-241)	156.5 (95-264)	153 (118-273)
TSH (mU/l)	1.58 (0.55-2.37)	1.75 (0.3-11.42)	2.09 (0.6-3.74)
Right IMT (mm)	0.7 (0.5-0.8)	0.8 (0.5-1.0)	0.7 (0.6-0.8)
Left IMT (mm)	0.7 (0.5-0.8)	0.8 (0.5-1.0)	0.7 (0.6-0.8)
Mean IMT (mm)	0.7 (0.5-0.8)	0.8 (0.5-0.9)	0.7 (0.55-0.75)
Plaque (%)	33.3	33.3	44.4

- Kruskal Wallis test. Statistically significant: p=0.006 for weight, p=0.006 and p=0.003 for BMI







Conclusions:

- In the literature:
  - Two studies with sitagliptin over 1 year of therapy decreased IMT significantly.
  - Although both decreased significantly, 12 weeks of vildagliptin therapy decreased IMT more than sitagliptin.
  - Six months of GLP-1 receptor analog therapy did not yield significant decrease in IMT.
- In our study despite small sample size and short duration, sitagliptin and vildagliptin had no and exenatide had slight effect on mean IMT in short term of therapy.
- Ongoing TRUST, PROLOGUE, and SPIKE studies will elucidate the effect of sitagliptin (over 100 patients, at least 1 year of therapy) on IMT.

References:

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