Clinical Determinants of Glycemic Response to Dipeptidyl Peptidase-4(DPP-4) Inhibitors in Type 2 Diabetes

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Introduction

There is considerable heterogeneity in glycaemic response to medications in type 2 diabetes (T2D).

Dipeptidyl peptidase-4(DPP-4) inhibitors are oral antihyperglycemic agents that are mainly used in combination with other anti-hyperglycaemic agents to treat T2D.

Glycaemic response to DPP-4Is has been shown to vary within and between study subjects of different ethnicities.

However, there are limited studies investigating determinants of response to DPP-4Is.

Methods

This study focuses on the anthropometric and clinical determinants of glycaemic response to treatment with DPP-4Is in T2D individuals (n=4996) from Tayside and Fife who are on stable treatment with DPP-4Is.

Association of baseline clinical and anthropometric variables with the change in HbA1c after 6-months of therapy was studied in non-insulin treated patients who started DPP-4 inhibitor as monotherapy or add on to other anti-hyperglycaemic drugs using step wise backward linear regression model.

Table 1 : Univariate Regression Model Estimates for Change in HbA1c(%) in patients using DPP-4Is

Variable	Estimate	Standard error	Pr(>|t|)
Age at diagnosis(years) (n=4996)	0.009	0.002	<0.001
Age at therapy(years) (n=4996)	0.008	0.002	<0.001
Body Mass Index (n=4636)	-0.011	0.003	<0.001
Sex F vs M (n=4996)	0.083	0.037	0.025
C-peptide (n=862)	0.024	0.042	0.574
HDL(mmol L) (n=4990)	-0.118	0.063	0.064
LDL(mmol L) (n=1991)	-0.068	0.036	0.056
Cholesterol(mmol L) (n=4990)	-0.061	0.018	<0.001
Triglyceride (mmol L) (n=2127)	0.000	0.019	0.987
BMI Change(n=4474)	0.048	0.018	0.010
Duration of Diabetes(years) (n=4996)	0.001	0.003	0.782
log(C-peptide) (n=862)	0.058	0.087	0.503
Drug Therapy-Mono(n=237)	-	-	-
Drug therapy –Dual (n=2680)	0.309	0.087	<0.001
Drug therapy Triple or more (n=2079)	0.282	0.088	0.001

Figure 1: Subjects in each category of antihyperglycemic drug therapy

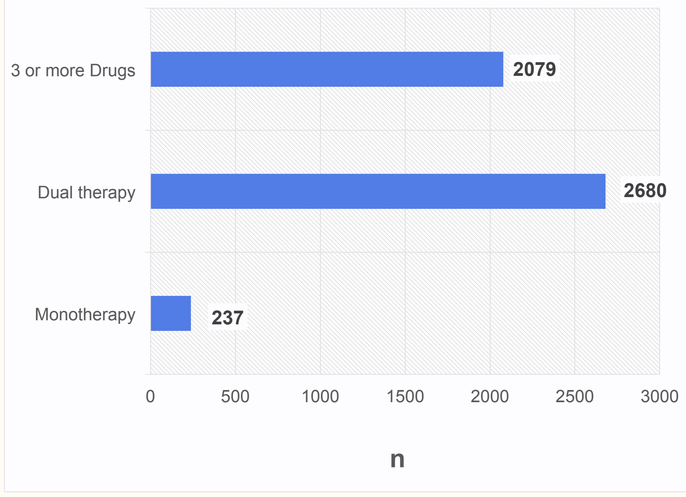

Table 2 : Multiple Regression Estimates

Variable	Estimate	Standard error	Pr(>|t|)
Age at diagnosis (Years) (n=4996)	0.007	0.009	<0.001
Body Mass Index (n=4636)	-0.008	0.003	0.004
BMI change (n=4474)	0.058	0.002	0.002
Drug therapy- Dual (n=2680)	0.414	0.116	<0.001
Drug therapy Triple or more(n=2079)	0.478	0.118	<0.001

Results

In univariate regression model- Age, Body Mass Index(BMI), Gender, Cholesterol and BMI change were found to be significant (Table 1). C-Peptide and the logarithm of C-peptide were not significant factors(Table 1).

In a model consisting of age at diagnosis, gender, BMI, HDL, Cholesterol and BMI change, combination therapy-

Age at diagnosis was found to be significant (β=0.007, P < 0.001) where older people at diagnosis respond better(Table 2).

Baseline BMI and BMI change are also associated with glycaemic response to DPP-4Is independently. BMI at baseline (β=-0.008, P=0.004) and the change in BMI (β=0.058,P= 0.002) were also associated with glycaemic response to DPP-4Is (Table 2).

Obese people at baseline had poor response and weight loss is positively correlated with greater response to treatment.

Maximum number of subjects were found to be on Dual therapy(Figure 1).

Compared to Monotherapy, subjects treated on dual, triple or more diabetic drugs were found to respond better to DPP-4Is. (β=0.414, P < 0.001 and β=0.478, P = 0.001) (Table 2).

Conclusion

While Age at diagnosis and weight loss and combination therapy are associated with greater response, Baseline BMI is correlated with reduced response . This is in line with previous reports showing association of markers of insulin resistance with glycaemic response to DPP-4Is.

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