Clinical Characteristics Affecting Lobeglitazone Response in Patients with Type 2 Diabetes

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Background

Lobeglitazone (Duvie) is a novel thiazolidinedione, currently used for the treatment of type 2 diabetes (T2DM) in Korea. We investigated clinical predictive parameters responsible for the glycemic response of lobeglitazone in patients with T2DM.

Subjects and Methods

A total of 423 patients with T2DM who were treated with lobeglitazone for more than 6 months were analyzed retrospectively. Good responders were defined when patients experience a decrease of hemoglobin A1c (Δ HbA1c) of $\geq 1\%$. Multivariate logistic analyses were performed to identify parameters predictive of lobeglitazone treatment.

Results

Table 1. Phenotype comparison between patients according to lobeglitazone response

Variables	Poor responder (n = 115)	Good responder (n = 120)	P
Age, years	62.4±12.0	63.8±12.7	0.304
Male sex	93 (62.4)	95 (55.6)	0.214
DM duration, years	6.0±3.7	5.8±3.8	0.657
Medication duration, days	347.6±114.0	349.9±116.9	0.857
Body mass index, kg/m ²	24.0±3.4	24.7±4.1	0.086
HbA1c, %	7.2±1.4	8.7±1.3	<0.001
FPG, mg/dL	143.2±52.7	172.6±57.9	<0.001
PP2, mg/dL	224.4±92.7	280.5±84.3	<0.001
Fasting C-peptide, ng/mL	2.4±1.8	3.2±2.2	0.007
Fasting insulin, μ U/mL	8.9±8.3	12.0±10.6	0.023
HOMA-IR	3.6±5.7	5.1±5.5	0.056
HOMA-B	45.1±37.7	59.2±77.1	0.104
Total cholesterol, mg/dL	158.1±40.2	165.5±38.8	0.097
Triglyceride, mg/dL	130.6±101.9	150.4±87.2	0.066
HDL-C, mg/dL	46.7±12.1	44.4±11.4	0.086
LDL-C, mg/dL	85.5±30.9	92.0±30.4	0.185
BUN, mg/dL	18.0±8.4	19.8±9.6	0.078
Creatinine, mg/dL	1.1±0.9	1.0±0.6	0.644
AST, IU/L	23.4±13.0	25.7±26.3	0.348
ALT, IU/L	24.7±18.7	29.2±36.8	0.182
Other antidiabetic drugs			
Insulin	34 (22.8)	51 (29.8)	0.157
Metformin	88 (59.1)	101 (59.1)	0.999
Sulfonylurea	39 (26.2)	39 (22.8)	0.484
DPP4 inhibitor	45 (30.2)	69 (40.4)	0.059

Table 2. Changes in anthropometric and biochemical parameters

Variables	Baseline	Follow up	P-value
HbA1c, %	7.5±1.1	6.9±1.0	<0.001
FPG, mg/dL	146.4±40.7	132.5±35.6	<0.001
PP2, mg/dL	230.5±73.2	207.2±67.3	<0.001
Fasting C-peptide	2.7±1.8	2.0±0.9	<0.001
Fasting insulin	10.8±12.1	8.0±5.0	<0.001
HOMA-IR	4.2±5.5	2.6±1.8	<0.001
HOMA-B	54.8±70.7	49.2±35.9	0.582
Total cholesterol, mg/dL	161.6±37.6	165.9±35.4	0.020
Triglyceride, mg/dL	146.5±86.3	133.4±81.3	0.003
HDL-C, mg/dL	44.7±11.0	48.6±12.2	<0.001
LDL-C, mg/dL	88.6±31.9	89.8±29.3	0.371
BUN, mg/dL	17.9±8.6	18.2±7.8	0.353
Creatinine, mg/dL	1.0±0.7	1.0±0.7	0.787
AST, IU/L	25.5±19.5	23.8±14.1	0.071
ALT, IU/L	28.9±28.4	23.9±17.9	<0.001
Body weight, kg	66.2±12.2	67.4±12.2	<0.001
Body mass index, kg/m ²	24.8±3.6	25.3±3.7	<0.001

Table 3. Multiple regression analysis for better glycemic response of lobeglitazone

Variables	Model 1		Model 2	
	β	P	β	P
Age, years	0.002	0.571	-0.001	0.804
Sex, female	0.172	0.103	0.077	0.506
Initial BMI, kg/m ²	0.040	0.005	0.032	0.038
DM duration, years	-0.021	0.148	-0.055	<0.001
Baseline HbA1c, %	0.563	<0.001	0.553	<0.001
Fasting C-peptide, ng/mL	0.088	0.019	0.066	0.042
Triglyceride, mg/dL	0.001	0.369	0.001	0.535

Model 1: unadjusted
Model 2: age, sex, initial BMI, diabetes duration, baseline HbA1c, fasting C-peptide level, and triglyceride adjustment.

Conclusion

After lobeglitazone administration for median 350 days, mean HbA1c levels were decreased by 0.6% from 7.5 ± 1.1% to 6.9 ± 1.0%. In the multivariate analysis, higher BMI, shorter diabetes duration, higher baseline HbA1c and fasting C-peptide level remained independent predictors for a good response (all P <0.05). Regarding adverse effects, weight gain was 1.3kg, from 65.6 ± 12.1kg to 66.9 ± 12.5kg, and there was no serious side effects.

With lobeglitazone treatment, a better response can be expected in obese T2DM patients with inadequate glycemic control, long-standing diabetes, and severe insulin resistance.