AD-0284) Therapeutic effect of 4 oral hypoglycemic agent in patients with type 2 diabetes mellitus who have limitation to insulin

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Abstract

Aim : The purpose of this study was to evaluate the clinical efficacy of four oral hypoglycemic agents combination therapy (4-OHA) in patients with poorly controlled type 2 diabetes mellitus (T2DM) who cannot accept insulin therapy.

Methods : Forty-seven patients with T2DM were enrolled according to the following criteria: 1) HbA1c > 8.5% (69 mmol/mol); 2) ongoing treatment with 3-OHA combination (metformin, sulfonylurea, and dipeptidyl peptidase-4 inhibitor); 3) limitations for the application of insulin therapy. The patients were administered the fourth OHA (pioglitazone) in addition to the previous treatment for 24 months. We evaluated changes in HbA1c, body weight, hypoglycemia events, and side effects. The control group consisted of 50 patients who underwent basal insulin therapy under identical clinical conditions.

Results : At study completion, there were no significant differences in HbA1c improvement between the 4-OHA group and the control group [-1.41 vs -1.56% (-15.4 vs -17.1 mmol/mol), P=0.207]. There were also no differences in hypoglycemic events (n=10 vs 14, P=0.298) and weight gain (+2.79 vs +2.30kg, P=0.21)

Conclusion : The 4-OHA combination therapy has sufficient glucose lowering effects in some patients. When insulin is not feasible, 4-OHA combination therapy may be considered as an alternative therapy.

Result

Background & Study subjects

- Diabetes patients with limited insulin therapy are actually present.
- There is still no additional treatment option for patients who cannot accept insulin therapy
- The effectiveness of the 4-OHA needs to be verified.
- Included criteria
 - HbA1c > 8.5% (69 mmol/mol) &
 - Received treatment with three OHAs for more than 6 months &
 - Can not receive insulin therapy despite past attempts

Table 1. Baseline clinical characteristics of subjects

Parameters	4-OHA (n=47)	Control (n=50)	p
Age (years)	62.6 ± 11.4	60.4 ± 9.9	0.314
Male sex, n (%)	24 (51.1%)	34 (68%)	0.101
Height (cm)	162.4 ± 0.1	163.9 ± 0.9	0.434
Weight (Kg)	66.7 ± 12.2	68.7 ± 11.8	0.218
BMI (Kg/m ²)	25.2 ± 3.8	25.9 ± 3.5	0.397
Duration of diabetes (yr)	14.5 ± 7.5	13.5 ± 5.6	0.470
Serum creatinine (mg/dL)	0.78 ± 0.21	0.83 ± 0.20	0.242
Initial HbA1c (%)	9.6 ± 1.0	10.1 ± 0.9	0.067
Comorbidity, n (%)			
HTN	22 (46.8%)	21 (42.0%)	0.205
CVD history	6 (12.8 %)	15 (30.0%)	
Oral hypoglycemic agents			
Sulfonylurea use			
Glimepiride, n (%)	33 (70.2%)	40 (80.0%)	0.496
/ mean dose (mg)	/ 7.0 ± 2.1	/ 7.3 ± 1.5	
Gliclazide, n (%)	14 (29.8%)	10 (20.0%)	0.189
/ mean dose (mg)	/ 253.3 ± 101.9	/ 146.0 ± 74.1	
Metformin use, n (%)	47 (100%)	50 (100%)	0.892
/ mean dose (mg)	/ 1938.3 ± 435.7	/ 1949.0 ± 326.7	
DPP4 inhibitor, n(%)			0.365
Sitagliptin (%)	25 (53.2%)	26 (52.0%)	
Vildagliptin (%)	8 (17.0%)	13 (26.0%)	
Linagliptin (%)	14 (29.8%)	11 (22.0%)	

Table 2. Comparison of clinical characteristics between good responder and non-responder in 4 oral hypoglycemic agents group, defined as decrease of HbA1c ≥ 2.0%

Parameters	Good responder (n=31)	Non-responder (n=16)	p
Age (years)	61.71 ± 11.08	64.44 ± 12.27	0.462
Male sex (%)			
Height (cm)	162.1 ± 9.0	162.9 ± 12.4	0.830
Weight (Kg)	67.96 ± 12.54	64.18 ± 11.49	0.308
Duration of diabetes (yr)	15.65 ± 7.16	12.19 ± 7.75	0.148
Initial HbA1c (%)	9.52 ± 0.84	9.75 ± 1.29	0.515
After HbA1c (%)	7.31 ± 0.55	9.39 ± 1.46	<0.05
Decreased HbA1c (%)	2.19 ± 0.87	0.35 ± 0.44	<0.05
Fasting glucose (mg/dL)	182.3 ± 10.9	189.5 ± 19.3	0.559
Creatinine (mg/dL)	0.77 ± 0.21	0.80 ± 0.22	0.564
C-peptide (ng/mL)	4.41 ± 3.46	5.62 ± 5.14	0.423
HOMA-IR	3.92 ± 3.18	5.86 ± 9.26	0.309
HOMA-beta	83.22 ± 56.01	65.20 ± 51.90	0.296

Figure 1. Change of mean HbA1c.

- No significant difference in the improvement of HbA1c between the 4-OHA group and control group (-1.41 % vs -1.56 % at 24 months, P=0.207).

Figure 2. Change of difference from baseline HbA1c

Figure 3. Change of mean body weight.

- No significant difference in the weight gain between the 4-OHA group and the control group (+2.79 kg vs +1.30kg at 24 months, P=0.21).

Summary

- 1.56% after 1 year and 1.41% after 2 years showed a decrease in HbA1c, when the addition of pioglitazone 15mg as a fourth drug to patients with type 2 diabetes who were uncontrolled blood glucose during three oral hypoglycemic agent(OHA) therapy (sulfonylurea, metformin, DPP4-inhibitor)
- 4-OHA therapy showed similar blood glucose lowering effect compared with the basal insulin-added control group
- If insulin treatment is not feasible, 4-OHA therapy may be considered a second option