Incretin secretion was not impaired in obese Korean children and adolescents with type 2 diabetes

So Hyun Park[a], Jae Hong Kim[a], Won Gyung Cho[b], Min Ho Jung[c], Sin Hee Kim[d], Gyung Sun Cho[e], Moon Bae Ahn[c], In A Jung[b], Yeon Jin Jeon[b] & Byung Kyu Suh[b]

[a]St. Vincent's Hospital; [b]Seoul St. Mary's Hospital; [c]Yeouido St. Mary's Hospital; [d] Incheon St. Mary's Hospital; [e]Bucheon St. Mary's Hospital, Republic of Korea, The Catholic University of Korea

OBJECTIVES

The role of incretins in type 2 diabetes (T2D) is controversial. This study investigated the association between incretin levels in obese Korean children and adolescents with T2D.

METHODS

We performed a 2-hr oral glucose tolerance test in obese children and adolescents with T2D and with normal glucose tolerance. Twelve obese children and adolescents with newly diagnosed T2D (DM1 group) and 12 obese age-matched subjects without T2D (NDM group) were included. An oral glucose tolerance test (OGTT) was conducted and insulin, C-peptide, glucagon, glucagon-like peptide-1 (GLP-1), and glucose-dependent insulinotropic polypeptide (GIP) were measured during the OGTT. Follow-up OGTT was done to 6 patients of the DM group (DM2 group) after three day discontinuation of oral hypoglycemic agent.

Table 1. Demographics and clinical characteristics of the subjects with obese type 2 diabetes at initial diagnosis (DM1), follow-up (DM2) and obese non-diabetes (NDM).

Characteristics	NDM (n=12)	DM1 (n=12)	DM2 (n=6)	*P* value (NDM vs DM1)	*P* value (NDM vs DM2)	*P* value (DM1 vs DM2)	*P* value (3 groups)
Age (years)	13.2 ± 2.2	14.4 ± 1.7		0.192			
Gender (%)				>0.999			
Male	7 (58.3)	8 (66.7)					
Female	5 (41.7)	4 (33.3)					
Tanner stage				0.400			
II–III	6 (50)	3 (25)					
IV–V	6 (50)	9 (75)					
BMI	30.0 ± 3.5	28.5 ± 3.9		0.237			
BMI Z-score	2.3 ± 0.5	1.9 ± 0.5		0.085			
Waist to hip ratio †	0.9 ± 0.1	0.9 ± 0.1	0.8±0.1	0.295	0.029	0.396	0.111
Total cholesterol (mg/dl)	172.4 ± 27.9	211.3 ± 43.7	154.8±42.3	0.015	0.399	0.035	0.018
LDL (mg/dl)	111.8 ± 24.9	135.7 ± 37.5	98.4±33.3	0.083	0.526	0.155	0.129
HDL (mg/dl)	40.3 ± 5.5	35.4 ± 13.2	42.6±11.1	0.248	0.958	0.370	0.424
Triglyceride (mg/dl)	102.0 ± 46.9	233.3 ± 392.9	62.8±36.5	0.326	0.044	0.028	0.040
FBS (mmol/l)	5.2 ± 0.5	12.2 ± 5.0	5.3±0.9	<0.001	0.742	0.002	<0.001
HbA1c (%)	5.5 ± 0.1	11.5 ± 2.2	6.0±0.6	<0.001	0.056	0.001	<0.001
HOMA-IR	8.0 ± 3.2	6.9 ± 3.0	3.4±4.3	0.507	0.017	0.035	0.033
HOMA- β	446.6 ± 202.1	52.5 ± 46.5	188.4±223.8	<0.001	0.017	0.044	<0.001
IGI (mU/mmol)	40.1 ± 18.0	1.9 ± 3.8	8.7±9.9	<0.001	0.003	0.017	<0.001

Figure 1. comparisons of the hormone secretion of the 3 groups

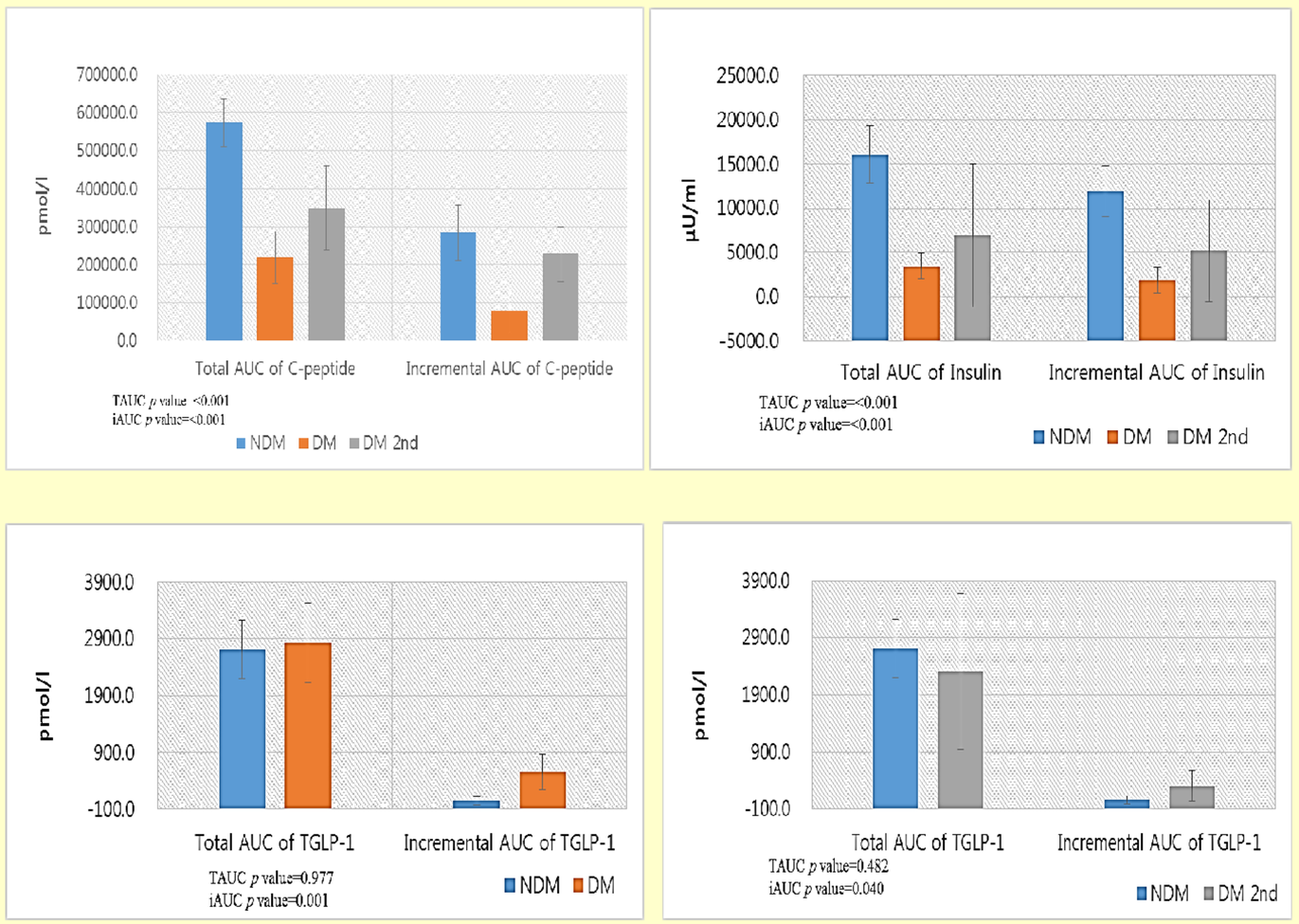
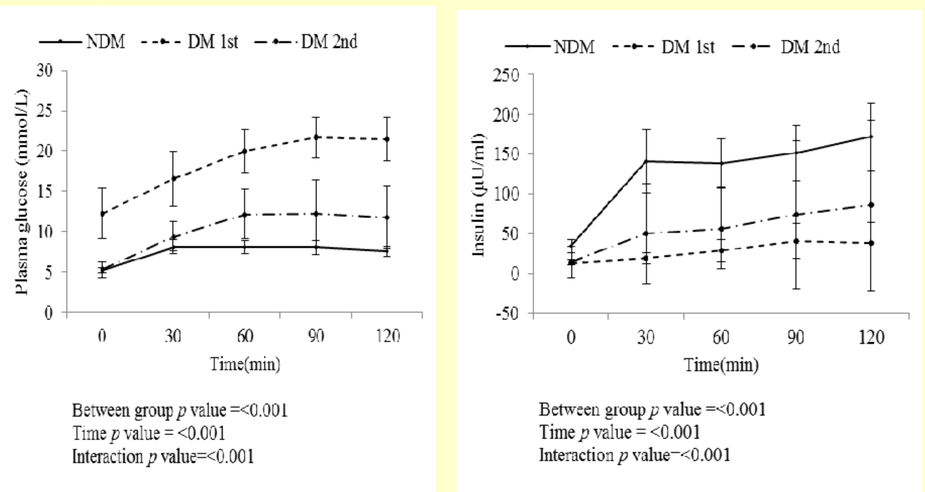


Table 2. comparisons of the hormone secretion of the 3 groups

	NDM (n=12)	DM1 (n=12)	DM2 (n=6)	comparing three groups	differences between the two groups		
					NDM vs DM1	NDM vs DM2	DM 1 vs DM2
				P value	*P* value	*P* value	*P* value
Insulin TAUC (μU/ml)	16039.0±1486.5	3431.0±666.7	6929.6±3147.5	<0.001	<0.001	0.022	0.242
C-peptideTAUC (pmol/l)	573425.0±28499.0	218862.5±30902.7	348210.0±42790.5	<0.001	<0.001	0.002	0.044
GlucagonTAUC (pmol/l)	1020.4±114.0	1177.1±189.4	972.5±203.6	0.841	0.708	0.888	0.607
TGLP-1 TAUC (pmol/l)	2712.2±233.8	2827.5±322.1	2305.7±531.0	0.579	0.977	0.482	0.281
iGLP-1 TAUC (pmol)	1227.4±150.4	1693.0±340.5	935.4±134.1	0.133	0.371	0.174	0.068
GIP TAUC (pmol/l)	2685.0±457.7	3340.4±511.2	3156.4±878.5	0.518	0.237	0.888	0.673
Insulin iAUC (μU/ml)	11884.9±1301.7	1848.1±667.9	5149.4±2232.9	<0.001	<0.001	0.013	0.147
C-peptide iAUC (pmol/l)	283994.4±33823.2	79053.2±26316.7	228130.0±27565.1	<0.001	0.001	0.281	0.008
Glucagon iAUC (pmol/l)	0.0±0.0	136.7±49.6	57.4±50.8	<0.001	<0.001	0.001	0.174
TGLP-1 iAUC (pmol/l)	54.3±33.9	552.1±138.3	298.4±106.4	0.003	0.001	0.040	0.349
iGLP-1 iAUC (pmol)	309.8±84.5	717.4±251.5	143.4±63.8	0.041	0.237	0.122	0.017
GIP iAUC (pmol/l)	1747.4±284.4	2714.9±471.9	2686.4±870.6	0.212	0.069	0.607	0.607

Figure 2. Basal and stimulated responses of plasma glucose (a) and insulin during the oral glucose tolerance test



RESULTS

The mean age of the patients was 13.8 ± 2.0 years, and the mean body mass index (BMI) Z-score was 2.1 ± 0.5. DM and NDM groups were comparable in age, sex, BMI Z-score, and waist:hip ratio. The DM1 group had significantly lower homeostasis model assessment of β (HOMA-β) and insulinogenic index (IGI) values (*P* < 0.001). The homeostasis model assessment of insulin resistance (HOMA-IR) index was not different between the two groups. Insulin and C-peptide secretions were significantly lower in the DM1 group than in the NDM group (P < 0.001). Total GLP-1 (TGLP-1) secretion was significantly higher in the DM1 group while intact GLP-1 (iGLP-1) and GIP secretion values were not significantly different between the two groups. Comparing DM1 and DM2 groups, FBS, BMI, HbA1c, HOMA-IR, and IGI values were significantly lower in the DM1 group than in the DM2 group (P < 0.05). HOMA- β was higher in the DM1 group than in the DM2 group (*P* = 0.017). TGLP-1 and GIP secretion values were not significantly different in the DM1 and DM2 group, however, iGLP-1 secretion was significantly lower in the DM2 group than in the DM1 group (*P* = 0.017). Comparing DM2 and NDM groups, TGLP-1 secretion was significantly higher in the DM2 group than in the NDM group (*P* = 0.04), however, iGLP-1 and GIP secretion values were not significantly different.

CONCLUSIONS

Impaired insulin secretion might be important in the pathogenesis of T2D in obese Korean children and adolescents, however, which may not be attributed to incretin secretion. Although patients had wash-out period, oral hypoglycemic agent might be able to influence on incretin secretion.

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SO HYUN PARK

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