

당뇨병 약물치료의 실제



김 철 식

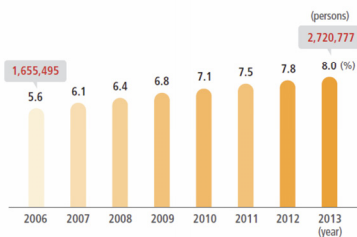
한림대성심병원 내분비내과

Medical Management of Hyperglycemia in Diabetes Mellitus

CS Kim, MD, PhD

Endocrinology Div., HUMC

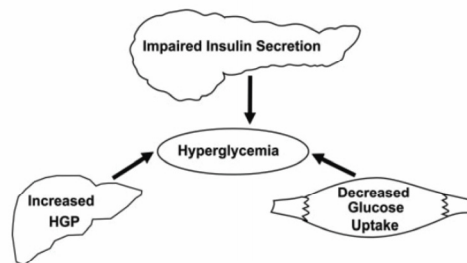
Trend in prevalence of diabetes in Korea



Prevalence
= [(Patients who had type 2 diabetes based on ICD-10 code and were being treated with antidiabetic agents)/(total subjects visiting hospitals or clinics or having health security service in each year)] X 100 (%)

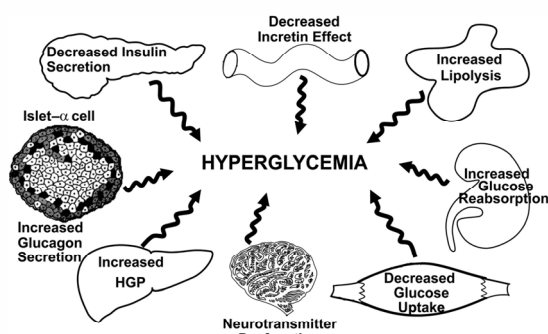
Korean Diabetes Fact Sheet 2015

Pathogenesis of type 2 diabetes: "the triumvirate"



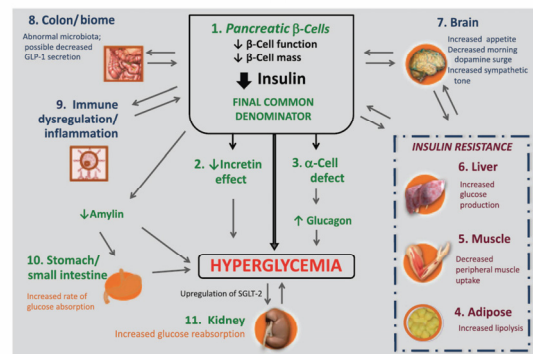
Diabetes 2009;58:773-95

"Ominous Octet"



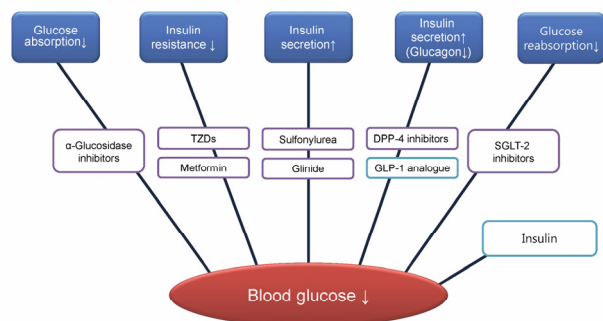
Banting Lecture. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. Diabetes 2009;58:773-95

"Egregious Eleven"



Schwartz SS et al., Diabetes Care. 2016 Feb;39(2):179-86

Anti-diabetes medications available in Korea



Case

- 45 year old man
- High blood glucose in health check-up
- PHx
 - HTN (4 yrs), Fatty liver disease, Smoking(-)
 - Prediabetes 2 years ago, no f/u
- FHx
 - Mother: T2DM
- Anthropometric data
 - Ht 173 cm, Wt 67 kg, BMI 22.4 kg/m²
 - WC 96 cm

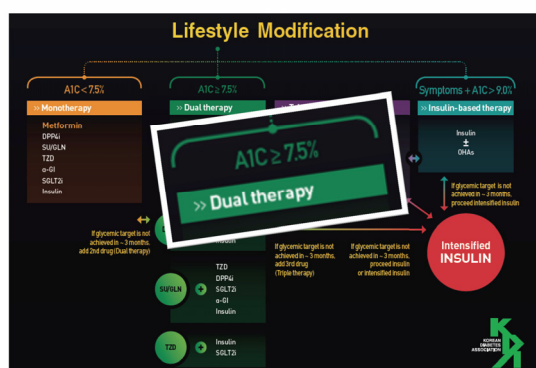
Case

- BP 125/75 mmHg
- Biochemical tests
 - FBS 143 mg/dL, PP2hr 246 mg/dL, Hb A1c 8.1%
 - TC/TG/HDL-C 230/267/39 mg/dL
 - calculated LDL-C 138 mg/dL
 - Insulin 8 μU/mL, C-peptide 1.3 ng/mL

Case

- Preferential treatment strategy?
 - ① Lifestyle modification only
 - ② Monotherapy
 - ③ Dual therapy
 - ④ Triple therapy
 - ⑤ Insulin monotherapy (or Insulin + OAD)

Treatment Guideline for Diabetes, KDA 2015



Case

- What are the medication given priority?
 - ① Metformin
 - ② Sulfonylurea
 - ③ Meglitinide
 - ④ α-glucosidase inhibitor
 - ⑤ Thiazolidinedione (TZD)
 - ⑥ Dipeptidyl peptidase-4 (DPP4) inhibitor
 - ⑦ sodium/glucose cotransporter-2 (SGLT2) inhibitor
 - ⑧ Glucagon-like peptide-1 (GLP-1) analogue
 - ⑨ Insulin

Considerations for selection

- Insulin resistance
- Insulin secretion

Patients

- Efficacy
- Adverse effects

Medications

Diagnosing Insulin Resistance

- **Clamp test**
- **Short insulin tolerance test**
- **Co-existence with**
 - Obesity
 - Abdominal obesity
 - Metabolic SD
 - PCOS
 - Acanthosis nigricans
- **HOMA-IR**
 - $\text{glucose} \times \text{insulin} / 405$, This patient, 2.8

Korean definition for the Metabolic Syndrome

Risk factor	Defining Level
Abdominal Obesity	Waist Circumference
Men	> 90 cm
Women	> 80 cm*
Triglycerides	$\geq 150 \text{ mg/dL}$
HDL cholesterol	
Men	< 40 mg/dL
Women	< 50 mg/dL
Blood pressure	$\geq 130/85 \text{ mmHg}$ or medication
Fasting glucose	$> 100 \text{ mg/dL}$ or medication

3 or more of these components are needed to define metabolic syndrome,
* Waist circumference cutoff point for women can be redefined.

당뇨병학회 대사증후군 소연구회 KDA 진료지침 2013

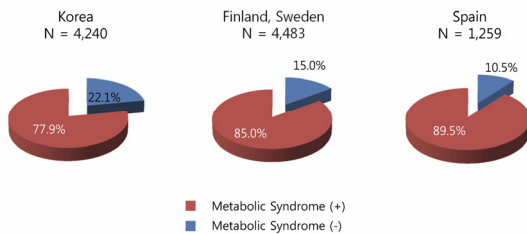
Clinical implications of metabolic syndrome



• CVD: cardiovascular disease
• T2D: Type 2 diabetes

Diabetes Care 2010;33:1865-1871
J Clin Endocrinol Metab 2004;89:2595-2600

Prevalence of metabolic syndrome in subjects of type 2 diabetes



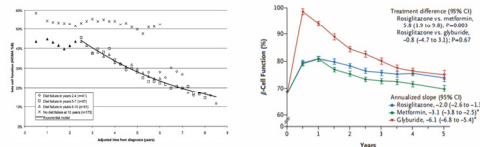
Korea Diabetes Association data, Korean Diabetes J 33:40-47, 2009
Botnia study, Diabetes Care 24:683-689, 2001
Rodriguez A. Et al., Endocrinol Nutr. 2010;57:60-70

Case

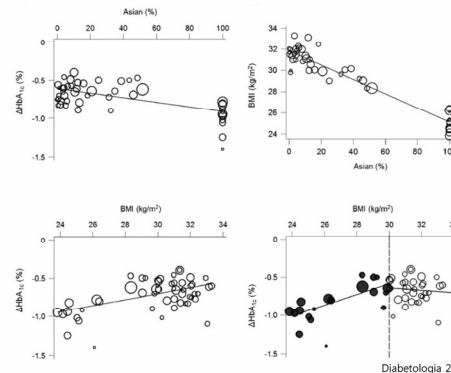
- Hx
 - HTN (4 yrs), Fatty liver disease, Smoking(-)
 - Prediabetes 2 years ago, no f/u
- Anthropometric data
 - Ht 173 cm, Wt 67 kg, BMI 22.4 kg/m²
 - WC 96 cm
- BP 125/75 mmHg
- Biochemical tests
 - FBS 143 mg/dL, PP2hr 246 mg/dL, Hb A1c 8.1%
 - TC/TG/HDL-C 230/267/39 mg/dL
 - calculated LDL-C 138 mg/dL
 - Insulin 8 $\mu\text{IU/mL}$, C-peptide 1.3 ng/mL

Diagnosing Insulin Secretory Function

- **HOMA-β (%)**
 - $(360 \times \text{insulin}) / (\text{glucose} - 63)$
 - This patient, 35%
- **C-peptide**
 - 1.3 ng/mL
- **Duration of diabetes**



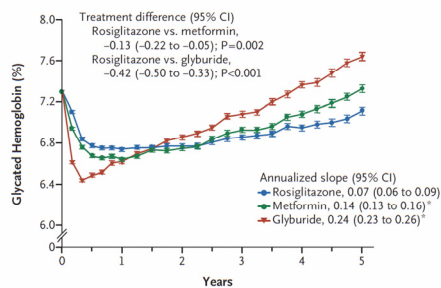
Glucose-lowering efficacy of DPP-4 inhibitors between Asians and non-Asians



Diabetologia 2013; 56(4): 696-708

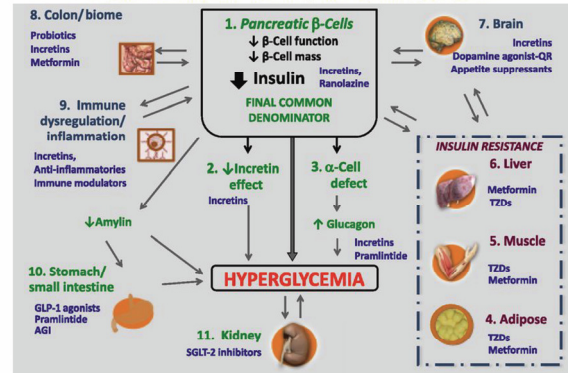
Durability of the medications

A Diabetes Outcome Progression Trial (ADOPT)



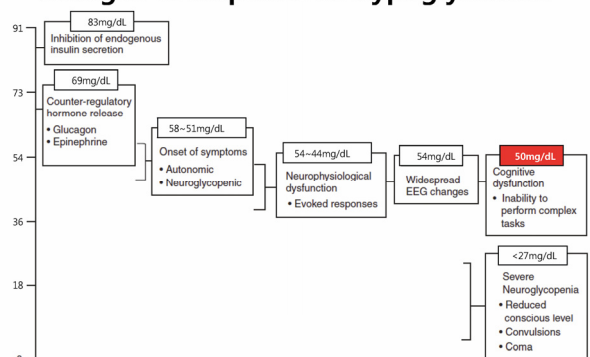
N Engl J Med 2006;355:2427-43

β-Cell-Centric Construct: Egregious Eleven Targeted Treatments for Mediating Pathways of Hyperglycemia



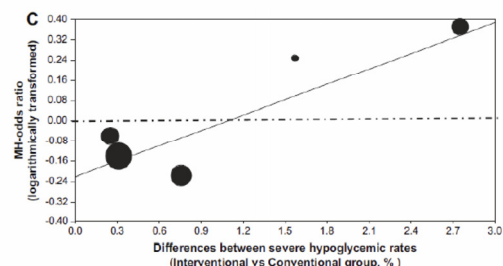
Stanley S. Schwartz et al. Dia Care 2016;39:179-186

Symptomatic and physiological changes in response to hypoglycaemia



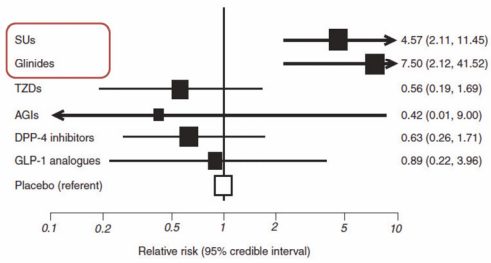
Adapted from Frier and Fisher in Hypoglycemia in Clinical Diabetes

Risk of severe hypoglycemia and CV death in patient with intensive treatment of diabetes



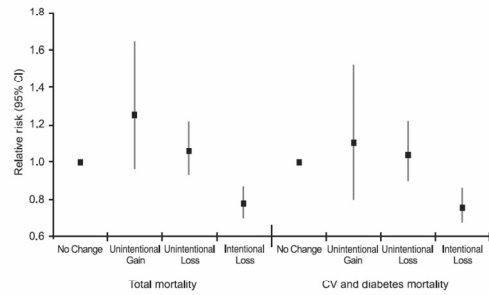
Nutrition, Metabolism & Cardiovascular Diseases (2009) 19, 604e612

Effect of antidiabetic medications on hypoglycemia in type 2 diabetes



JAMA 2010;303:1410-18

Impact of weight gain on outcomes in type 2 diabetes



Current Medical Research & Opinion 2011;27:1431-1438

Medication specific weight change

Weight Gain	Weight Neutral	Weight Loss
Insulin SU Meglitinide TZD*	Metformin* α-Gi DPP4i	GLP-1 analogue SGLT-2 inhibitor

Anti-diabetes medications available in Korea

