Glucagon-like peptide-1 (GLP-1) stimulates insulin secretion and then somatostatin secretion in rat islets.

Seungjoon Oh[1,2], So Young Park[2], Kwang Sik Suh[2], Sung-Woon Kim[1,2]

[1]Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine; [2]Research Institute of Endocrinology, Kyung Hee University Hospital, Seoul, Korea

Abstract

- **Objective :** GLP-1 is known to stimulate insulin and somatostatin secretion in pancreatic islet cells. The exogenous somatostatin inhibits insulin secretion, but GLP-1 increases insulin secretion in spite of stimulating somatostatin secretion from d-cell. So, we investigated whether there exists a time difference of insulin and somatostatin secretion after GLP-1 stimulation or insulin secretion depends on secreted GLP-1 or somatostatin concentration inside the islets.
- **Methods:** We isolated pancreatic islets from five 8-week-old Sprague Dawley rats by collagenase digestion. The islets were incubated in RPMI1640 medium before experiments. In vitro, insulin and somatostatin measured at 5, 10, 30 minutes depending on glucose (2.7, 5.5 and 16.7 mM as hypo-, normo-, and hyperglycemic condition respectively) and GLP-1 concentrations (0, 0.1, and 10 ng/mL) from culture media using ELISA kit. Each well contained 30 islets per well.
- **Results:** Insulin secretion showed continuously increased by time and GLP-1 concentration at any glucose concentration. Somatostatin secretion was increased significantly 10 minutes later after GLP-1 administration at hypo- and normoglycemia. However, in hyperglycemia, insulin secretion showed the same pattern compared with the other glycemic conditions, but somatostatin was maximally stimulated until 10 minutes and decreased without GLP-1 administration. Adding the GLP-1, somatostatin was increased continuously until 30 minutes. This suggested hyperglycemic condition itself might need more insulin secretion in the ß-cell than somatostatin secretion in d-cell. Therefore, we observed time lag of intraislet somatostatin secretion after GLP-1 stimulation.
- **Conclusion:** We observed earlier GLP-1 induced insulin secretion in ß-cell than somatostatin secretion in d-cell of rat islets. Hyperglycemic condition might primarily secrete insulin and inhibit somatostatin secretion inside the islets.

Background

- GLP-1 is known to stimulate insulin and somatostatin secretion in pancreatic islet cells.
- The exogenous somatostatin inhibits insulin secretion. But GLP-1 increases insulin secretion in spite of stimulating somatostatin secretion from beta-cell.
- Purpose
  - ❖ existence of a time difference of insulin and somatostatin secretion inside the islets after GLP-1 stimulation
  - ❖ insulin secretion rate in accordance with GLP-1 or somatostatin concentration inside the pancreatic islet cells

Materials and Methods

- The pancreatic islets were isolated form 8-week-old Sprague Dawley rats by collagenase digestion and incubated in RPMI 1640 medium.
- In vitro, insulin and somatostatin measured at 5, 10, 30 minutes depending on
  - ❖ **glucose concentration**
    - Hypoglycemia (2.7 mM)
    - Normoglycemia (5.5 mM)
    - Hyperglycemia (16.7 mM)
  - ❖ **GLP-1 concentration**
    - 0 ng/mL
    - 0.01 ng/mL
    - 10 ng/mL
- 30 islets per well
- Analysis with ELISA kit.

Results

- Hypoglycemia (2.7 mM) (Table 1, Figure 1A)
  - ❖ Insulin secretion
    : continuously increased by time and GLP-1 concentration.
  - ❖ Somatostatin secretion
    : increased significantly 10 minutes later after GLP-1 administration.
- Normoglycemia (5.5 mM) (Table 2, Figure 1B)
  - ❖ Insulin secretion
    : continuously increased by time and GLP-1 concentration.
  - ❖ Somatostatin secretion
    : increased significantly 10 minutes later after GLP-1 administration.
- Hyperglycemia (16.7 mM) (Table 3, Figure 1C)
  - ❖ Insulin secretion
    : continuously increased by time and GLP-1 concentration.
  - ❖ Somatostatin secretion
    : maximally stimulated until 10 minutes and decreased without GLP-1 administration.
    : increased continuously until 30 minutes after GLP-1 administration.

Table 1. In hypoglycemia, insulin and somatostatin concentration depending on GLP-1.

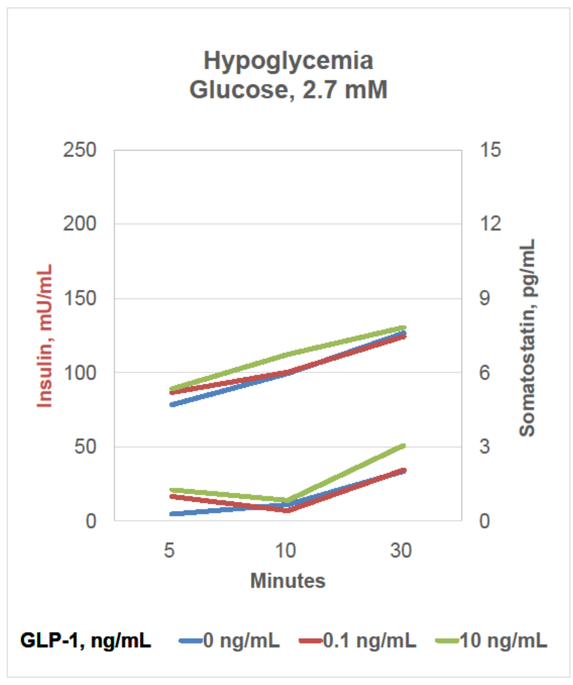
Hypoclycemia (glucose 2.7 mM)				
		5 min	10 min	30 min
GLP-1 0 ng/mL	Insulin(mU/mL)	78.4	99.5	126.7
	Somatostatin(pg/mL)	0.28	0.67	2.02
GLP-1 0.1 ng/mL	Insulin(mU/mL)	86.7	100.3	124.4
	Somatostatin(pg/mL)	0.99	0.42	2.07
GLP-1 10 ng/mL	Insulin(mU/mL)	89.1	112.3	130.5
	Somatostatin(pg/mL)	1.26	0.84	3.06

Table 2. In normoglycemia, insulin and somatostatin concentration depending on GLP-1.

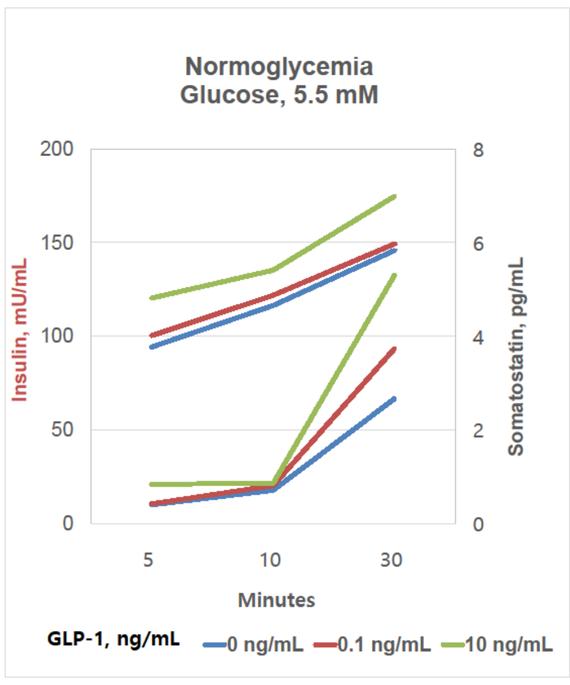
Normoglycemia (glucose 5.5 mM)				
		5 min	10 min	30 min
GLP-1 0 ng/mL	Insulin(mU/mL)	94.2	116.4	145.8
	Somatostatin(pg/mL)	0.4	0.71	2.67
GLP-1 0.1 ng/mL	Insulin(mU/mL)	100.3	121.8	149.3
	Somatostatin(pg/mL)	0.42	0.81	3.74
GLP-1 10 ng/mL	Insulin(mU/mL)	120.3	135.2	174.7
	Somatostatin(pg/mL)	0.84	0.86	5.31

Table 3. In hyperglycemia, insulin and somatostatin concentration depending on GLP-1.

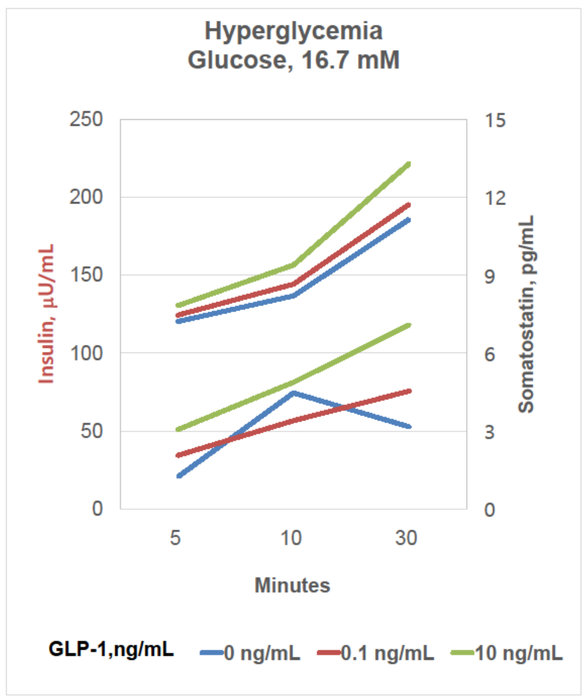
Hyperglycemia (glucose 16.7 mM)				
		5 min	10 min	30 min
GLP-1 0 ng/mL	Insulin(mU/mL)	120.3	136.7	185.7
	Somatostatin(pg/mL)	1.25	4.47	3.17
GLP-1 0.1 ng/mL	Insulin(mU/mL)	124.4	144.2	195.3
	Somatostatin(pg/mL)	2.07	3.4	4.54
GLP-1 10 ng/mL	Insulin(mU/mL)	130.5	156.5	221.4
	Somatostatin(pg/mL)	3.06	4.88	7.09



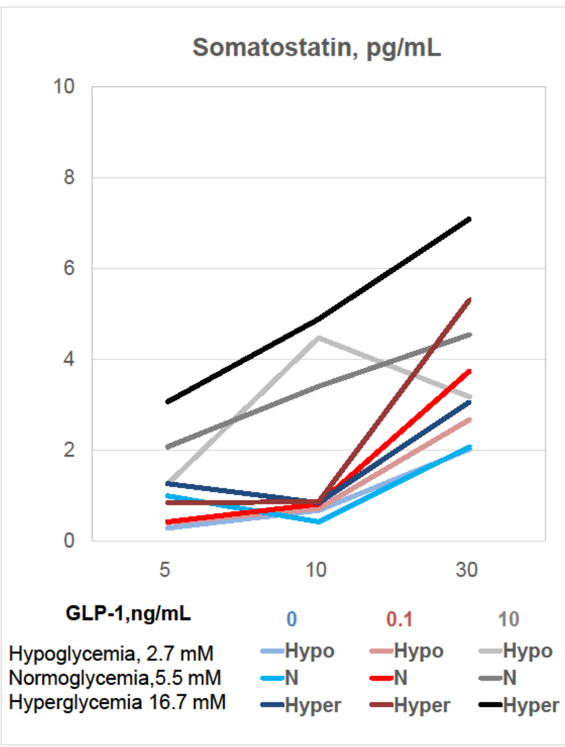
A



B



C



D

Figure 1. Insulin and Somatostatin concentration depending on GLP-1. hypoglycemia (A), normoglycemia(B) , hyperglycemia(C), somatostatin secretion rate depending on GLP-1 and glucose concentraion.

Conclusion

- Hyperglycemic condition itself might need more insulin secretion in the ß-cell than somatostatin secretion in α-cell.
- GLP-1 induced insulin secretion in ß cell is earlier than somatostatin secretion in α-cell of rat islets.

17 ECE
158--EP
Reproduction, endocrine disruptors and signalling
Sung-Woon Kim
DOI: 10.3252/pso.eu.17ece.2015
Poster presented at: ECE2015 16-20 May 2015 DUBLIN, IRELAND 17th EUROPEAN CONGRESS OF ENDOCRINOLOGY