Review Article

REGULATION OF BLOOD GLUCOSE DURING FASTING

Hamid Javaid Qureshi and Naila Hamid

Abstract : Muslims fast in the holy month of Ramadan, some also fast in Shawal and other months. After intake of sehri, blood glucose increases but as fasting continues, it falls. The main control of transition from feasting to fasting and vice versa is two pancreatic hormones, insulin and glucagon. Insulin is secreted from beta cells of pancreatic islets after sehri (food) intake and energy is stored. When blood glucose falls due to fasting, glucagon is secreted from alpha cells of pancreatic islets to release energy and blood glucose rises. During prolonged fasting, epinephrine released by sympathetic stimulation and cortisol released from adrenal cortex to maintain blood glucose level.

Keywords: Fasting, Blood Glucose, Insulin, Glucagon and Pancreatic islets.

Introduction

Fasting during the holy month of Ramdan is obligatory for all the Muslims. Some also fast during the month of Shawal and other months. There are metabolic responses leading to hyperglycemia after intake of sehri and as fasting continues, hypoglycemia develops that also leads to metabolic changes. The most important control of transition from feasting to fasting and vice versa is two pancreatic hormones insulin and glucagon.[1] After intake of food (sehri), insulin is secreted from beta cells of pancreatic islets. Insulin is a small protein having a molecular weight of 5808. Insulin is first formed as preproinsulin which is converted into proinsulin having a molecular weight of 9000. It consist of 3 peptide chains; A, B and C. Most of the proinsulin is further cleaved in Golgi apparatus to form insulin composed of A and B peptide chains connected by disulfide linkages and C chain peptide called connecting peptide (C-peptide). The insulin and C-peptide are packed in the secretory granules and secreted into the blood **Fig1**.

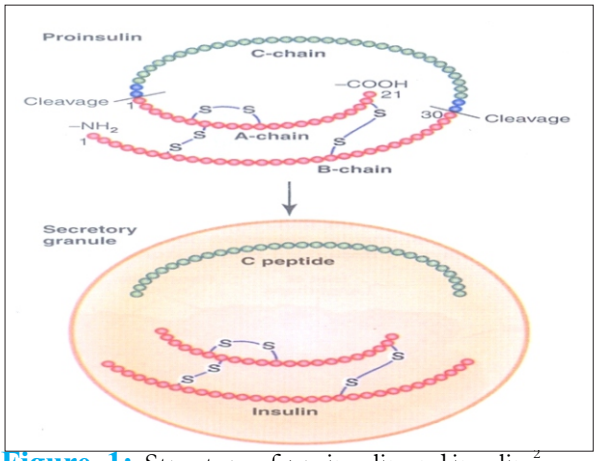

Figure -1: Structure of proinsulin and insulin.[2]

Functional activity of insulin depends upon intact disulfide linkages.[2] C-peptide concentration in the plasma can be measured by radioimmune assay and it indicates beta cells function in patients receiving exogenous insulin. Patients with type I diabetes usually have greatly decreased levels of C-peptide.[3]

Insulin secretion is stimulated by increased plasma glucose, gastrointestinal hormones like gastrin, secretin, cholecystokinin and glucose dependent insulinotrophic hormone, increased plasma aminoacid concentration arginine and lysine and hormones such as glucagon, growth hormone and cortisol.[2] Even before glucose has been reabsorbed, the gastrointestinal hormones reach the pancreatic beta cells through the blood to stimulate strongly insulin secretion. These hormones are called incretins.[1,4] After its secretion, Insulin circulates in the blood in an unbound form. It has an average plasma half life of 6 minutes, so it is mainly cleared from the circulation within 10 to 15 minutes insulin is degraded by the enzyme insulinase mainly in the liver, to a lesser extent in the kidney and muscles.[5] Insulin secretion is inhibited by potassium depletion, beta adrenergic blockers, fasting, alpha adrenergic activity and hypoglycemia.[3] When plasma glucose level is < 75 80 mg/dL, beta cells stop insulin secretio **Fig 2.**

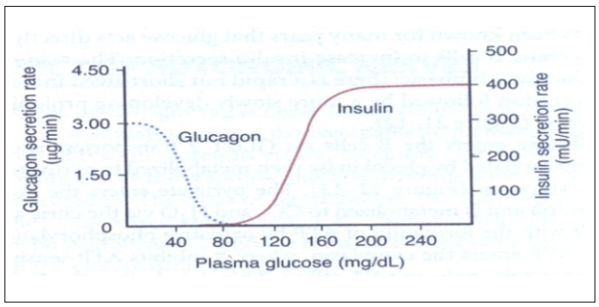

Figure-2: Effect of plasma glucose on insulin and glucagon Secretion.[3]

Fasting plasma insulin level is 10 20 μ U/mL. After a meal, it may reach to a peak of 100 μ U/mL. In a normal human. The total daily secretion of insulin may be as much as 40 U/day.[6] Beta cells increase their rates of insulin secretion within 30 seconds of exposure to increased concentration of glucose and can shut down secretion as rapidly.[7] When plasma glucose increases, it is transported into beta cells of the pancrease by the glucose transporter (GLUT 2). Inside the cells, glucose is phophorylated to glucose6phosphate, that is subsequently oxidized to form adenosine triphosphate (ATP), which inhibits ATP sensitive potassium channels of the cell membrane there by opening voltage gated calcium channels. This produces calciums influx that stimulates fusion of vesicles with the cell membrane and secretion of insulin into extracellular fluid by exocytosis **(Fig-3).**

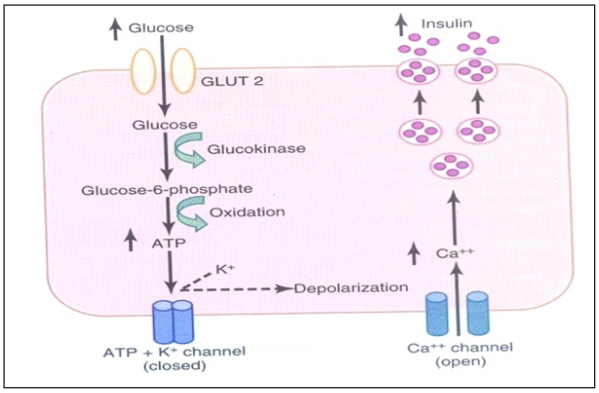

Fig-3: Basic mechanism of insulin secretion from beta cells by glucose stimulation.[2]

Somatostatin and norepinephrine (by activating alpha adrenergic receptors) inhibit exocytosis of insulin. Sulfonylurea drugs stimulate insulin secretion by binding to the ATPsensitive potassium channels and blocking their activity. This results into depolarization that triggers insulin secretion. Insulin binds with insulin receptors in the membrane of target cells, there is activation of tyrosine kinase resulting into the cellular effects.[2] Insulin is "hormone of energy storage". or "hormone of abundance" it increases stores of carbohydrates, fats and protein.[1,3] It is hypoglycemic hormone, promotes uptake of glucose by the liver cells, muscle and adipose tissue. It also increases glucose utilization. It is mainly anabolic hormone.[8] insulin primarily exerts it effects by acting on non-working skeletal muscle, liver and adipose tissue.[9] It increases glycogen synthesis by promoting the activity of enzyme glycogen synthase in the liver. Glycogen content of liver can increase upto 5 6% of the liver mass (100 grams of stored glycogen). Insulin also promotes glycogen storage in the muscle.

Insulin promotes conversion of excess glucose in the liver into fatty acids. It increases triglyceride synthesis, which are packed as very low density lipoproteins and transported via blood to the adipose tissue and deposited as fat **(Fig-4)**. Insulin inhibits action of hormone sensitive lipase in adipose tissue to prevent break down of fats to release fatty acids.[2]

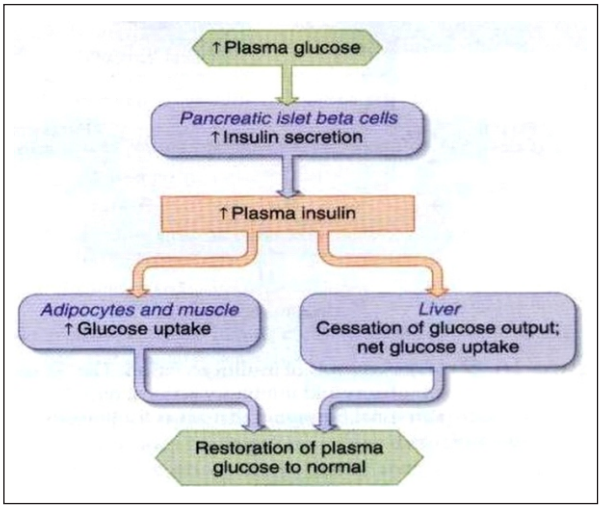

Fig-4: Nature of plasma glucose control over insulin secretion. As glucose levels increase in plasma (e.g., after a meal containing carbohydrate), insulin secretion is rapidly stimulated. The increase in insulin stimulates glucose transport from extracellular fluid into cells, thus decreasing plasma glucose concentrations. Insulin also acts to inhibit hepatic glucose output.[1]

Insulin promotes protein synthesis and growth. It stimulates transport of amino acids into cells, promotes DNA transcription and translation of messenger RNA. It inhibits protein catabolism. There is synergistic action of growth hormone and insulin to promote the growth.[3] Due to fasting, when plasma glucose decreases, glucagon is secreted from alpha cells of pancreatic islets. It is a "hormone of energy release". It is a hyperglycemic hormone. It is a polypeptide having a molecular weight of 3485. Glucagon acts on the target cells through formation of cyclic AMP.[2] Carbohydrate stores (liver and muscle glycogen) are the first energy stores to be metabolized during starvation.[10] Glucagon has a half life of 5-10 minutes in the circulation. It is degraded in many tissues particularly by the liver. When plasma glucose falls below 80 90 mg/dL, glucagon secretion increases. In addition to decreased plasma glucoses,

exercise and beta adrenergic stimulation also stimulate glucagon secretion.[3]

Glucagon causes break down of glycogen (glycogenolysis) in the liver by activating the enzyme phosphorylase and increases plasma glucose.2 Increases gluconeogenesis in the liver to increase plasma glucose. In the absence of food intake (fasting), glycogen stored in the liver is sufficient to maintain blood glucose for about 12 hours.[11] Glucagon by activating adipose cell lipase causes breakdown of triglycerides (lipolysis) to mobilize

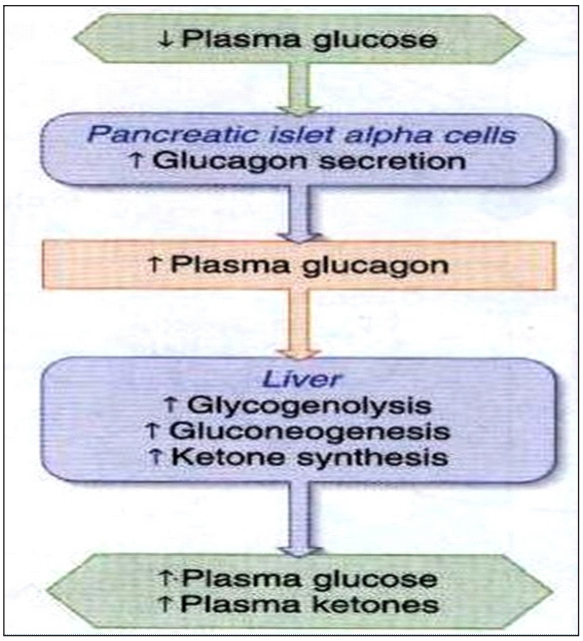

Fig-5: Nature of plasma glucose control over glucagon secretion.[1]

Large quantities of fatty acids available to the energy system of the body **Fig-5**. It also causes formation of ketone bodies (ketogenesis).[3]

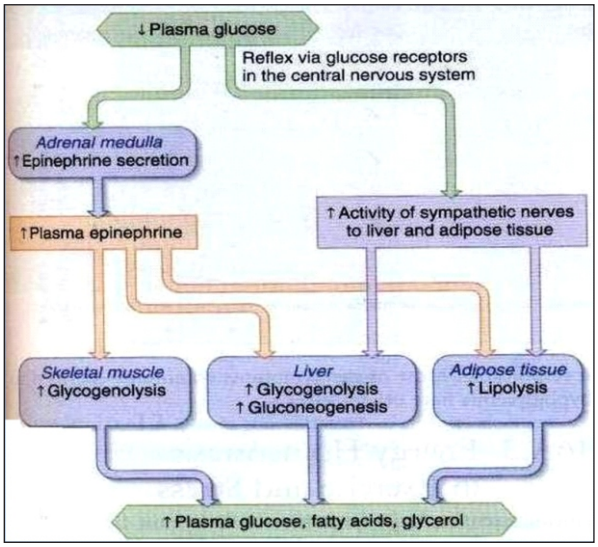

Fig-6: Participation of the sympathetic nervous system in the response to a low plasma glucose concentration.[1]

If hypoglycemia is severe, it leads to sympathetic stimulation that through epinephrine releases glucose from the liver to correct hypoglycemia.[2] **Fig-6** In fasting, cortisol maintains blood glucose by stimulating gluconeogenesis.[6.]

Conclusion

The main control of blood glucose during fasting is through the pancreatic hormones; insulin and glucagon. Regulation of blood glucose level during fasting is very important especially in patients of diabetes mellitus. The dose of hypoglycemia drugs should be modified as per requirement at sehri and aftari.

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References

1 Widmaier EP. Raff H. Strang KT. Regulation of organic metabolism and energy balance. In: Vander's Human Physiology 12th edition. New York. Mc Graw Hill; 2011: 560563

2. Hall JE. Insulin, glucagon and diabetes mellitus. In: Guyton and Hall Textbook of Medical Physiology. 12th edition. New Delhi. Elsevier; 2011: 941949

3. Barrett KE, Barman SM. Boitano S. Brooks HL. Endocrine functions of pancreas. In: Ganong's Review of Medical Physiology. 23rd edition. New Delhi. Tata Mc Graw Hill; 2010: 318326

4. Bijlani RL and Manjunatha S. Pancrase. In: understanding Medical Physiology 4th Ed. New Dehli Jaypee. 472474.

5. Koeppen, BM. Hormonal regulation of energy metabolism. In: berne & levy Physiology. 6th Ed. New Dehli, Elsevier 676677

6. Tendon OP. Tripathi Y. Kumar A. Mandal MB. Ravi K. venkatesh D. Hormonal regulation of growth and development. In: Best & Taylor's Physiological Basis of Medical Practice 13th edition. Philadelphia. Wolters Kluwer; 2012: 894899

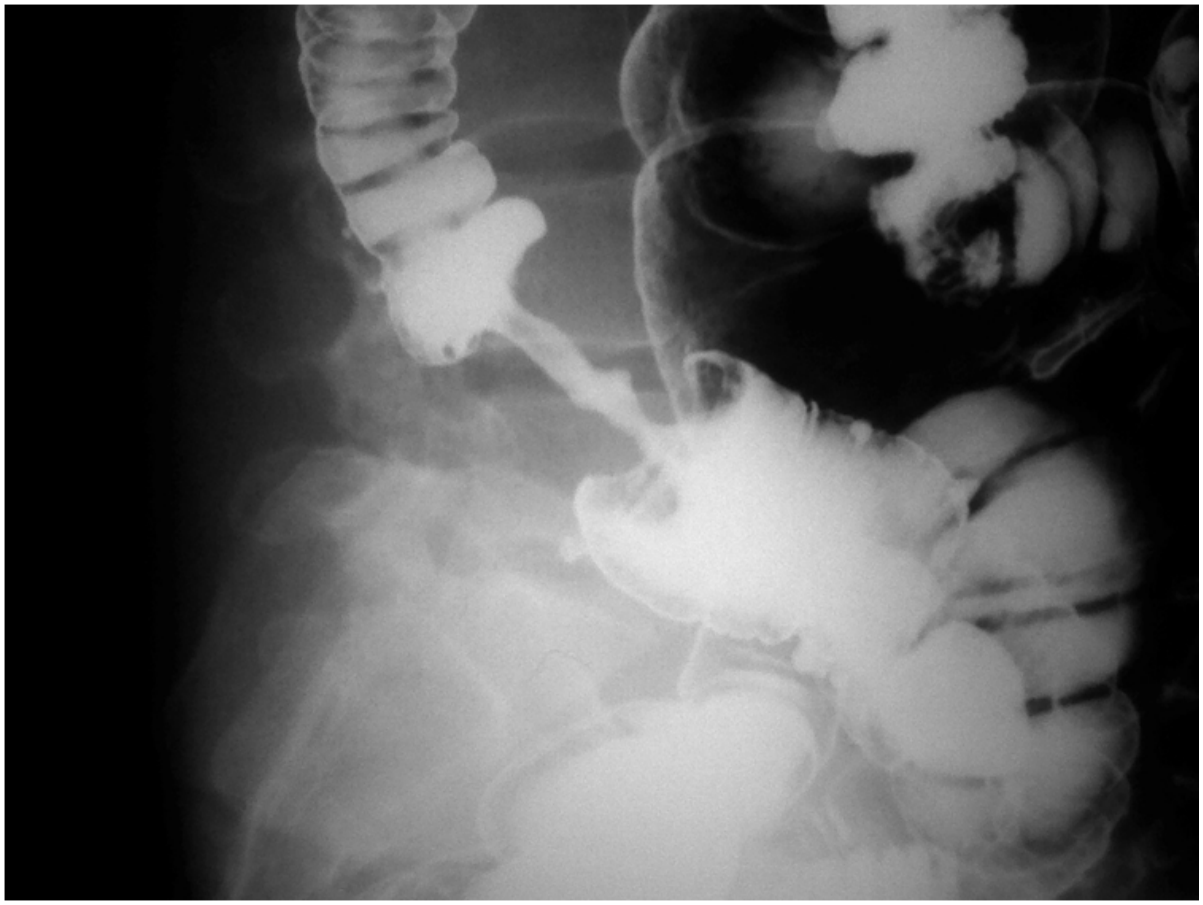
7. Johnson LR. The pancreatic blets

In: Essential Medical Physiology New Dehli, Elsevier; 2006. 655-656
8. Chaudhuri SK. Growth and old age. In: Concise Medical Physiology 6th edition. Delhi. New Central Book Agency; 2011:307310
9. Sherwood L. The peripheral endocrine glands. In prinipla of humar physiology 7th Ed. New Dehli, Cengagee Learning; 2010: 716720
10. Peterson OH. Energy metabolism In: Humar Physiology 5th Ed. Victoria, Black well Publishing 2007; 599600
11. Hall JE Dietary alances; regulation of feeding; obesity and staroation; vitamins and minerals, In: Guyton and Hall Testbook of Medical Physiology. 12th edition. New Dehli, Elsevier; 2011: 852
cartilage. 2004; 12: 20-30.

Picture Quiz

WHAT IS DIAGNOSIS?

50 year male has history of chronic diarrhea with intermittent blood in stools. What sign is evident in following radiograph?



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