The Role of Gastric Inhibitory Polypeptide in the Regulation of Metabolism and Body Physiology

Novi Margareta

1Department of Internal Medicine, Kartini Hospital, Kupang, Indonesia

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*Corresponding author:
Novi Margareta

E-mail address:
novi.margareta@gmail.com

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1. Introduction

The regulation of metabolism and body physiology is a complex process and is very important for the internal balance and optimal function of the organism. In this context, hormones act as biochemical messages that coordinate various aspects of metabolism and body function. One hormone that has a central role in this process is gastric inhibitory polypeptide (GIP), also known as Glucose-Dependent Insulinoactive Polypeptide. The regulation of metabolism and body physiology is a complex correlation of biochemical processes and hormonal signals that work together to maintain the organism's internal balance. In this case, gastric inhibitory polypeptide (GIP) plays a central role as one of the key hormones that contributes to the regulation of the body's response to food intake and the control of blood glucose levels.1,2

Produced by cells in the small intestine, mainly in the duodenum and jejunum, GIP has been the subject of intensive research due to its important role in regulating the body's response to food intake and controlling blood glucose levels after meals. GIP plays a role in stimulating the release of insulin from beta cells in the pancreas, especially after intake of foods containing glucose or fat. This insulin response is important for optimizing glucose use by body cells and maintaining blood glucose balance, preventing uncontrolled blood glucose spikes.
consuming foods containing carbohydrates, which can increase blood glucose concentrations. The insulin response regulated by GIP helps avoid excessive spikes in blood glucose that can have detrimental effects on health, especially in the long term.\(^3\)

Gastric inhibitory polypeptide (GIP) also has a significant impact on various aspects of the body’s metabolism and physiology. This hormone plays a complex role in the process of absorbing nutrients from the digestive tract into the bloodstream and other body tissues. Apart from that, GIP can also influence the development and regulation of adipose (fat) cells. One important impact of GIP is its influence on the absorption of nutrients, especially glucose and fat, from the digestive tract into the bloodstream. This hormone can increase glucose transport into body cells, thereby helping reduce blood glucose levels after eating. It is an integral part of the body’s response to food intake, which helps maintain energy balance and avoid disturbances in glucose homeostasis. In addition, GIP also has implications for the regulation of adipocyte oogenesis (formation of adipose cells) and fat accumulation in the body. Some studies suggest that this hormone may contribute to the formation and development of adipose cells, which play an important role in energy storage. Thus, GIP has the potential to influence body weight and overall body composition.\(^4\)

**Gastric inhibitory polypeptide (GIP)**

Gastric inhibitory polypeptide (GIP), also known as Glucose-Dependent Insulinaotropic Polypeptide, is a peptide hormone produced by cells in the small intestine, especially in the duodenum and jejunum. GIP has an important role in regulating the body’s response to food intake and controlling blood glucose levels after eating. GIP is one of the incretin hormones, meaning that it stimulates the release of insulin from the beta cells in the pancreas. This response mainly occurs after eating and helps optimize glucose absorption by body cells. GIP works by interacting with receptors on various types of cells, especially beta cells in the pancreas and epithelial cells in the small intestine.\(^5\)

In addition to its role in insulin release, GIP also has an impact on the absorption of nutrients from the digestive tract and can influence the growth and regulation of adipose (fat) cells. However, GIP’s influence is not limited to that. This hormone also has complex interactions with the rest of the endocrine system, and responses can vary depending on individual health conditions, such as obesity and diabetes. GIP is one of the key elements in the regulation of metabolism and body physiology, and understanding how this hormone works has provided important insights into how the body regulates blood glucose levels and nutrient use after meals.\(^6\)

The process of gastric inhibitory polypeptide (GIP) synthesis occurs in small intestinal cells, especially in the duodenum and jejunum. GIP synthesis begins with transcription of the GIP gene found in intestinal cell DNA. The GIP gene contains the genetic information necessary to produce the GIP precursor, the initial molecule that will be converted into the final GIP hormone. After transcription, the precursor GIP (also known as pro-GIP) is formed in the cell nucleus. This precursor contains the peptide sequence that will form active GIP but in a longer and inactive form. The GIP precursor then undergoes further processing in the endoplasmic reticulum and Golgi apparatus of the cell. During this stage, unneeded parts of the precursor are cut off, resulting in a shorter, biologically active GIP molecule. After processing, active GIP molecules are packaged in small vesicles inside the cell. These vesicles contain GIP, which is ready to be released when needed. When food enters the small intestine, hormonal and nerve signals stimulate the release of GIP from these cells. When food reaches the duodenum and jejunum, which are the main production sites of GIP, vesicles containing GIP release this hormone into the bloodstream. GIP will then circulate to various target organs, such as the pancreas, to influence the body’s response to food. By going through this series of stages, the initial GIP molecules produced by intestinal cells undergo processing and release into active hormones in the bloodstream.\(^7\)

**Stimulation of insulin release**

When food reaches the small intestine, especially the duodenum and jejunum, the process of digestion
and nutrient absorption begins. Nutrients such as glucose and fat contained in food are broken down and absorbed through the walls of the small intestine. The epithelial cells lining the intestinal wall have various detection mechanisms to recognize the presence of these nutrients. This detection is an important signal to initiate hormonal responses, including the release of hormones such as Gastric Inhibitory Polypeptide (GIP), which plays an important role in regulating the body's response to food intake and controlling blood glucose levels after eating. When nutrients, especially glucose and fat, are present in sufficient quantities in the small intestine, the epithelial cells in the intestinal wall respond by producing and releasing Gastric Inhibitory Polypeptide (GIP) into the bloodstream.

The released GIP then circulates through the bloodstream and reaches the pancreas. In the pancreas, GIP interacts with the GIPR receptor located on the surface of beta cells in the islets of Langerhans. The interaction between GIP and the GIPR receptor triggers the activation of signaling pathways in beta cells. One important pathway is the activation of G protein (G protein) and an increase in cAMP (cyclic adenosine monophosphate) concentrations. An increase in cAMP activates the Protein Kinase A (PKA) enzyme. PKA plays a key role in intracellular signal transduction. Activation of PKA initiates a series of biochemical changes in beta cells. PKA activation leads to increased calcium (Ca²⁺) permeability in beta cells. This results in increased calcium flow into the cells. Higher calcium in beta cells triggers the mobilization of insulin-containing vesicles to the cell surface. These vesicles contain insulin that has been stored in beta cells. The process of mobilizing insulin vesicles leads to the release of insulin from beta cells into the bloodstream. The released insulin will be transported to various parts of the body through the bloodstream. After reaching target cells, such as muscle and liver cells, insulin interacts with its receptors and facilitates glucose uptake into the cells. This helps lower blood glucose levels that have increased due to food intake. GIP-induced insulin release has glucose-dependent properties, meaning that it is more active when blood glucose levels are high, such as after eating. This response helps maintain blood glucose balance after meals and prevents excessive glucose spikes.⁹,¹⁰

**Blood glucose regulation**

After eating, especially after the intake of foods containing glucose or fat, GIP is produced in response to nutrients present in the small intestine. GIP then stimulates the release of insulin from beta cells in the pancreas. One important aspect of the GIP-induced insulin response is its "glucose-dependent" nature. This means that GIP-induced insulin release is more intense when there is an increase in blood glucose, such as after a meal, and less active when blood glucose levels are normal. The insulin response induced by GIP helps control blood glucose spikes after meals. This is important because uncontrolled blood glucose spikes can cause diabetes complications, such as organ and tissue damage.¹¹

GIP contributes to more precise regulation of insulin production and release according to the body's needs. This helps prevent excessive increases in insulin levels that can cause metabolic problems. Understanding the role of GIP in optimizing insulin responses after meals is key in the management of diabetes, especially type 2 diabetes. Therapies targeting incretin hormones, such as GIP, have become a focus in efforts to improve blood glucose control in diabetes patients. Blood glucose balance is an important factor in general health, and the role of GIP in optimizing the insulin response after meals is one important mechanism that helps prevent metabolic disorders and complications associated with diabetes.¹²

**Nutrient absorption**

GIP does have an important role in optimizing the process of glucose and fat absorption in the small intestine. GIP has the ability to influence the activity of membrane transporters in small intestinal cells. These membrane transporters are special proteins involved in transporting nutrients, such as glucose and fat, across cell membranes into intestinal cells to then be absorbed into the bloodstream. GIP can stimulate more efficient glucose absorption by small intestinal epithelial cells. This means that more glucose from the food consumed can be taken up and
absorbed by the body, which can then be used as an energy source or stored in the form of glycogen in the liver. Apart from affecting glucose absorption, GIP can also affect the absorption of fat from food. It helps the body absorb fatty acids and other nutrients necessary for a variety of biological functions, including cell membrane formation and energy production.\textsuperscript{13}

By increasing the efficiency of nutrient absorption, GIP contributes to better nutrient utilization by the body. These nutrients are important fuel for optimal metabolic processes, growth, and body function. Regulation of nutrient absorption by GIP also has an impact on the body’s energy balance and body weight regulation. The body’s ability to take in nutrients from food more efficiently can have an impact on weight management and overall body metabolism. By optimizing the absorption of glucose and fat from food, GIP contributes to the efficient utilization of nutrients in the body. This is important in maintaining energy balance, optimizing body function, and supporting growth and development processes.\textsuperscript{14}

**Effect on fat metabolism**

GIP is believed to have an influence on adipose cells or fat cells. Although the exact mechanisms remain the subject of further research, there are indications that GIP may influence the development and function of adipose cells. There is evidence that GIP may play a role in influencing the formation and growth of adipose cells. Adipose cells are a storage site for fat in the form of triglycerides, and they also have a role in the regulation of fat metabolism and related adipocytokines. Leptin and adiponectin are hormones produced by adipose cells and play a role in the regulation of body weight and metabolism. Several studies indicate that GIP may influence the expression and release of these hormones, impacting body weight regulation and insulin sensitivity.\textsuperscript{15}

GIP works together with other incretin hormones, such as glucagon-like peptide-1 (GLP-1), in regulating the body’s response to food intake. These incretin systems collectively influence insulin release, blood glucose regulation, and energy metabolism. Although much remains to be understood about the role of GIP in the regulation of fat metabolism and its relationship to adipose cells, research continues to uncover deeper mechanisms and effects. This is an exciting area of research and has the potential to provide better insight into how hormones such as GIP interact with overall body metabolism.\textsuperscript{16}

**Relationship with other hormones**

GIP and GLP-1 are the two main incretin hormones secreted by the digestive tract after food intake. Although both have unique roles, they work synergistically to optimize the body’s response to food. Both of these hormones stimulate the release of insulin from beta cells in the pancreas, each with a different response pattern. GIP focuses more on insulin release after meals, especially carbohydrate-containing meals, while GLP-1 emphasizes the insulin response to high blood glucose levels. Apart from stimulating the release of insulin, the incretin hormone also has the effect of inhibiting the release of glucagon from alpha cells in the pancreas. Glucagon is a hormone that increases blood glucose levels, so inhibiting its release helps maintain blood glucose balance.\textsuperscript{17}

GIP and GLP-1 also have an effect on gastric emptying after eating. They help slow the rate of gastric emptying so that food is digested and absorbed more slowly. This helps control blood glucose spikes after meals. In addition to their influence on the pancreas, GIP and GLP-1 also have an impact on the overall regulation of the digestive tract system, including the movement of food through the intestines and the production of gastric acid. Because of their important role in regulating insulin and blood glucose responses, incretin hormones such as GIP and GLP-1 have become therapeutic targets in the management of type 2 diabetes. Drugs that modulate the action of these hormones can help improve blood glucose control. The complex interactions between GIP, GLP-1, and other factors form an intricate system for regulating the body’s response to food. A good balance between the release of these hormones is important for maintaining metabolic health and preventing diabetes problems.\textsuperscript{18}
Impact on energy balance

GIP plays a role in regulating glucose and fat metabolism in a broader way. In addition to stimulating insulin release, GIP can also influence the insulin response to blood glucose, as well as the absorption of glucose and fat from the digestive tract. This impacts how the body uses and stores energy from nutrients. Regulation of glucose and fat metabolism by GIP has an impact on the body’s energy balance. The efficiency of nutrient absorption and use regulated by GIP can impact the amount of energy available to the body. When energy balance is disturbed, this can contribute to unhealthy weight problems. GIP affects adipose cells, which have an important role in storing energy in the form of fat. In several studies, GIP has been associated with the regulation of growth and development of adipose cells. Further research is needed to understand the exact mechanism.19

There is research linking high GIP levels to insulin resistance, which is a characteristic of type 2 diabetes. Although this association still needs to be further investigated, it shows the complexity of GIP’s role in insulin metabolism and resistance. In some conditions, such as obesity and type 2 diabetes, the role of GIP in the regulation of body weight and metabolism has been the focus of research. Understanding how GIP affects these metabolic diseases may help develop more effective treatment strategies. Although the role of GIP in the regulation of body weight and energy balance is still under further research, understanding its relationship with the metabolism and growth of adipose cells has become an interesting subject of study in an effort to understand the complexity of the body’s regulation of nutrition and energy.20

2. Conclusion

Gastric inhibitory polypeptide (GIP) has a very important role in regulating metabolism and body physiology related to food intake and controlling blood glucose levels. GIP is produced by cells in the small intestine in response to the presence of nutrients, especially glucose and fat.

3. References


