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Perioperative Insulin Resistance

Essay

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By

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List of Abbreviations

Abb.	Full term
ACTH	*Adrenocorticotrophic hormone*
ADA	*American diabetes association*
AGEs	*Intracellular advanced glycation end products*
BUN	*Blood urea nitrogen*
CAD	*Coronary artery disease*
CRP	*C-reactive protein*
CVD	*Cardiovascular disease*
DAN	*Diabetic autonomic neuropathy*
DKA	*Diabetic ketoacidosis*
DM	*Diabetes mellitus*
DM-1	*Type 1 diabetes*
DM-2	*Type 2 diabetes*
EASD	*European association for the study of diabetes*
FFA	*Free fatty acid*
FPG	*Fasting plasma glucose*
GAD65	*Glutamic acid decarboxylase autoantibodies*
GDM	*Gestational diabetes*
GFR	*Glomerular filtration rate*
GIK	*Glucose insulin-potassium*
GLUT4	*Glycose transporter 4*
HbA1C	*Glycated hemoglobin*
HDL	*High density lipoprotein*
HIV	*Human immunodeficiency virus*
IAs	*Insulin autoantibodies*
ICAs	*Islet cell autoantibodies*

IDDM	*Insulin dependent diabetes mellitus*
IDF	*International diabetes federation*
IFCC	*International federation of clinical chemistry and laboratory medicine*
IFG	*Impaired fasting glucose*
IFT	*Impaired glucose tolerance*
IGF-BP	*Insulin-like growth factors binding protein*
IgG	*Immunoglobulin G*
IL-1	*Interleukin I*
IL6	*Interleukin 6*
IMGU	*Impaired insulin mediated glucose uptake*
IR	*Insulin resistance*
IV	*Intravenous*
LADA	*Latent autoimmune diabetes in adult*
MAPK	*Mitogen activated protein kinase*
MODY	*Maturity-onset diabetes in youth*
NIDDM	*Non insulin-dependent diabetes mellitus*
NMR	*Nuclear magnetic resonance*
NO	*Nitrous oxide*
OGTT	*Oral glucose tolerance test*
PAJ-1	*Plasminogen activator inhibitor-1*
PONV	*Post operative nausea and vomiting*
SJS	*Stiff joint syndrome*
TG	*Triglyceride*
TIVA	*Total intravenous anaesthesia*
TNF-α	*Tumor necrosis factor α*
TZD	*Thiazolidinediones*
VLDL	*Very low density lipoprotein*
WHO	*World Health Organization*

INTRODUCTION

Elective surgery causes a marked, transient reduction in insulin sensitivity. The degree of the reduction is related to the magnitude of the operation, the type and duration of surgery performed, and perioperative blood loss. Also the degree of postoperative insulin resistance (IR) has significant influences on the length of hospital stay ***(Throll et al., 1999).***

Development of hyperglycemia after major operations is very common and is modulated by many factors. These factors include perioperative metabolic state, intraoperative management of the patient, and neuroendocrine stress response to surgery ***(Inzucchi, 2000).***

Insulin resistance (IR) is a state in which there is an insensitivity of the peripheral tissue (e.g., muscle, liver, adipose tissue) to the effect of insulin. There is a threefold increase in risk for coronary artery disease and stroke in subjects with IR when compared with individuals who have normal glucose tolerance ***(Isomaa et al., 2001).***

Acute insulin resistance can develop perioperatively and contribute significantly to hyperglycemia. Hyperglycemia is associated with poor outcomes in postsurgical patient. IR is a feature of the catabolic reactions after major surgery because the postoperative increase in the circulating levels of catabolic

hormones increases the production of glucose and weakens its peripheral use ***(Schricker et al., 2005).***

The underlying pathophysiology is not yet fully understood, although hyperglycemia predicts post-surgical morbidity and mortality. Apparently perioperative insulin resistance has a complex pathophysiology and tissue-specific differences have to be considered. Multiple causative factors and intracellular signalling pathways have been identified driving the development of systemic perioperative insulin resistance ***(Thorell et al., 1999).***

Aim of the work

To highlight causes and mechanisms of insulin resistance development in the perioperative period. Also, we will discuss the perioperative management of diabetic patients.

PATHOPHYSIOLOGY OF INSULIN RESISTANCE

Insulin Hormone:

Insulin is secreted by the B-cells of pancreatic islets in response to elevation in blood glucose levels. It is a protein consisting of 51 amino acids contained within two peptide chains; α chain and β chain. The chains are connected by two disulphide bridges **(figure 1)**. In addition, there is an intra-chain disulphide bridge that links positions 6 and 11 in the (α) chain. The molecular weight of human insulin is 5808 ***(Eckel et al., 2005).***

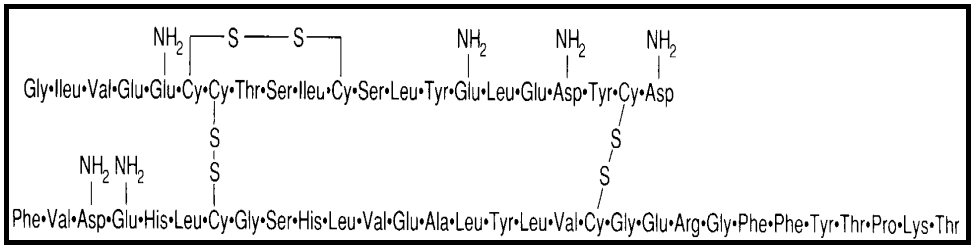

Figure (1): Human insulin molecule ***(Guyton and Hall, 2006).***

Insulin Secretion:

When insulin is secreted into the blood, it circulates almost entirely in an unbound form; it has a plasma half-life that averages only about 6 minutes, so that it is mainly cleared from the circulation within 10 to 15 minutes. Except for that portion of the insulin that combines with receptors in the target cells, the remainder is degraded by the enzyme insulinase mainly in the liver, to a lesser extent in the kidneys and muscles, and slightly in most other tissues ***(Guyton and Hall, 2006)***.

The human pancreas secretes 40-50 units of insulin per day in normal adults. The basal concentration of insulin in the blood of fasting human averages 10 Mu/ml (0.4ng/ml). In normal subjects, insulin seldom rises above 100Mu/ml after standard meals. The increase in peripheral insulin concentration begins 8-10 minutes after ingestion of food and reaches peak concentration in peripheral blood by 30-45 minutes **(figure 2)**. This is followed by a rapid decline in postprandial blood glucose level, which returns to baseline values by 90-120 minutes ***(Karam, 1997)***.

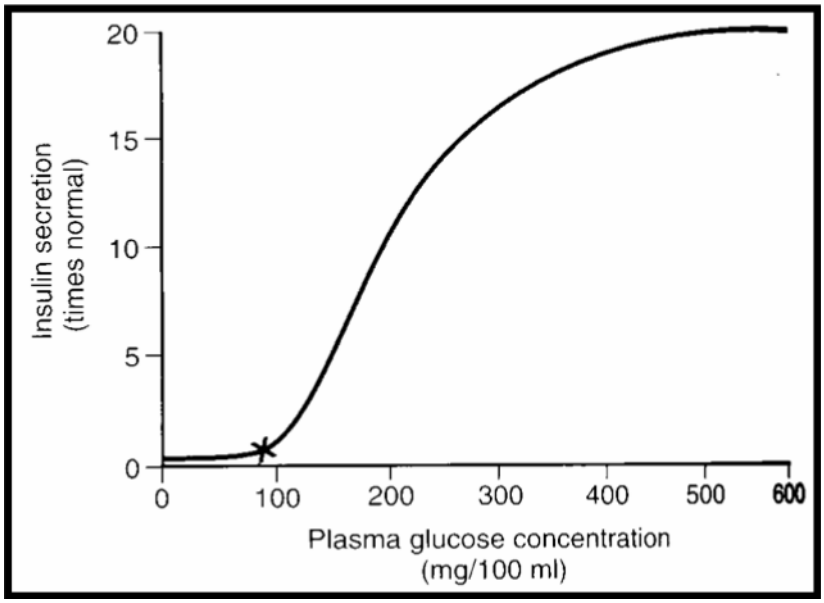

Figure (2): Approximate insulin secretion at different glucose levels ***(Guyton and Hall, 2006)***.

Glucose is known to enter β-pancreatic cells by diffusion, which is facilitated by a specific membrane protein termed glucose transporter-2. By virtue of its relatively low affinity for glucose, this protein more effectively facilitates transport of glucose during hyperglycemia than at the lower levels of blood glucose as during fasting state ***(Goldfine and Pilch, 1992)***.

Factors involved in regulation of insulin secretion, can be divided into three categories (table 1): ***Direct stimulants***, which are known to stimulate insulin release directly. **Amplifiers**, which appear to potentiate the response of the β-cell to glucose and **inhibitors** of insulin release. The action of the amplifier substances, many of which are gastrointestinal hormones

stimulated by ingestion of meals, explains the observation that insulin response to an ingested meal is greater than the response of intravenously administered substrates ***(Karam, 1997)***.

Table (1): Regulation of insulin release in humans ***(Karam, 1997).***

Stimulants of insulin release	• Glucose, mannose. • Leucine. • Vagal stimulation. • Sulfonylureas
Amplifiers of glucose-induced insulin release	***1. Enteric hormones:*** Glucagon-like peptide. Gastrin inhibitory peptide. Cholecystokinin. Secretin, gastrin. ***2. Neural amplifiers:*** Beta-adrenergic stimulation. ***3. Amino acids:*** arginine.
Inhibitors of insulin release	***1. Neural:*** α-adrenergic effect of catecholamines. ***2. Humoral:*** somatostatin. ***3. Drugs:*** Diazoxide, phenytoin, vinblastine, colchicines.