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GENERAL INFORMATION

Insulin resistance in surgery

Olle Ljungqvist*

Department of Surgery, Örebro University Hospital, Örebro, Sweden

KEYWORDS
Insulin resistance;
Postoperative metabolic response;
Enhanced recovery after surgery

Abstract
Insulin resistance is a condition in which the effect of insulin falls below normal, affecting glucose metabolism, lipids and proteins. In surgery it presents after an injury is established or during surgical intervention.
Depending on the level of trauma, insulin resistance may last for weeks. The best method to evaluate insulin resistance is the hyperinsulinemic-euglycemic clamp technique.
With ERAS (Enhanced Recovery After Surgery) programmes and objectives such as preoperative glucose administration, minimally invasive surgery and pain control, insulin resistance is reduced by 50% during abdominal surgery.

PALABRAS CLAVE
Resistencia a la insulina;
Respuesta metabólica posquirúrgica;
Enhaced Recovery After Surgery

Resistencia a la insulina en cirugía

Resumen
La resistencia a la insulina es una condición en donde la acción de la insulina está por debajo de lo normal y afecta al metabolismo de la glucosa, los lípidos y las proteínas. En cirugía se presenta después del establecimiento del daño o bien durante el proceso quirúrgico.
Dependiendo del nivel del trauma, la resistencia a la insulina puede durar semanas. El mejor método para evaluar la resistencia a la insulina es el denominado clamp hiperinsulinémico normoglucémico.
Con los programas y objetivos de ERAS (Enhaced Recovery After Surgery, por sus siglas en inglés), tales como la administración de glucosa preoperatoria, la cirugía de invasión mínima y el control del dolor, la resistencia a la insulina se reduce hasta un 50% durante la cirugía abdominal.

*Correspondence to the author: Department of Surgery, Örebro University Hospital, Örebro 70185, Sweden.
Email: olle.ljungqvist@ki.se

Background

Insulin resistance develops within minutes of any damage or injury to the body, such as trauma, sepsis[1] and elective surgery[2]. This change in metabolism has been shown to be associated with the development of major postsurgery complications[3]. Current knowledge of metabolic balance control in surgical patients places an emphasis on the control of metabolism as key to caring for these patients[4].

Insulin resistance is a term used to describe a metabolic situation where the effect of insulin is below normal for any of the metabolism's important functions[4] including metabolism of glucose, fats and proteins and although this is the full meaning of the term, insulin resistance is commonly used to describe the ineffectiveness of insulin to maintain glucose values.

Insulin resistance manifests as dose-dependent in response to the magnitude of the operation[2] and its duration[5]; laparoscopy instead of open surgery reduces insulin resistance[6] as does the anaesthetic technique[7,8]. It lasts for ~3 weeks after an open abdominal procedure such as cholecystectomy[9].

The metabolism of glucose in postoperative insulin resistance and the development of complications

Most research into insulin resistance is performed with glucose. Glucose values are increased after surgery and reach very high values if glucose infusions are administered without insulin. In non-severe cases, the absorption of glucose is quickly stimulated with insulin, primarily by activating specific glucose transporters in muscle and fat. After surgery there is a significant blocking of the activation of these transporters called GLUT4. Within the cell, there is also a blocking of the storage of glucose and glycogen, which depletes energy in the muscle. At the same time there is a rapid release of glycogen in the liver, which occurs similarly in the muscle where energy reserves are also exhausted. In the liver, glucose production is supported by the increase of gluconeogenesis from lactate, glycerol and amino acids. Therefore, the liver and periphery raise glucose levels, which is very similar to what happens in patients with type 2 diabetes mellitus.

Diabetes studies have shown that although insulin absorption is low in sensitive cells such as muscle and fat, other cells that assimilate glucose according to extracellular concentration, immune cells, endothelial and neural, present an increase in absorption. In diabetes, Brownlee[10] has proposed a mechanism where these cells participate in the complications of diabetes. Briefly, for the assimilation of insulin, independent cells have transporters that recover external glucose values. In situations of glucose overload, these cells can also be overloaded. Without these cells' storage capacity, the glycolytic pathway may become saturated and lead to the production of oxygen free radicals, which will eventually cause changes in gene expression, increasing inflammation and dysfunction. In recent studies in surgical patients, many of the intracellular changes observed in diabetic patients occurred a few hours after surgery[11,12]. Interestingly, although the cells involved and diabetic complications are the same as they are in postoperative patients (Table 1), the period differs between the two, relative to the rate of insulin resistance, throughout the years in diabetes and minutes after surgery. Complications can take months or years in diabetics, whereas its development can take days or weeks. Even so, the complications are very similar and include infections, cardiovascular problems and others up to certain neutral points,suggesting that they have a common pathophysiological basis. The field is interesting and important for future research.

Protein metabolism and their recovery after surgery

In a healthy person, insulin mainly affects muscle proteins, reducing their catabolism. However, insulin also stimulates the absorption of proteins and its synthesis in the muscle when accompanied by amino acids, for example, after the consumption of proteinous foods[13,14]. Resistance to insulin for protein turnover also develops after surgery[15]. Strength and muscle mass is lost[16,17]. This loss, along with the simultaneous depletion of energy sources and the inability to carry external glucose, explains fatigue and the difficulty to move frequently observed after major surgery.

Modification of insulin resistance

As mentioned briefly, there are several ways to modify insulin resistance. This author believes that this is one of the main ways to achieve these objectives[4]— called 'Enhanced Recovery After Surgery' (ERAS). Table 2 shows several treatments known to influence insulin resistance and the specialist responsible for its application. From this table it becomes clear that there must be a joint effort to ensure the least amount of stress or insulin resistance in surgical patients. This is the essence of the ERAS protocols[18]. Interestingly, when the ERAS study guides[19,20] or the most recent from the ERAS society[21-23] are put to the test, it is shown that improvements depend on their strict adherence and application[24]. When their use increases from 50 to 90% in almost 1,000 patients with colorectal cancer (50/50), the duration of insulin resistance decreases from an average of 9.5 days to <6 dayssix and complications from 46 to 18%. This shows that the guidelines make a difference. It is very probable that the effect is related to surgical stress and lower insulin resistance[4].

Table 1 Cells and tissue affected by glucose elevations with clinical manifestations in diabetes and surgery

Cells/tissue	Complication
Immune cells	Infection, increased inflammation
Endothelial cells	Cardiac, vascular
Neural cells	Polyneuropathy
Kidney	Failure

Table 2 List of perioperative treatments known to impact the action of insulin and resistance

Treatment	Effect of IR	Professionals responsible
Fasting of carbohydrates at night treatment	Carbohydrate treatment reduces IR by 50%	Anaesthetist
Laparoscopic surgery	Reduces IR >50%	Surgeon
Pain control	Pain increases IR	Surgeon/anaesthetist/nurse
Epidural anaesthesia	IR can be reduced by up to 50%	Anaesthetist
Postoperative food	Improves IR	Surgeon/nurse

IR: insulin resistance.

Determination of insulin resistance

In insulin resistance studies, using the correct method is very important. Unfortunately, the use of simple, cheap and uncomplicated methods generally leads to confusing results. The only reliable way to assess insulin resistance is the gold standard, the hyperinsulinemic-euglycemic clamp technique where the insulin action on the glucose metabolism is studied on observed values after ingestion of food, i.e., normal physiological values[25]. Other methods cited in the literature include the HOMA and QUICKI, which use baseline glucose and insulin and do not reflect the results using the ERAS clamp method. This causes confusion in the literature because the authors who use these simplified methods tend to use them as if they were one and the same. Although numerous studies using the clamp method demonstrate that the treatment reduces insulin resistance after surgery by 50%[26], other studies in similar patient groups using HOMA did not detect this difference[27]. This is explained by the fact that the main flaw of postoperative insulin resistance is due to the drastic decrease of the incorporation of glucose, which decreases dramatically and is responsible for ~90% of the total change. This part of insulin resistance is not detected by other methods and results in confusion when no insulin resistance is found.

Conclusions

Insulin resistance during surgical procedures is common. Glucose metabolic disorders and protein losses are amongits consequences. These begin minutes after the trauma. ERAS programmes quickly reduce insulin resistance by reducing operative trauma and pain.

Conflict of interest

The author declares no conflict of interest.

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