

A grand dame with hidden aces: The non-diabetic uses of insulin

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ABSTRACT

This brief communication reviews the non-diabetic uses and utility of insulin. It highlights the lesser known uses in medicine, psychiatry, surgery and diagnostics that this versatile peptide has.

Key words: Applied pharmacology, insulin, non-traditional uses

INTRODUCTION

The discovery of insulin is thought to be one of the most dramatic turns in the medical history. Insulin is the most important anabolic hormone in the body.^[1] Over the past century, researchers have discovered multiple pleiotropic effects and actions of this molecule. While extensive work has been published, on a regular basis, about advances in biochemistry, physiology, and pharmacology of insulin, no review has targeted the spectrum of non-diabetic uses of this hormone. Some of the many non-diabetic uses of insulin are presented here [Table 1].

DIAGNOSTICS

Several hormones including insulin are used as an essential component of synthetic growth media for cell culture.^[2] They promote growth of mammalian cells by increasing the permeability of cell membranes to glucose and making nutrients available to the cells. Although invariably every mammalian cell will require insulin for survival, the degree

Table 1: Non-diabetic uses of insulin

Diagnostic	Therapeutic	Surgical
Growth media for cell cultures	Solutions for total parenteral nutrition	Reduction of surgical complications
Organ preservation solutions	Glucose-insulin-potassium solution	
Insulin tolerance test for GH deficiency	Weight loss, weight gain and muscle building	
Narcoanalysis	Antidote for calcium channel blocker therapy Insulin potentiation therapy Deep insulin coma therapy Ectodermal healing Wound healing Anti-aging	

of requirement varies with different cell lines. Insulin is also used for similar reasons in organ preserving solutions. Organs extracted for transplant purposes are preserved in insulin containing solutions.

Insulin tolerance test is the most reliable provocative test for growth hormone deficiency.^[3] An insulin tolerance test is age independent and reproducible. Insulin is administered into the patient and blood samples are taken after every 15 minutes over the next hour to determine whether the growth hormone levels have risen in response to insulin. Since growth hormone is a counter-regulatory hormone and is released when blood glucose level falls below normal,

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an insulin tolerance test deliberately lowers the blood glucose level to check whether there is an increase in the release of growth hormone. Failure of release of growth hormone would suggest growth hormone deficiency.

PSYCHOLOGY

Insulin is also used in narcoanalysis to reduce an individual's self-control over one's thoughts and cause him to reveal the thoughts or memories which he would otherwise have suppressed.^[4] The central nervous system has an absolute requirement for glucose. A reduction in blood glucose level causes a decrease in all the higher mental functions. Narcoanalysis uses this principle to reduce the higher mental control on the thoughts or memories. This would cause the subject to reveal the required information which he might not have disclosed ordinarily. It is useful for psychiatric and forensic purposes. The legal status of narcoanalysis is still debatable.

NUTRITION

The solutions used for total parenteral nutrition often contain a small amount of insulin.^[5] Regular insulin added to parenteral nutrition solution manages hyperglycemia, improves absorption of nutrients and reverses negative protein balance. Insulin availability in such solutions ranges from 10 to 95%. Rapid infusion of the parenteral nutrition, as is the usual case, would cause severe hypoglycemia if the insulin were not there to cause the glucose to be absorbed rapidly into the cells. It also prevents other complications such as muscle wasting which are common in bed-ridden patients.

CARDIOLOGY

Glucose–insulin–potassium solution (GIP or GIK solution) is given after a myocardial infarction to increase the usage of glucose by the myocardium and maintain the integrity of membrane ionic pumps.^[6] The GIP solution provides the glucose needed by the myocardium in reperfusion conditions and protects the cellular membrane and keeps the membrane pumps functional. It prevents changes in intracellular concentrations of sodium, potassium and calcium ions, thus preventing cardiac arrhythmias. Insulin also has direct anti-inflammatory and anti-apoptotic effects. Although most studies have shown positive results, GIP solution has not received as wide an acceptance among cardiologists as one might predict and is therefore not very commonly used.

BODY BUILDING

Insulin has also been used by many as a substance of

abuse for body building.^[7] Insulin with growth hormone is being used by many athletes and body builders for increasing their muscle mass. When supplied with growth hormone, it causes an increase in lean body mass since both the hormones are highly anabolic. Since insulin has a very short half-life in the body, it is exceedingly difficult to detect insulin abuse using laboratory tests. This knowledge is attracting more and more athletes toward this illegal practice. Insulin supplied exogenously or produced endogenously also has an effect of suppressing ghrelin. Ghrelin is responsible for stimulation of appetite. Therefore, this leads us to believe that exogenously supplied insulin will result in suppression of appetite and weight loss.^[8] However, unsupervised administration of insulin into a non-diabetic may lead to many serious downfalls in the blood glucose level which may prove to be fatal. Therefore, these practices are very dangerous.

POISONING

In a few patients with calcium channel blocker poisoning (verapamil and amlodipine–atenolol combination) who were unresponsive to conventional therapy, insulin–dextrose infusion has been used.^[9] Insulin–dextrose solution led to stabilization of their hemodynamic profiles and accelerated their recovery. Insulin induces positive inotropy by provision of glucose to myocytes and reduces peripheral vascular resistance.^[10]

MALIGNANCY

Insulin potentiation therapy (IPT) is a controversial, innovative cancer treatment which combines insulin with low-dose chemotherapy to prevent toxic effects and chemoresistance.^[11] With IPT, dose-related adverse effects of chemotherapeutic drugs are prevented and anti-neoplastic effects are increased specifically. However, its effectiveness is still debatable and this has limited its wide usage.

PSYCHIATRY

Deep insulin coma therapy (DICT) for schizophrenia was an extremely rigorous method where the patients were injected with insulin to induce severe hypoglycemia for 10–15 minutes.^[12] Thereafter, the hypoglycemia was reversed by infusing glucose. This treatment was continued for a few days or until the patient's symptoms disappeared. It was said to be useful for treating schizophrenia but carried an enormous amount of risk. This treatment was discredited in the late 1950s.

WOUND HEALING

Insulin has a specific healing effect on the cells which are embryologically derived from the ectoderm.^[13] The insulin is applied topically or injected in much smaller quantities than those used for diabetics. Some of the many organs which may benefit from the use of insulin are the sensory organs, central and peripheral nervous system, vestibule and palate of mouth, tongue, nose, nails, hairs, sweat and sebaceous glands, eyes and the ears.

Zinc protamine insulin (ZPI) has been shown to accelerate wound healing in open wounds, surgical incisions and lacerations.^[14] Insulin is required for cellular proliferation in devitalized tissues. After the exudate and necrotic tissue has been removed, insulin accelerates the metabolism of adjacent layer and stimulates it to regenerate and proliferate. It also arrests bacterial growth and enhances phagocytosis, thus lowering the chances of infection.

AGEING

Insulin has also been associated with an increased release of Klotho, the anti-aging protein.^[15] This suggests the possibility that insulin might be involved in the processes of anti-aging and longevity. It is an area which needs further research before it can be used practically.

SURGERY

It is known that surgery induces a catabolic state with insulin resistance.^[16] Aggressive insulin therapy postoperatively or postoperative carbohydrate loading has been shown to significantly reduce hospital stays, lower the occurrences of surgical complications and a return to normal activities faster.^[16] The exact mechanism behind this observation is unknown.

CONCLUSION

Insulin has conventionally been associated with diabetes. Surely enough, the discovery of insulin did change the course of treatment of diabetes altogether and even today its major use comes in diabetes, but the diversity of applications of insulin suggests that it has the potential of curing many more diseases than previously anticipated.

The many non-diabetic uses of insulin should also be investigated; since there may be many more aces hidden in this old lady.

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