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Co-Relation of Steriods in Diabetic and COVID-19 Patients

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

An unusual rise in blood glucose linked with the use of glucocorticoids in a patient with or without a prior history of diabetes mellitus is referred to as steroid-induced diabetes mellitus. The term steroid refers to a group of chemicals that have varied physiological effects. Hydrocortisone are a class of hormones that comprises both lab-made and naturally occurring hormones. Steroids are naturally occurring hormones in the human body. Corticosteroids have a wide spectrum of effects, from solely glucocorticoid to solely mineralocorticoid, and steroid compounds are chosen based on their suitability for a particular therapy. A drug may have anti-inflammatory resources, it could also have mineralocorticoid action, which lowers blood pressure. Steroids are drugs that have been used extensively in a variety of conditions. Glucocorticoids, despite being frequently recommended for their anti-inflammatory and immunosuppressive characteristics, have a number of side effects, with hyperglycemia being one of the most common and representative. In diabetic individuals, corticosteroids are generally contraindicated due to the danger of altering glucose control and

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resulting in severe decompensation. However, if given early and in a well-controlled regimen, corticosteroid medication can be useful in some patients. With good knowledge of the pharmacokinetics of the glucocorticoid utilized, glucose disequilibrium after withdrawal can be predicted.

Keywords: DIABETIC; blood glucose; public health; glucocorticoids.

1. INTRODUCTION

Steroids have been used for a variety of purposes since their discovery in 1935. Initially, these adrenal gland isolates were considered to be solely effective in patients with Addison disease [1]. Numerous of the therapeutic functions of steroids nowadays are linked to their anti-inflammatory and immune-modulating effects. Steroid unintended consequence are prevalent and problematic, ranging from moderate acne to Cushing syndrome, if left untreated, this can develop to diabetic mellitus and clearly life-threatening heart illness [2]. Side effects can take place at any dose and are dependent on how the medicine is delivered [1].

The term steroid refers to a group of chemicals that have varied physiological effects. Corticosteroids are a chemical class that includes both lab-made and spontaneously generated hormones. Mineralocorticoids regulate salt and water levels, while glucocorticoids govern metabolism and inflammation in general. Corticosteroids have a variety of actions, ranging from glucocorticoid to mineralocorticoid, and steroid molecules are chosen based on their suitability for a particular therapy. A substance possibly will have significant anti-inflammatory qualities, it may also have mineralocorticoid activity, which has a negative impact on blood pressure [1].

Steroids are naturally occurring hormones in the human body. Steroids hormones are man-made that are identical to those originate naturally by the body. Corticosteroids are a type of steroid that is used to treat disease. They are not the same as anabolic steroids, which are used by some sportsmen and bodybuilders. The effects of anabolic steroids vary greatly. Many different medical disorders are treated with steroid medications. It can be administered as lotions/gel, nasal sprays, inhalers, tablets, or injections [3]. Corticosteroids are utilized to treat dangerous swelling, but they can also cause DM, which is known as steroid diabetes. Steroid users who are already in danger for type 2 DM or who require to use steroids for extended periods of time are the most vulnerable to steroid-induced diabetes [4].

In diabetics, steroids can raise blood sugar levels. It can also cause non-diabetic people to have higher blood sugar levels. This can happen because steroid treatment causes the liver to produce more sugar, steroids make it difficult for sugar to leave the bloodstream, and the body may develop insulin resistant while on steroids [5].

2. MECHANISTIC PHARMACOLOGY AND PHYSIOLOGY OF STEROIDS

Steroids' anti-inflammatory activities are thought to be due to their inhibition of phospholipase A2, an enzyme involved in the synthesis of inflammatory chemicals [6]. Steroids have been demonstrated to alter gene expression, translation, and enzyme activity in studies [7]. In a nutshell, they exert their physiologic effects via a variety of metabolic routes [7]. One of these pathways is the induction of lipocortins, which are a type of protein. Inflammatory mediators produced such as leukotrienes and prostaglandins is inhibited by glucocorticoids, which effectively terminate the inflammatory cascade [6,8]. Glucocorticoids have a wide range of adverse effects, indicating that they can affect a variety of physiological systems. Exogenous glucocorticoids can directly produce hypopituitarism via negative feedback control of the hypothalamic-pituitary-adrenal (HPA) axis (Addison disease) [2,9]. Their impact on glucose metabolism may result in tissue insulin resistance and elevated fasting glucose levels [2,9]. Glucocorticoids act directly on osteoclasts, affecting bone resorption and limiting calcium absorption in the gastrointestinal tract, resulting in osteoopenia and osteoporosis [2,9]. Because glucocorticoids can have such a wide range of impacts on a patient's physiology, particularly on the HPA axis, a practitioner must proceed with caution while discontinuing their use. If you've been taking steroids for less than a week, you can stop taking them without tapering. Tapering should be done in accordance with clinical parameters and the illness for which the drug

was prescribed, with doses lasting 1-3 weeks [10]. When a patient has been on glucocorticoids for more than three weeks, the aim is for the practitioner to immediately taper to physiologic doses, then progressively reduce the quantity while monitoring adrenal function [11]. Patients who are taking equivalent doses of 30 mg of hydrocortisone daily or who have established HPA axis dysfunction and are stressed should receive an increased dose of steroids every 6 hours for 24 hours, followed by a 50% reduction in the previous maintenance dose per day [9].

Mineralocorticoids, which are represented endogenously by aldosterone and deoxycorticosterone, affect electrolyte (sodium and potassium) levels to produce volume changes [2]. Unlike glucocorticoid production, mineralocorticoid production is predominantly controlled by the renin-angiotensin-aldosterone system rather than the HPA axis. The HPA axis' product adrenocorticotropic hormone, on the other hand, has only a minor effect on aldosterone secretion [2].

2.1 Mechanisms of Action of Corticosteroids

Glucocorticoids activate the cytoplasmic glucocorticoid receptor, which translocates to the nucleus and serves as an important regulator of the proinflammatory process that is initiated through NF-κB signaling. NF-κB =nuclear factor-κB; IκBα = inhibitory protein of NF-κB; GC = glucocorticoid; GR = glucocorticoid receptor; GRE = glucocorticoid response elements [12].

2.2 How Do Steroids Work?

The adrenal glands is produced by the synthetic versions of hormones, which are positioned directly above each kidney, are known as steroids. When steroid is taken in higher doses than the body normally produces, it can cause a variety of side effects.

- **Decrease inflammation**. Inflammation take place when the body's immune system reacts to a wound and sickness. The region may become aching, hot, red, and swollen when the skin and tissues beneath the epidermis are impacted. Inflammation is typically beneficial to your health, but it can also be harmful. Steroids can be used to treat inflammatory diseases like asthma and eczema.
- **Decrease the activity of the immune system**, the body's innate anti-infective and anti-sickness defense. This could benefit people with autoimmune diseases like rheumatoid arthritis, autoimmune hepatitis, and systemic lupus erythematosus (SLE), which are caused by the immune system attacking the body in the wrong way.

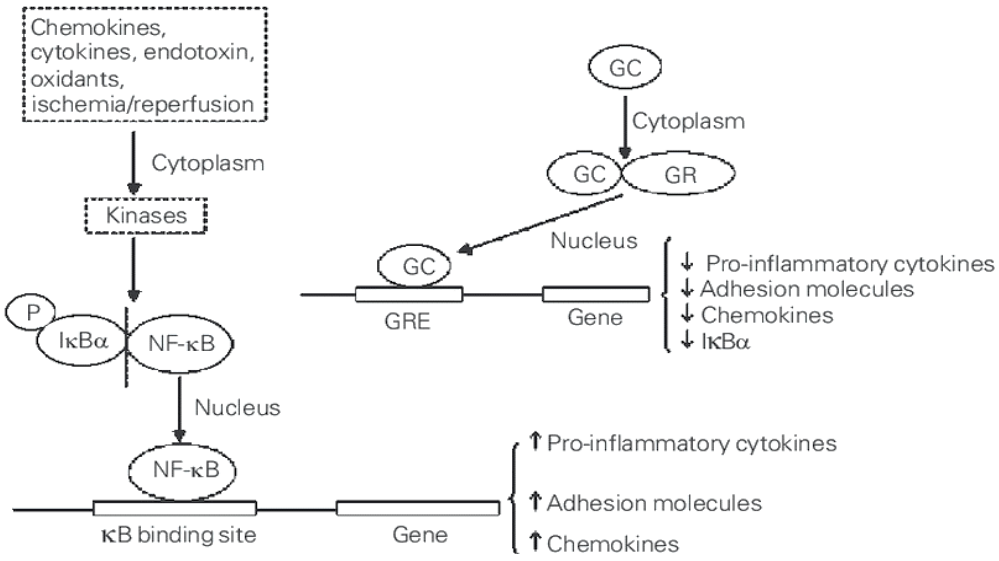

Fig. 1. Mechanisms of action of corticosteroids

2.3 Types of Steroids

Steroids come in different types of form. They are:

2.3.1 Oral steroids

Oral steroids decrease swelling and are used for managing numerous different type of conditions, including:

a. Asthma.
b. Crohn's disease.
c. Ulcerative colitis
d. Arthritis
e. Multiple sclerosis.
f. Adrenal insufficiency.
g. Hypopituitarism.
h. As part of the treatment for various cancers.

2.3.2 Topical steroids

Topical steroids include those used for the skin, nasal sprays and inhalers.
Topical steroids for the skin come in the form of creams, ointments, and lotions. Various skin problems are treated with topical steroids. Fingertip units are widely used to determine the amount of topical steroid to administer.

This steroids can also be given as:

a) Uveitis causes swelling on the surface of the eye, which can be treated with eye drops.
b) Rectal foam or suppositories can be used to treat ulcerative colitis (proctitis) or Crohn's disease that affects the rectum.

2.3.3 Nasal steroid spray

These are the medications which are prescribed to relieve nasal congestion and stuffiness. They're most commonly used to treat nasal allergies like hay fever. Steroid Nasal Sprays is a separate booklet that you should read.

2.3.4 Steroid inhalers

Steroids breathed are also known as inhaled corticosteroids. Inhaled steroids, often known as corticosteroids, are used to treat lung inflammation. They're used to treat asthma and other respiratory illnesses such as chronic obstructive pulmonary disease (COPD). These steroids are hormones that the body produces on its own. They're not the same as anabolic steroids, which are used by certain people to bulk up. The most prevalent illnesses for which they are prescribed are asthma and COPD (chronic obstructive pulmonary disease).

2.3.5 Steroid injections

Joint pain and rheumatoid arthritis can be treated with steroid injections. They can also be used to treat soft tissue diseases such tendon irritation and tennis elbow. See the companion booklet titled Steroid Injections for further details [3].

2.4 Side Effects of Steroids

Oral steroids have a higher rate of side effects, which can include [3]:

- Pre-diabetes or type 2 diabetes.
- Dyspepsia (Indigestion).
- Acid reflux (Heartburn).
- Increased appetite, which may cause weight gain.
- Insomnia.
- Increased risk of infections, especially viral infections such as shingles or measles.
- Osteoporosis (Weakening of the bones).
- Hypertension (High blood pressure).
- Cushing's syndrome is caused by an overabundance of steroid in the body, which can cause thinning of the skin, easy bruising, and stretch marks, among other things.
- Eye problem, such as glaucoma and cataracts.
- Mental illness, including:
- A shift in mood and etiquette - eg, feeling irritable or anxious.
- Depression.

2.5 How Do Steroid Medications Affect Blood Glucose Levels?

Some diabetics may need steroid drugs to treat other ailments such asthma, arthritis, autoimmune diseases, and dermatitis, or as part of chemotherapy.

This medicines can be used to relieve pain and inflammation, as well as to prevent nausea during medical operations (such as chemotherapy).

These hormones (also known as corticosteroids) are produced by the body to aid in the battle against stress, injury, and disease. Steroid drugs work in the same way that hormones generated by the body do. Cortisone, hydrocortisone, prednisolone, prednisone, and dexamethasone are only a few examples of steroid drugs.
These medications can be taken in various ways, including:

- ✓ orally (as tablets or liquid)
- ✓ by using inhaler
- ✓ by injection (into a joint, vein or muscle)
- ✓ eyes drop or ears drop
- ✓ as a cream applied to the skin.

The levels of blood glucose are likely to rise if a person has diabetes and is taking steroid medication. Insulin resistance can be caused by steroid medications, which allow the liver to release stored glucose into the bloodstream, causing blood glucose levels to rise.

The time it takes for these medications to start affecting the levels of blood glucose varies depending on how we take them.

Steroids taken orally: Within a few days of taking oral steroids, blood glucose levels may begin to rise. The effect of steroids on blood glucose levels varies depending on the time, amount, and kind of steroid used. Blood glucose levels may rise quickly after a steroid treatment and remain elevated for 3-10 days [13].

3. CORTICOSTEROIDS IN DIABETES PATIENTS INFECTED WITH COVID-19

According to a review of medical history, signs and symptoms, demographic data, laboratory and CT results from 174 consecutive COVID-19 patients, diabetes is a risk factor for COVID-19 and a poor prognostic predictor of the condition [14].

According to a comprehensive study report published in 2010, the overall prevalence rates of diabetes and prediabetes in Chinese adults are 11.6 percent and 50.1 percent, respectively, suggesting that 113.9 million people have diabetes and 493.4 million people have prediabetes [15]. These estimates are believed to be far higher now than they were ten years ago, when COVID-19 first emerged in China at the end of 2019. As a result, COVID-19-infected patients with diabetes and prediabetes form a large group in China that need specific attention and treatment.

Inflammatory cytokines such as interferon and interleukins are decreased in people with diabetes. Downregulation of these cytokines disturbs the host's internal milieu, switches Th1 cells to Th2, changes macrophage and lymphocyte function, and alters the activity of mucosal endothelium cells on the innate immune system's front line. When a virus infects a person, all of these changes weaken the body's barrier and immune system. Immune system dysregulation could possibly be to responsible for the disease's prolonged course and slow recovery in critical individuals.

An important component of the renin–angiotensin–aldosterone system is angiotensin-converting enzyme 2 (ACE2) (RAAS), is involved in the detection and internalisation of COVID-19 infection. Insulin resistance or decreased insulin production are caused by the overexpression of ACE2 in various organs, including the pancreas [16].

Low-dose (30–80 mg/day) and short-term (3–5 days) methylprednisolone is a common therapeutic method in clinical practice, based on the 17-year-old lesson of the SARS pandemic. However, a study indicated that low-dose, short-term therapy has no significant effect on pulmonary exudation or cytokine storm prevention [17].

3.1 What Factors Contribute to the Risk of Complications and Death in Diabetic Individuals Who Get Covid-19 Infection?

In people with uncontrolled diabetes, the body's immunity is weakened. Due to a lack of immunity, when the virus enters the body, it is unable to resist and fight the COVID-19 infection as well as persons without diabetes. As a result, a hyperinflammatory response known as a cytokine storm develops. This leads the body to generate a variety of harmful cytokines and inflammatory compounds, causing multi-organ damage, which is why diabetics have been recorded to have severe respiratory problems, cardiovascular problems, acute kidney and liver damage, and even death. When blood sugar levels rise rapidly, diabetic ketoacidosis might develop [18].

Diabetes treatment has remained unchanged, however it has become more intensive. For people with mild diabetes and mild COVID-19, nothing has changed, and patients are still taking the same medications. If the diabetes or COVID-19 infection is severe enough that the patients must be admitted to the hospital, they must be started on insulin, which is normally given many times a day. This is exacerbated by the use of steroids in severe cases of COVID-19, which causes blood sugar levels to rise, necessitating a higher dose of both antidiabetic medicines and insulin [18].

COVID-19-related new-onset diabetes can be caused by a number of factors.

- ✓ People may experience a new start of diabetes as a result of stress, anxiety, or depression.
- ✓ Diabetes can be triggered by weight gain caused by an improper diet and a lack of exercise.
- ✓ Steroids, especially high doses of dexamethasone used in severe COVID-19 instances, can cause new onset DM as well as an acute exacerbation of pre-existing mild diabetes..
- ✓ A condition known as "Covid induced diabetes." Although clear confirmation for this is currently lacking, it is thought that the coronavirus can directly destroy pancreatic cells.

3.2 What Role may a Diabetologist Play in the Post-COVID-19 Care Strategy?

COVID-19 has instilled in everyone the importance of proper diabetes care. As a result, the diabetologist must raise public awareness about how to effectively manage diabetes. This may aid in the prevention of COVID-related complications as well as diabetes-related issues such as diabetic eye disease, renal disease, cardiovascular disease, nerve problems, and so on. As a result, a greater emphasis on educating diabetic patients and raising awareness about diabetes and the repercussions of inadequate diabetes management is required [18].

3.3 Clinical Consequences of Corticosteroid usage in COVID-19 Patients: a Comprehensive Review and Meta-Analysis

In this systematic review and meta-analysis on the effectiveness and safety of corticosteroids in COVID-19 patients, the pooled estimate of observational retrospective studies and RCTs confirmed the positive effect of corticosteroids therapy on mortality in COVID-19 disease, as first reported in the RECOVERY trial. Furthermore, the need for mechanical ventilation in COVID-19 patients who were already respiratoryly compromised was reduced in corticosteroid-treated COVID-19 patients. Although the data from the studies was insufficient to draw any firm conclusions, the corticosteroid group may exhibit symptoms of virus clearance delays, as well as an increase in antibiotic use and infection [19].

4. CONCLUSION

As the therapeutic benefits of glucocorticoids are expanded across medical fields, the incidence of steroid-induced or steroid-exacerbated diabetes will continue to climb. Both steroid-related and non-steroid-related diabetes benefit from early detection and risk factor modification. Diagnosed poor fasting glucose or impaired glucose tolerance prior to starting chronic glucocorticoids can assist identify those who would benefit from steroid-sparing medication or, if that is not an option, blood glucose monitoring while starting therapy. The COVID-19 pandemic has opened our eyes on the importance of controlling hyperglycemia. The focus of diabetes management over the years has moved towards an individualized approach towards reduction of cardiovascular disease, kidney disease and microvascular complications. Uncontrolled diabetes a silent killer, needs timely appropriate management for better health care outcomes - both short and long term. Future diabetes prevention and treatment efforts will be guided by more study into the exact mechanism of steroid-induced insulin resistance.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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