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A CASE REPORT ON PREDNISOLONE INDUCED HYPERGLYCEMIA IN CHRONIC KIDNEY DISEASE AND ROLE OF CLINICAL PHARMACIST

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ABSTRACT

Prednisolone is a 1, 2-dehydrocortisol which is highly potent synthetic glucocorticosteroid which has minimal mineralocorticoid activity. Like immunosuppressive or anti inflammatory agent Prednisolone can also be used, which indicated in the treatment of various conditions, including congenital adrenal hyperplasia, psoriatic arthritis, systemic lupus erythematous, bullous dermatitis herpetiformis, seasonal or perennial allergic rhinitis. Majorly it causes Cushing Syndrome, peptic ulceration, edema, hypokalemia, muscle weakness, behavioral changes. Hyperglycemia is the most common side effect of Glucocorticoids and more representative. A 60 year old male patient was consulted in the nephrology department with chief complaints of shortness of breath, past medical history of patient includes hyperntension, diabetis mellitus, chronic kidney disease, In-order to prevent serious adverse drug reactions of this drug, close monitoring during treatment course, creating awareness, recognition of the problem and careful management of all patients who receive this medication are essential.

KEYWORDS: Prednisolone, hyperglycemia, adverse drug reaction.

INTRODUCTION

Drugs like steroids have been used in a variety of conditions like both acute and chronic[1] extensively. At supraphysiological doses, they reduce the synthesis of pro-inflammatory cytokines, T-cell function, and antibody Fc receptor expression, which activate anti-

inflammatory and immunosuppressive processes, making them the cornerstone in treatment of numerous inflammatory diseases.[2,3]

Their use is limited, despite their efficacy by the wide variety of side effects, majorly partited into three classifications: idiosyncratic, gradual and immediate. Immediate effects include fluid retention, blurred vision, mood changes, insomnia, weight gain, and modulation of the immune response. Endocrine metabolism, especially hyperglycemia, osteopenia with subsequent osteoporosis, dyslipidemia, central obesity, and adrenal suppression are more gradual effects noticed. Acne, dyspepsia and skin thinning are considered of gradual onset. Avascular necrosis, cataracts, open-angle glaucoma and psychosis[3-5] are some of the idiosyncratic effects observed.

Steroids are the main cause of drug-induced hyperglycemia.[4] hyperglycemia in patients with known diabetes mellitus (DM) they not only exacerbate, but also cause DM in patients without documented hyperglycemia before the initiation of glucocorticoids (GC) therapy,[1,6] with an incidence that can reach up to 46% of patients, and increases in glucose levels up to 68% compared to baseline.[7-9] Furthermore, in some populations they can precipitate acute complications such as nonketotic hyperosmolar state, and diabetic ketoacidosis[10] and in a few instances death, especially in patients with pre-existing DM.

This is the case report of 60 year old male patient who consulted nephrology department with the chief complaints of shortness of breath. Prednisolone is available in the form of oral and parental forms (IM). It's readily absorbed into gastrointestinal tract; peak plasma concentration is 1-2 hours after administration. 90% shows high protein binding. Biological half-life of prednisolone is 2-3 hours, with 65% of excreted in the urine either in free form or glucoconjugate.

CASE REPORT

A 60year old male patient was consulted in nephrology department with chief complaints of shortness of breath, past medical and social history of patient includes; he was a known case of DM type2, HTN,CKD, and alcoholic The prescribed medication for the patient are included in the table 1. the patient was treated in, in patient department(IPD) of a nephro center with care. The list of prescribed from the day are given in the table, on the second day prescription doctor introduced the Tab wysolone (prednisolone)40mg orally. On the 3rd day after the fasting blood sugar examination of patient was seen to be 297mg/dl (100-125mg/dl)

which was 140mg/dl on the 2nd day RBS examination. Based on the above information we have suspected it as possible ADR (hyperglycemia). upon a literature review on prednisolone pharmacology and its effects that support the occurrence of hyperglycemia. The relationship between the effect and drug have also done dechallenge test i.e. drug was withdrawn from the treatment regimen, and prescribed

Table 1: Showing the day wise prescription of the patient.

S. no	Drug	ROA	Dose	Freq	Day1	Day2	Day3
	R.B.S				140mg/dl	297mg/dl	140mg/dl
01	Inj Ceftriaxone & Tazobactam	I.V	1gm	B.D	✓	✓	✓
02	Inj torsemide	I.V	20mg	B.D	✓	✓	✓
03	Tab metolazone	P/O	5mg	B.D	✓	✓	✓
04	Multivitamins & antioxidants	P/O	1 cap	O.D	✓	✓	✓
05	Inj pantaprazole	I.V	40mg	O.D	✓	✓	✓
06	Inj ondansetron	I.V	4mg	O.D	✓	✓	✓
07	Neb-salbutamol+budesonide	Nasal			✓	✓	✓
08	Tab-prednisolone	p/o	40mg	O.D	×	✓	✓
09	Calcium gluconate +ca lactate+cholecalciferol	P/O	10ml	TID	×	✓	✓
10	INJ- insulin	S.C	30 units	B.D	×	×	✓

DISCUSSION

GC's provide a substrate for oxidative stress metabolism increasing lipolysis, proteolysis, and hepatic glucose production.[4] After GC administration, mechanism responsible for intolerance of glucose is similar to that of type 2 DM since steroids increase insulin resistance depends on the dose and type used,[14,15] which can be up to 60%-80. There is the enzymatic activity of 11β-hydroxysteroid dehydrogenase% among the notable factors that modify the biological effects of steroids, which is classified into two types: type 1, expressed in liver and adipose tissue and amplifies the local action of steroids to convert cortisone to cortisol, and type 2, which predominates in renal tissue and reduces the effect of converting cortisol to cortisone.[4] Skeletal muscle is responsible for 80% of postprandial glucose represents storage and the largest reserve of glycogen in the body. Its storage is totally dependent on the presence of insulin and the availability of the glucose transporter type 4 (GLUT4) glucose transporter in the cell membrane. Insulin resistance is induce by steroids, which interfere with signaling cascades, within muscle cells mainly the GLUT4 transporter, with the subsequent 30%-50% reduction in insulin-stimulated glucose uptake and a 70% reduction in insulin-stimulated.

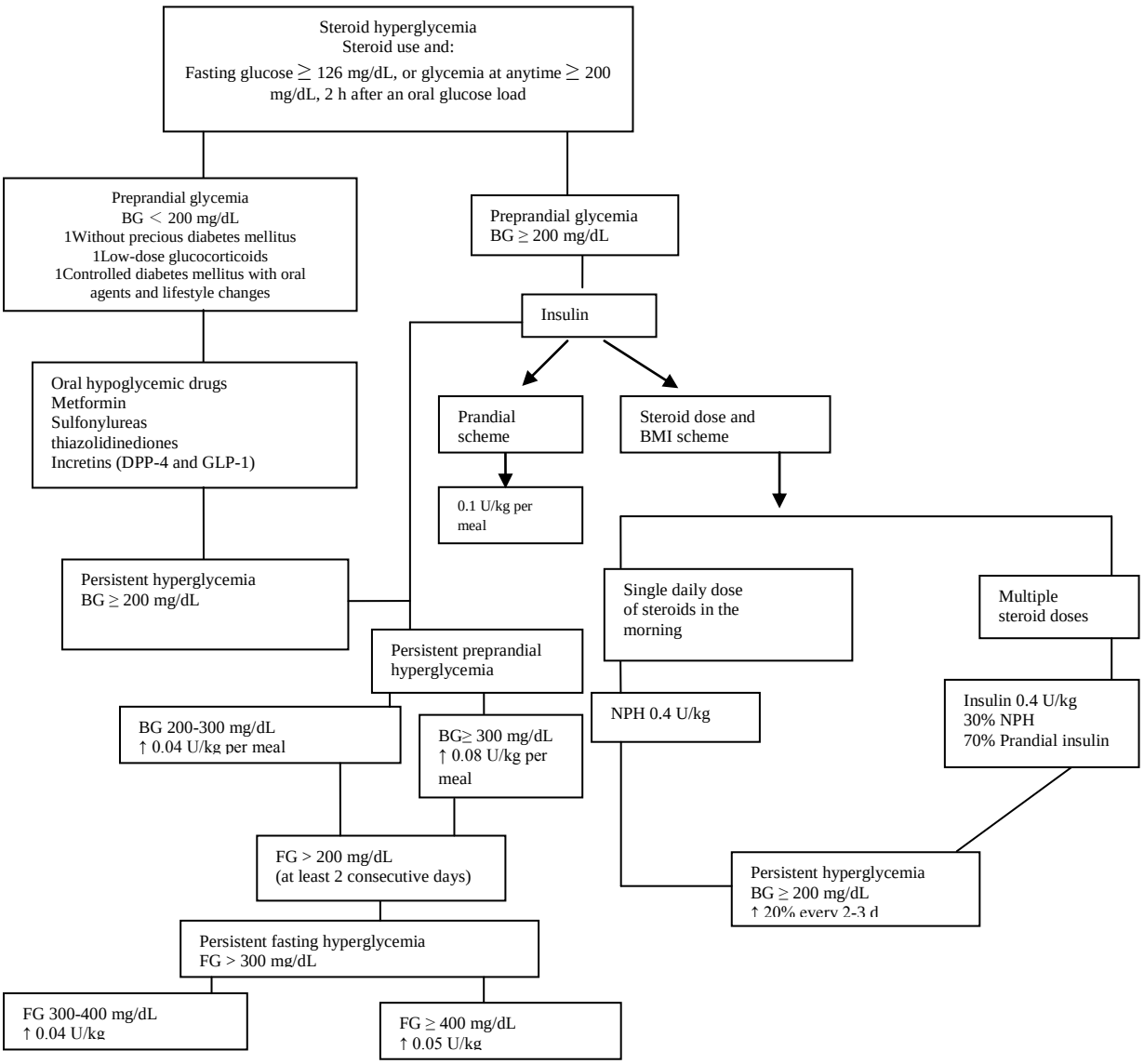
These promote the accumulation of intramyocellular lipids (acetyl coenzyme A, diacylglycerol and ceramide), reducing the entry and storage of intramuscular glucose.[4] The liver maintains euglycemia in the fasting state, *via* gluconeogenesis and glycogenolysis, effects that are counteracted by insulin after food intake. Insulin is effected by the metabolic effects through GC's antagonism, through the induction of enzymes particularly in the postprandial state that promote gluconeogenesis, increased mitochondrial activity, increased lipolysis and proteolysis, the enhancement of the effects of counter regulatory hormones, such as and epinephrine, glucagon and the induction of insulin resistance *via* the nuclear peroxisome proliferator-activated receptor (PPAR) α.[4,21,25] Steroids have direct effects on various adipokines: (1) glucose tolerance is influencing by promoting the expression of resistin and adipokinines; (2) insulin sensitivity is promoted by decreasing the expression of adiponectins; and (3) stimulating of leptin expression and secretion. Finally, they are responsible for increasing triglyceride hydrolysis in adipocytes.[4] These effects have the final result of increased plasma levels of non-sterified fatty acids, which accumulate within muscle cells and reduce glucose uptake by interfering with insulin signaling.[24,25] the function of pancreatic beta cells through the reduction of GLUT2 is alterd by GC'S and glucokinase receptor expression at the same time activity of glucose-6-phosphate dehydrogenase is increasing, with the consequent alteration in β-oxidation. Insulin synthesis is reduced additionally, and through the induction of beta cell apoptosis. it is thought that they reduce cell mass .Likewise, in response to the decrease in insulin sensitivity, the pancreatic beta cell normally increases insulin secretion to maintain glucose homeostasis, but at times this increase is not sufficient to compensate for the insulin resistance resulting in hyperglycemia.[4,15] With the subsequent state of hyper insulinism based on the aforementioned, GC's increase insulin resistance. In healthy subjects, this mechanism is compensated by an increase in pancreatic insulin secretion, causing serum glucose levels to remain within normal range.[14] However, in susceptible populations, such as normoglycemic individuals with reduced insulin sensitivity and a low rate of production of the same prior to steroid use, this offsetting effect is lost, resulting in hyperglycemia[4] (Table 1).

CONCLUSION

In a variety of medical conditions GCs are drugs that have been widely used. Despite their medical efficacy, steroid induced hyperglycemia remains as a common potentially harmful problem that must be considered when using any type a dose of GC. Little is known, despite its frequency about the impact of hyperglycemia associated with steroid use on clinical

comorbidity and mortality. Early detection and effective treatment in these patients requires, proper knowledge in understanding the mechanisms involved in steroid hyperglycemia is essential. Appropriate guidelines that establish there commendations for the diagnosis and treatment of steroid diabetes are needed in order to prevent all the complications associated with the hyperglycemic state. Insulin must be the treatment of choice in most of the cases, in cases of serum glucose > 200 mg/dL is mostly used. Nevertheless an individualized approach must be taken in each patient in order to consider lifestyle modifications and oral hypoglycemic drugs as alternative therapeutic options.

ROLE OF CLINICAL PHARMACIST IN MONITERING BLOOD GLUCOSE LEVLES: SEE IN FLOW CHART



CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

ADR: Adverse Drug Reaction; DM- diabetes type II, HTN- hypertension, CKD- chronic kidney disease.

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