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PREDNISOLONE : A MULTIPURPOSE GLUCOCORTICOID

Damini V. Chandile*, Lokesh G. Barade, Harshal L. Tare

TSPM'S Trimurti Institute of Pharmacy, Jalgaon, Maharashtra, India.

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For Correspondence:

Damini V. Chandile

TSPM'S Trimurti Institute of Pharmacy, Jalgaon, Maharashtra, India

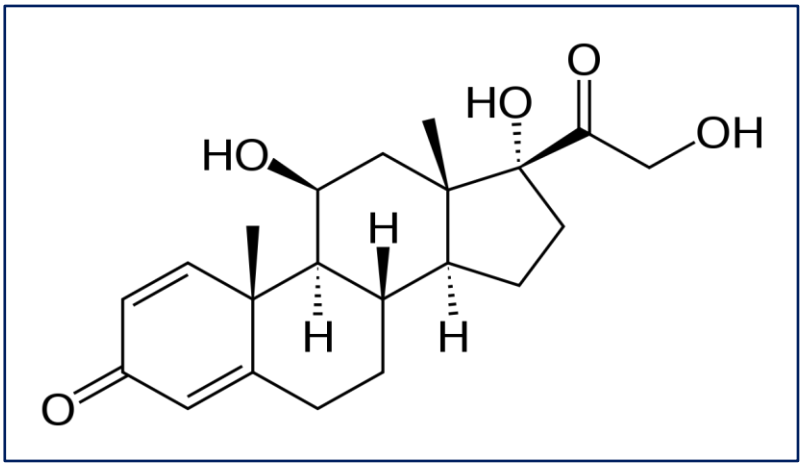
E-mail:

daminichandile@gmail.com

ABSTRACT

Prednisone is a drug which belongs to the pharmacological category of systemic corticoids. It is a pro-drug that is converted in prednisolone in the liver, has an anti-inflammatory effect four times more powerful than hydrocortisone. Though it is a multipurpose drug it has several side effects also. Nowadays prednisolone is getting used widely but it is showing adverse reactions also. In this review we will study about both advantages of prednisolone and side effects of prednisolone.

Introduction:



Prednisolone is a steroidal anti-inflammatory drug with predominant glucocorticoid and low mineral corticoid activity.[1] It is important to take this medication as prescribed. To avoid stomach upsets this medicine should be taken with meal, snack or a glass of milk. It is risky to stop prednisolone without guidance of a doctor. Predniosolone is a very effective medication. More effects are related to the size of the dose and the length of the time that the child is on the medication. It used in the treatment of a wide range of inflammatory and auto-immune diseases such as asthma, multiple sclerosis, rheumatoid arthritis and auto immune hepatitis etc. Prednisolone can increase glomerular permeability to proteins in patients with a nephritic syndrome. Glucocorticoid treatment is regularly used in patients with a nephrotic syndrome due to minimal change disease or membranous nephropathy.[2]

Prednisolone is also known as 'disease modifying anti-arthritic drugs' because of its anti-inflammatory action by inhibiting gene transcription for COX-2, cytokinesis, cell adhesion molecules, and inducible NO synthetase.[3] This medication reduces body's ability to fight off infections and may hide more obvious signs of illness like fever. Corticosteroids play an important role in the treatment of acute exacerbation of asthma.[7]

Mechanism of action:

Prednisolone is a synthetic adrenocorticoid steroid drug with predominantly glucocorticoid properties. Some of these properties reproduce the physiological actions of endogenous glucocorticosteroids, but others do not necessarily reflect any of the adrenal hormones normal functions; they are seen only after administration of large therapeutic doses of the drug. The pharmacological effects of prednisolone which are due its glucocorticoid properties include: promotion of gluconeogenesis; increased deposition of glycogen in the liver; inhibition of the utilization of glucose; anti-insulin activity; increased catabolism of protein; increased lipolysis;

stimulation of fat synthesis and storage; increased glomerular filtration rate and resulting increase in urinary excretion of urate (creatinine excretion remains unchanged); and increased calcium excretion. Depressed production of eosinophils and lymphocytes occurs, but erythropoiesis and production of polymorphonuclear leucocytes are stimulated. Inflammatory processes (edema, fibrin deposition, capillary dilatation, migration of leukocytes and phagocytosis) and the later stages of wound healing (capillary proliferation, deposition of collagen, cicatrization) are inhibited. Prednisolone can stimulate various components of gastric juice. Suppression of the production of corticotropin may lead to suppression of endogenous corticosteroids. Prednisolone has slight mineralocorticoid activity, whereby entry of sodium into cells and loss of intracellular potassium is stimulated. This is particularly evident in the kidney, where rapid ion exchange leads to sodium retention and hypertension.[4]

Pharmacokinetics:[4]

1. Absorption
2. Distribution
3. Metabolism
4. Excretion

1. Absorption:

Oral administration of single doses of 30 mg prednisolone base equivalent of Orapred ODT, and Pediapred Solution to 21 adult volunteers yielded comparable pharmacokinetic data.

Table 1. Comparison of Mean Pharmacokinetic Parameters (%CV) in Healthy Volunteers following a Single Dose of 30 mg Orapred ODT and Pediapred Solution,

Dose* (30 mg prednisolone base equivalent)	$AUC_{0-\infty}$ (ng.hr/ml) (± S.D.)	C_{max} (ng.hr/ml)** (±S.D.)
Pediapred Solution	2426.1 (360.0)	461.33 (77.94)
Orapred ODT	2408.1 (361.5)	420.91 (78.28)

*Administered under fasting conditions.

**Mean values of 21 normal volunteers.

2. Distribution:

Prednisolone is 70-90% protein-bound in the plasma and the volume of distribution is repeated as 0.22-0.7 L/kg.

3. Metabolism:

Prednisolone is reported to be metabolized mainly in the liver and excreted in the urine as sulfate and glucuronide conjugates.

4. Excretion:

Prednisolone is eliminated from the plasma with a mean (+/- SD) half-life of 2.6 (+/- 0.27) hours.

Inactive Ingredients of prednisolone:

The tablets contain lactose monohydrate, magnesium stearate, microcrystalline cellulose, pregelatinized starch and sodium starch glycolate.

Prednisolone Oral Solution contains alcohol, citric acid, disodium edetate, fructose, hydrochloric acid, maltol, peppermint oil, polysorbate 80, propylene glycol, saccharin sodium, sodium benzoate, vanilla flavor and water.[5]

Indications and usage:[5]

1. Endocrine Disorders
2. Rheumatic Disorders
3. Collagen Diseases
4. Dermatologic Diseases
5. Allergic States
6. Ophthalmic Diseases
7. Respiratory Diseases
8. Hematologic Disorders
9. Neoplastic Diseases
10. Edematous States
11. Gastrointestinal States
12. Miscellaneous

CLASSICAL SIDE EFFECTS[6]

1. Infectious disorders

Prednisolone is widely prescribed in dialy medical practice, transcending speciality limits. The frequency and the heretogeneity of de adverse reactions attributed to prdnisone are substantial, although this relation is not proven or totally cleared in some cases, the manifestations vary from tenuous and transitory symptoms to debilitating and even lethal consequences. As it often happens in more pharmaceutical approaches, the side effects are proportional to dosage and length of the therapy.[6]

2. Endocrine and Metabolic Complications

Prednisolone enhances the appetite and provokes liquid retention, causing weight gain. Gonadic function is frequently altered. In men, corticosteroids inhibit gonadotropin secretion, including abnormal levels of testosterone and manifestations like decreased libido and diminution of body

hair. In women, the lower responsivity to Luteinizating Hormone and Gonadotropin-Releasing Hormone causes menstrual irregularities and amenorrhoea.

3. Fluid and Electrolyte Balance

Generally, prednisone administration relates to water and sodium retention, as well as potassium depletion, which may even cause a hypokalemic alcalosis. Diet modifications and blood pressure monitoring are essential measures.

4. Musculoskeletal Implications

Because of protein metabolism modifications, muscle weakness and loss of bulk may occur, usually in mild forms and affecting more prominently the lower limbs, these complications may even arise as severe disability, striking proximal muscles and causing wide mobility impairment. It is shown that more than one third of the patients treated with glucocorticoids during 5 to 10 years develop osteoporosis. The bone loss is more intense at the first 6 months of therapy and is greater at the trabecular bone. Even low doses of prednisolone like 2.5mg/day can culminate in bone loss.

5. Hematological Disorders

Prednisolone treatment increases white blood cell count, affecting differently the leukocyte subtypes, monocytes, limphocytes and eosinophils are decreased, while polymorphonuclears are increased.

6. Cardiovascular System

Hypertension is the most observed cardiovascular side effect of glucocorticoids. Fibrinolysis activity modification, blockage of nitric oxide formation and elevated triglycerides and total cholesterol serum levels induce endothelial dysfunction and cause higher rates of thromboembolic complications in patients treated with systemic glucocorticoids.

7. Dermatologic Affections

Excessive androgen liberation, fibroblast activity inhibition and immunosuppression are the main etiologic factors involved in the dermatological modifications. Skin infections, acne, thinning and increased skin fragility, hirsutism, poor wound healing, facial erythema and easy bruisability are common skin abnormalities during sustained prednisone therapy.

8. Gastrointestinal Tract

Singly prednisolone has low probabilities of provoking peptic ulcer disease or digestive hemorrhage, but it is also known that glucocorticoids in general are related to gastric intolerance and that it may cause peptic ulcer disease or digestive hemorrhages when associated with other risk factors, such as smoking and use of non-steroidal anti-inflamatories.

9. Ophthalmological Complications

Posterior subcapsular cataracts is the most eminent ophthalmological side effect of corticosteroid therapy, the suspension of drug administration does not guarantee regression of the dysfunction; children are more vulnerable to this event. Glaucoma may occur on patients under chronic use of prednisone as well.

Warnings:

1. Cardio-Renal:

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses.

2. Endocrine:

Corticosteroids can produce reversible hypothalamic-pituitary adrenal (HPA) axis suppression with the potential for corticosteroid insufficiency after withdrawal of treatment. Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients.

3. Infection:

a) General:

Patients who are on corticosteroids are more susceptible to infections than are healthy patients. Infection with any pathogen (viral, bacterial, fungal, protozoan or helminthic) in any location of the body may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect cellular immunity, humoral immunity or neutrophil function.

b) Fungal infections

Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections unless they are needed to control life-threatening drug reactions.

c) Special Pathogens:

Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogens, including those caused by Amoeba, Candida, Cryptococcus, Mycobacterium, Nocardia, Pneumocystis, Toxoplasma.

d) Tuberculosis:

The use of prednisone in active tuberculosis should be restricted to those of fulminating or disseminated tuberculosis in which the corticosteroid is used for management of the disease in conjunction with an appropriate antituberculous regimen.

e) Vaccination:

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered. However, the response to such vaccines may be diminished and cannot be predicted.

f) Viral Infections:

Chickenpox and measles can have a more serious or even fatal course in pediatric and adult patients on corticosteroids. In pediatric and adult patients who have not had these diseases, particular care should be taken to avoid exposure.

i) Ophthalmic:

Use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to bacteria, fungi or viruses.

Precautions:[5]

a) General precautions:

The lowest possible dose of corticosteroids should be used to control the condition under treatment. When reduction in dosage is possible, the reduction should be gradual.

b) Gastrointestinal:

Steroids should be used with caution in active or latent peptic ulcers, diverticulitis, fresh intestinal anastomoses, and nonspecific ulcerative colitis, since they may increase the risk of a perforation.

c) Neuro-Psychiatric: l

Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that they affect the ultimate outcome or natural history of disease.

d) Information for patients:

Patients should be warned not to discontinue the use of corticosteroids abruptly or without medical supervision. As prolonged use may cause adrenal insufficiently and make patients dependent on corticosteroids.

e) Pregnancy:

There are no adequate and well-controlled studies in pregnant women. Corticosteroids should be used during pregnancy only if the potential risk to the foetus. Infants born to mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

f) Pediatric Use:

The efficacy and safety of corticosteroids in the pediatric population are based on the well-established course of effect of corticosteroids, which is similar in pediatric and adult populations. Like adults, pediatric patients should be carefully observed with frequent measurements of blood pressure, weight, height, intraocular pressure and clinical evaluation for the presence of infection, psychosocial disturbances, thromboembolism, peptic ulcers, cataracts and osteoporosis.

g) Geriatric Use:

Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy. In particular, the increased risk of diabetes mellitus, fluid retention and hypertension in elderly patients treated with corticosteroids should be considered.

Conclusion:

Though prednisolone is a multipurpose drug; it has more side effects also. It is necessary to take this medicine when prescribed but not in excess quantity. The main side effect is psychosis, mood swings etc. Pregnant womens should avoid taking this drug as it can show the signs of hypoadrenalism in foetus. Continuous consuming of prednisolone can make the habbit of corticosteroids to the patients.

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