

A REVIEW ON DEXAMETHASONE AND ITS SIGNIFICANCE

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ABSTRACT

Dexamethasone is a globally used corticosteroid in treatment rheumatic problems, skin diseases and cancers. It was first discovered by Philip Showalter Hench in 1957 and was approved for medicinal use in 1961. It is one among the list of essential medicines released by World Health Organization (WHO). National Institutes of Health (NIH), US and National Health Service, UK have recommended use of Dexamethasone in patients with severe COVID-19 symptoms and are on external oxygen supply. This article aims to discuss the structure of Dexamethasone, its pharmacokinetics, applications in the various fields of medicine, side effects and brief the role of Dexamethasone in the treatment of COVID-19. This article highlights the latest research developments in the use of Dexamethasone for the treatment of COVID-19. Lack of sufficient data on SARS-CoV-2 relating it to the symptoms and treatment makes it extremely significant for new age researchers to build upon the already established antiviral drugs such as Dexamethasone.

KEYWORDS: COVID-19, Corticosteroids, Dexamethasone, Glucocorticoids, Pandemic.

INTRODUCTION

In December 2019, Wuhan, Hubei province, China, became the epicenter of COVID-19 pandemic caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2).^[1] There are several reports of using corticosteroids in the setting of severe coronavirus infections including SARS-CoV-2 and MERS. There is however less data on safety and efficacy of corticosteroids in COVID-19 and its application to treat SARS and MERS infection in Controversial.^[2,3] Reports of efficacy of corticosteroids in patients with SARS-CoV infections have resulted in widespread use of the therapy to treat COVID-19, especially for people with severe infection hospitalized in the ICU. Presently there is significantly less data on the safety and efficacy profiles of corticosteroids like Dexamethasone.^[4]

Dexamethasone is a type of corticosteroid medication used in the treatment of several disordered conditions, including the ones that closely mimic cortisol, the hormone naturally produced by adrenal gland in humans, rheumatic problems, a number of skin diseases, severe allergies, asthma and chronic obstructive lung disease. It is an established anti-inflammatory drug, commonly used to treat conditions in which the body's immune system does not function properly leading to inflammation and tissue damage. Dexamethasone reduces the production of the cytokines and prostaglandins, chemicals that cause inflammation. It is also used to treat nausea and vomiting

in cancer patients that is caused as a side effect to the administration of chemotherapy drugs.^[5]

National Institutes of Health (NIH), US and National Health Service, UK has now recommended the use of Dexamethasone in patients who are severely affected with COVID-19 and are mechanically ventilated or under oxygen supply.^[6]

Structure of Dexamethasone

Dexamethasone is a fluorinated steroid, a 3-oxa-Delta-(1), Delta-(4)-steroid, a glucocorticoid, a 20-oxo steroid, an 11beta-hydroxy steroid, a 17alpha-hydroxy steroid and a 21-hydroxy steroid [see Fig 1]. It is derived from a hydride of a Pregnane.^[7] It is a synthetic member of the class of glucocorticoids and is used globally as an adrenergic, antiemetic, antineoplastic, xenobiotic, an immunosuppressant and an anti-inflammatory drug.

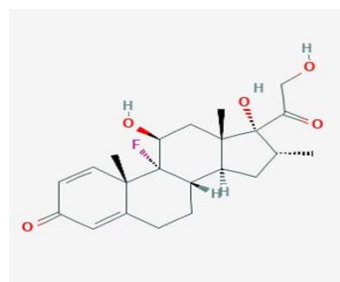


Fig. 1: Structure of Dexamethasone.

Pharmacokinetics

Pharmacokinetics is a branch of pharmacology that deals with study of all the physiological effects of body on the drug administered. It involves Absorption, Distribution, Metabolism and Excretion of the drug.

Absorption of Dexamethasone: Dexamethasone is largely an orally administered drug that readily gets absorbed in the small intestine. However the variable onset and duration of action depends on other parenteral modes of drug administration such as Intra-articular space, Intra muscular or Intra vascular modes. An Intra vascular administered drug is absorbed at the highest rate.

Distribution of Dexamethasone: Dexamethasone is distributed from blood into muscle cells, liver, skin, intestine and kidneys. Dexamethasone is bound weakly to plasma proteins; transcortin and albumin. Only the unbound portion is active.

Metabolism of Dexamethasone: Dexamethasone is metabolized in the liver to inactive glucuronide and sulfate metabolites through Phase 1 and Phase 2 enzyme systems.

Excretion of Dexamethasone: Inactive metabolites and small amounts of unmetabolized drug is excreted by the kidneys. Insignificant quantities are also excreted in feces. The biologic half-life of Dexamethasone is 36 to 54 hours.^[8]

Applications of Dexamethasone**1. As Anti-inflammatory agent**

Dexamethasone is used as treatment to inflammatory and autoimmune disorders such as rheumatoid arthritis and bronchospasm. Idiopathic thrombocytopenic purpura, a decrease in numbers of platelets due to an immune problem, responds to 40 mg of Dexamethasone daily for four days.

It is also given in small amounts before and/or after some forms of dental surgery, such as the extraction of the wisdom teeth, an operation which often leaves the patient with puffy, swollen cheeks.

Dexamethasone is commonly given as a treatment for croup in children, as a single dose can reduce the swelling of the airway to improve breathing and reduce discomfort.

It is injected into the heel when treating plantar fasciitis, sometimes in conjunction with triamcinolone acetone.^[9]

2. As Anti – Cancer agent

Patients on cancer chemotherapy are often given dexamethasone to counteract certain side effects of the treatment. In brain tumors (primary or metastatic), dexamethasone is used to counteract the development of

edema, which could eventually compress other brain structures. It is also given in cord compression, where a tumor compresses the spinal cord.

Dexamethasone is also used as a direct chemotherapeutic agent in certain haematological malignancies, especially in the treatment of multiple myeloma, in which dexamethasone is given alone or in combination with other chemotherapeutic drugs.^[10]

3. In Pregnancy

Dexamethasone is administered to women at risk of premature delivery to promote maturation of the fetus lungs. However dexamethasone administration has been associated with low birth weight, although not with increased rates of neonatal death.

Dexamethasone has also been used during pregnancy as an off-label prenatal treatment for the symptoms of congenital adrenal hyperplasia (CAH) in female babies. Early prenatal CAH treatment has been shown to reduce some CAH symptoms, but it does not treat the underlying congenital disorder. Experimental use of dexamethasone in pregnancy for fetal CAH treatment was discontinued in Sweden when one in five cases suffered adverse effects.

A small clinical trial found long-term effects on verbal working memory among the small group of children treated prenatally, but the small number of test subjects means the study cannot be considered definitive.^[11]

Role of dexamethasone in treatment of covid-19

Five observational studies were published evaluating the use of dexamethasone in COVID-19 infection with controversial results; and only one randomized clinical trial showed a decrease in the mortality by 35% in patients with mechanical ventilation and by 20% in others with supplemental oxygen.^[12,13] Dexamethasone is vital to avoid corticosteroids in the initial, stable, mild-to-moderate patients with COVID-19 infections.^[13,14] Studies have also related Dexamethasone to the massive release of cytokines and tumor necrosis factor α .^[15,16] Dexamethasone has a protective effect in severe COVID-19 infections. However, large-scale clinical trials that are ongoing might throw light on the clinical effectiveness of corticosteroids in COVID-19 infection.^[13]

Side Effects

The exact correlation of side effects of dexamethasone is not available, hence the estimates to the side effects is based on available documentation on dexamethasone.

Some common side effects associated with administration of Dexamethasone are: Acne, Insomnia, Vertigo, Increased appetite, Weight gain, Impaired skin healing, Depression, Euphoria, raised intraocular pressure, Vomiting, Dyspepsia, Confusion, Amnesia and Hypertension.

The adverse effects of dexamethasone can also be related to the adverse effects of related corticosteroids such as Irritability, Nausea, Malaise, Headaches, and Cataract (in cases of long-term treatment it occurs in about 10% of patients). Sudden withdrawal after long-term treatment with corticosteroids can lead to: Adrenal insufficiency, Hypotension, Fever, Myalgia, Arthralgia, Rhinitis, Conjunctivitis, Painful itchy skin nodules, Weight loss or even Death.^[17]

CONCLUSION

Corticosteroids and their biologically active synthetic derivatives differ in their metabolic (glucocorticoid) and electrolyte-regulating (mineralocorticoid) activities. These are employed at physiological doses for replacement therapy when endogenous production is impaired. In addition, glucocorticoids such as Dexamethasone potently suppress inflammation, and their use in a variety of inflammatory and autoimmune diseases makes them among the most frequently prescribed drug. The effects of Dexamethasone are numerous and make the study appropriate under the present scenario.

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