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A REVIEW ON THE USE OF CORTICOSTEROIDS

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ABSTRACT

Corticosteroids [CS] are used to treat various diseased conditions such as inflammatory diseases including allergic diseases and hypersensitivity reactions. Cortisol is produced in the adrenal gland and a variety of other hormones are produced through cholesterol metabolism. They are elaborated in the regulation of different processes such as metabolism electrolyte regulation inflammation, and stress responses based on their major effects. Corticosteroids act as anti-inflammatory, antiproliferative, immunosuppressive, and show vasoconstrictive effects. Prolonged use of corticosteroids leads to hormonal changes within the body which may cause a wide range of side effects. Once corticosteroids are prescribed the patient should be monitored regularly and reviewed to assess the response to the treatment with adjusting the dose at a minimum. When corticosteroids are used thoroughly as intensive therapy or for prolonged courses, a tapering strategy is recommended to prevent signs and symptoms of adrenal insufficiency due to hypothalamic-pituitary-adrenal axis suppression.

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INTRODUCTION:

Corticosteroids are potent anti-inflammatory and immune-modulatory agents used to treat various disease conditions. In some cases, produce immediate or delayed hypersensitivity reactions [1]. Corticosteroids are a class of biological negotiators produced in the adrenal gland and synthesized from cholesterol [2]. A variety of other hormones, including cortisol, mineralocorticoid, aldosterone, and male and female sex hormones, are produced through the common pathway of cholesterol metabolism [3]. They are involved in the control of various processes such as metabolism electrolyte regulation inflammation, and stress responses based on their major effects, they are divided into two main groups: glucocorticoids and mineralocorticoids used in the treatment of various pathological conditions and diseases [2].

EPIDEMIOLOGY:

Glucocorticoids are mostly given drugs in modern medicine [4]. 40% of patients taking oral corticosteroids in the UK are with skin diseases (6%), musculoskeletal conditions

(6%) and neurological conditions (3%) which are the next most common conditions being treated with OCS. Despite the associated risks, data show that oral corticosteroids are used by 0.9% of the adult UK population at any one time [5]. Topical corticosteroids were introduced about 50 years ago. They represent an important milestone in dermatologic therapy [6]. The therapeutic uses of corticosteroids were demonstrated firstly by Edward Kendall and Philip Hench in 1948 [7]. During the 1950s it was discovered that hydrocortisone, a natural glucocorticoid hormone, could reduce inflammation and proliferation in some skin disorders [8]. Since the first isolation of cortisol in 1950, corticosteroids have been demonstrated to be highly effective in the treatment of acute inflammation and chronic inflammatory diseases [5].

CLASSIFICATION:

I. GLUCOCORTICOIDS:

Short-acting: cortisone, hydrocortisone. Intermediate-acting: prednisolone, methylprednisolone, triamcinolone, deflazacort.

Long-acting: dexamethasone, betamethasone.

II. MINERALOCORTICOIDS:

Aldosterone, desoxycorticosterone, fludrocortisone [9].

Primary effects of glucocorticoids (GCs): Anti-inflammatory: Inhibits the action of inflammatory mediators (transrepression), or by blocking anti-inflammatory mediators (transactivation)

Immunosuppressive: which stops the delayed hypersensitivity reactions by directly affecting T-lymphocytes

Anti-proliferative: Inhibition of DNA synthesis and skin cell turnover

Vasoconstrictive: Inhibit the action of histamine and other vasoconstrictive mediators [10].

THERAPEUTIC USES: Corticosteroids acts as anti-inflammatory, antiproliferative, immunosuppressive, and vasoconstrictive effects.

1. DERMATOLOGIC DISORDERS: Topical corticosteroids are the cornerstone of treatment. These effects are mediated through their binding to intracellular corticosteroid receptors and regulation of gene transcription of numerous genes, particularly those that code for pro-inflammatory cytokines [11].

2. RESPIRATORY DISORDERS: These drugs are very effective in reducing the frequency of days with symptoms, improving lung function, and reducing the frequency of hospitalization for asthma and the risk of a life-threatening attack. It shows anti-inflammatory action which inhibits the inflammatory cytokines [12].

3. NEOPLASTIC DISEASE: Corticosteroids like methylprednisolone and dexamethasone were used as antiemetic agents for decades [13]. Reduced release of 5-HT3 from blood cells upon administration of steroids as well as direct effects on cellular 5-HT3 receptor expression have been suggested as important factors [14,15].

4. RHEUMATIC DISORDERS: Intra-articular corticosteroids may show their anti-inflammatory effect by down-regulating the genetic expression of several pro-inflammatory proteins [16].

Mechanism of Action (Anti-Inflammatory and Immunosuppressive Effects):

The steroid molecule scatters across cell membranes and attaches to glucocorticoid receptors, which causes a conformational change in the receptor. The receptor glucocorticoid complex is allowed to move into the cell nucleus, where it dimerizes and binds to glucocorticoid response elements. Glucocorticoid response elements are associated with genes that either suppress or stimulate transcription, which results in ribonucleic acid and protein synthesis; these effects are called Trans repression or transactivation, respectively [17]. Ultimately, these agents inhibit transcription factors that

control the synthesis of pro-inflammatory mediators, including macrophages, eosinophils, lymphocytes, mast cells, and dendritic cells [18,19,20]. Another important effect is the inhibition of phospholipase A2, which is responsible for the production of numerous inflammatory mediators [21].

The main routes of administration of corticosteroids are:

- Oral: prednisone, prednisolone, methylprednisolone, betamethasone, hydrocortisone, dexamethasone
- Parenteral (intravenous or intramuscular): methylprednisolone, triamcinolone, dexamethasone
- Inhalation (aerosol): beclometasone, budesonide, flunisolide, fluticasoneTopically (e.g. application to the skin) e.g., beclometasone, betamethasone, clobetasol

In addition, corticosteroids may also be administered by intra-articular, ocular, nasal, rectal (enema), in-ear or spinal methods [22].

Tapering of Corticosteroid Therapy:

When corticosteroids are utilized thoroughly as intensive therapy or for long-term courses, a tapering strategy is recommended to prevent signs and symptoms of adrenal insufficiency due to hypothalamic-pituitary-adrenal axis suppression. General instructions regarding the need to consider a tapering regimen are:

(1) Prednisone 30 mg daily for minimum 2 weeks,

(2) Any dose of any systemic corticosteroid for at least 1 month, or when signs and symptoms of hypothalamic-pituitary-adrenal axis suppression are already present. Some clinicians use tapering to avoid exacerbation of the condition that is being treated [3].

❑ **SIDE EFFECTS:**

Long term corticosteroid use leads to hormonal changes within the body which can cause side effects

INHALED CORTICOSTEROIDS:

There is a range of local side effects that include perioral dermatitis [23] tongue hypertrophy, [24] oral and oropharyngeal candidiasis [25,26,27] pharyngeal inflammation, laryngeal disorders [28], cough during inhalation, and a sensation of thirst.[29] The pharyngeal disease tends to present with pain, irritation, or soreness in the throat. Pain during swallowing (odynophagia), and, patients may present with dysphagia. The most frequent side effect is hoarseness of the voice (dysphonia) due to the action of the steroid inhaler on the larynx. Cough can be troublesome for this same reason.

SYSTEMIC CORTICOSTEROIDS:

Dermatological: Thin, fragile skin, Mild hirsutism, Bruising, Facial erythema, increased sweating

Haematological: Polymorphonuclear leucocytes increased, Lymphocytes decreased, Polymorphonuclear leucocytes increased, Lymphocytes decreased

Fluids and electrolyte imbalance: The patient should be warned about the development of a cushingoid habitus (moon faces, buffalo hump, and central obesity), weight gain, and growth suppression [30].

ORAL CORTICOSTEROIDS:

Sleeplessness, mood swings, anxiety, a sense of well-being, a sense of fullness, weight gain, and stomach upset.1–10 Severe mood changes and psychotic reactions, raises blood pressure, raises blood sugar levels [31]

TOPICAL CORTICOSTEROIDS:

Striae distensae, Cutaneous atrophy, Stellate pseudo scars, Telangiectasia, Purpura, Erythema, Rosacea, Acneiform dermatoses, Rebound erythema, Demodicidosis, Milia, Cataracts, Tinea, Candidiasis, Scabies, Hypertrichosis, Hypopigmentation, Contact dermatitis, Tachyphylaxis[32]

MANAGEMENT FOR CORTICO-STEROID INDUCED SIDE EFFECTS:

The following measures should be considered for a patient who is about to begin steroid therapy or who is already on treatment:

• Take on a weight-bearing exercise (such as brisk walking)
• Stop smoking
• Avoid excess alcohol intake
• Hormone replacement therapy is considered for post-menopausal and amenorrhoeic women [33].
• In the recent reports of an increased risk of breast carcinoma, we need to discuss with the patient.
• Corticosteroid-induced bone loss is due to reduced calcium absorption from the gut and increased urinary loss.

Recent studies have shown that calcium and vitamin D supplements are beneficial in preventing bone loss [34].

Advising patients is the key to the safe use of long term systemic corticosteroids and it recommends discussing the following points with the patient:

• Not to stop taking corticosteroids suddenly
• Consult a doctor if they become ill of the increased susceptibility to infections, especially chickenpox
• Read and keep the patient information leaflet
• Always carry the steroid treatment card and show it to any health professional involved in their treatment.

In addition, the following suggestions may help to minimize some side effects:

• A single morning dose,
• An early diet which should be low calorie, low sodium, and high potassium
• Awareness of possible errors on high doses.
• Once corticosteroid therapy is started the patient should be monitored regularly and reviewed to assess the response to the treatment with adjustments to keep the dose at a minimum [30].

CONCLUSION:

Patients with corticosteroid-induced side effects should be treated by dose adjustment. Long-term corticosteroid use leads to hormonal changes which can cause a wide range of side effects. Advise patients on the safe use of long-term corticosteroids. Corticosteroids are mainly used to treat dermatological disorders, respiratory disorders, neoplastic disorders, and rheumatic disorders. Recent studies have shown eradicate drug abuse which leads to severe side effects. By evaluating side effects and educating patients about corticosteroids use and increase patient knowledge will decrease side effects due to corticosteroidal drug abuse.

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