Topical Glucocorticoids – A Review

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Abstract:
The topical glucocorticoids represent the treatment of choice for many types of inflammatory dermatoses. Despite the extensive use of this class of drugs as first line therapy the mechanism of their action is uncertain. It is clear that the multiplicity of actions of the topical Glucocorticoids is an important facet of their scope in the treatment of dermal disorders. Current understanding of the molecular mechanisms of Glucocorticoids action has advanced significantly over the past decade with the realisation that multiple systems are responsible for transduction of Glucocorticoids effects at a molecular level. Several inflammatory enzymes induced in inflammation are sites of inhibitory action of the Glucocorticoids , and the possibility that this occurs in the skin will be discussed paying particular attention to the inducible phospholipase A2 , nitric oxide synthase and cyclooxygenase systems.

Key Words : Glucocorticoids, dexamethasone, inflammation, nitric oxide synthase, cyclooxygenase, phospholipase A2.

INTRODUCTION:
A variety of synthetic glucocorticoids, some far more potent than cortisol, have been created for therapeutic use. They differ in both pharmacokinetics and pharmacodynamics. Because they permeate the intestines easily, they are administered primarily, but also by other methods, such as topically on skin. More than 90% of them bind different plasma proteins, though with a different binding specificity. Endogenous glucocorticoids and some synthetic corticoids have high affinity to the protein transcortin whereas all of them bind albumin (1). In the liver, they quickly metabolize by conjugation with a sulfate or glucuronic acid, and are secreted in the urine. Topical glucocorticoids are the most commonly prescribed topical medications for the treatment of rash, eczema, and dermatitis. Topical glucocorticoids have anti-inflammatory properties, and are classified based on their vasoconstriction abilities. Topical refers to external application of the drug to the surface for localized action. It is more convenient mode of delivering the drugs to skin, oropharyngeal/nasal, mucosa, eyes, ear canal, anal canal, vagina, and etc. Nonabsorbable drugs given orally for action on gastrointestinal mucosa, inhalation of drugs for action on bronchial mucosa and irritating solutions/jelly's applied to urethra are other forms of topical medications. In dental practice antiseptics, astringents, haemostatics are often applied as paints, toothpastes, mouthwashes, gargles. Glucocorticoids are a class of steroid hormones that bind to the glucocorticoid receptor, which is present in almost every vertebrate animal cell. The name glucocorticoid derives from its role in the regulation of the metabolism of glucose, its synthesis in the adrenal cortex, and its steroidal structure. Glucocorticoids cause their effects by binding to the glucocorticoid receptor.

TOPOCAL GLUCOCORTICOID:
Any synthetic steroid derivative exhibiting the same function as the naturally occurring corticosteroid hormone, formulated for topical application. Topical glucocorticoids are applied to the skin where it exerts its effect, however, glucocorticoids can be absorbed systemically after being applied locally (2). Topical glucocorticoids are mainly used for the localized treatment of inflammation of the skin and help relieve symptoms such as itching, swelling and redness. A topical glucocorticoid is a medication that is applied to body surfaces such as the skin or mucous membranes and they are available in creams, foams, gels, lotions and ointments. They are applied to the surface of tissues other than the skin, such as eye drops applied to the conjunctiva, and ear drops placed in the ear, or medications applied to the surface of a tooth.

MECHANISM OF ACTION :
The Glucocorticoids have many actions such as; anti-inflammatory, immunomodulatory, vasoconstrictor, gluconeogenic, antimitotic to. It is believed that several of these actions contribute to the therapeutic efficacy of these drugs in the treatment of skin disease (3). Indeed it is often this multi-pronged attack that endow glucocorticoids with the considerably greater therapeutic potency above other modes of treatment (4). Due to the diversity of conditions that the Glucocorticoids may be used to treat it is important to appreciate that any particular action of a Glucocorticoids may be beneficial in the treatment of one disease yet responsible for a confounding side effect in another. For instance, the anti-mitotic nature of Glucocorticoids is the property upon which their use in psoriasis is based, yet in the treatment of other inflammatory dermatoses results in skin atrophy and may often be the reason for cessation of topical Glucocorticoids treatment. Topical Glucocorticoids are prescribed for the treatment of many inflammatory conditions and today represent the drug type of choice for the treatment of most dermal inflammatory disease. This is not to say that the topical Glucocorticoids are a panacea for all skin disease, but perhaps may be regarded as the most effective single class of drugs providing such broad spectrum therapeutic benefit (5). The anti-inflammatory action of the topical Glucocorticoids has variously been attributed to several different mechanisms, and it is now clear that it is a combination of the different properties of the Glucocorticoids that act in concert to provide the therapeutic advantages of this class of drugs in the treatment of inflammatory skin disease.
Additionally both the anti-mitotic and vasoconstrictor nature of the GCs are properties which, most likely, contribute to resolution of certain inflammatory skin disease. The anti-mitotic effect is believed to confer the beneficial effects of topical Glucocorticoids in the treatment of psoriasis, a disease characterized by a high cell turnover rate (6). The vascular effect i.e. vasoconstriction, also termed blanching when applied to the skin surface, has been suggested to contribute to the anti-inflammatory effects of these drugs by virtue of the decreased blood flow to the inflamed site. Additionally it is this blanching response which forms the basis of the standard assay for the assessment of the potency of topical Glucocorticoids.

**Mechanisms of Anti Inflammatory Action of the Topical Glucocorticoids:**

Inhibition of phospholipase A2 activity decreases production of lipid mediators (prostaglandins, leukotrienes, platelet-activating factor), cyclooxygenase induction decreased prostaglandin production, nitric oxide synthase induction decreases nitric oxide production, cytokines production Suppresses cell mediated inflammation mass cell activity and reduction of mass cell number decreases levels of mast cell inflammatory mediators (histamine, 5-HT), Vasconstriction decreases local blood flow.

**Inflammatory Dermal Diseases Treated With Topical Glucocorticoids:**

Treatment of choice for topical glucocorticoids are Eczema, Contact dermatitis, Atopic dermatitis, Lichen planus, Lichen simplex chronicus, Chroinc dermatitis, Neurodermatitis, Insect and arthropod bites, Burns and sunburns, Keloids. Usefull alternative or adjunctive therapy Include of Psoriasis, Seborrhoeic dermatitis, Chronic lupus, erythematous, Alopecia areata, Acne. Isolated examples of successful treatment such as Bullous pemphigoid, Cutaneous mastocytosis, Vitiligo.

**MEDICAL USES:**

Synthetic therapeutic drugs with corticosteroid-like effects are used in a variety of conditions, ranging from brain tumors to skin diseases. Dexamethasone and its derivatives are almost pure glucocorticoids, while prednisone and its derivatives have some mineralocorticoid action in addition to the glucocorticoid effect. Fludrocortisone is a synthetic mineralocorticoid. Hydrocortisone is available for replacement therapy, e.g. in adrenal insufficiency and congenital adrenal hyperplasia (7). Synthetic glucocorticoids are used in the treatment of joint pain or inflammation, temporal arteritis, dermatitis, allergic reactions, asthma, hepatitis, systemic lupus erythema toss, inflammatory bowel disease, sarcoidosis and for glucocorticoid replacement in Addison's disease or other forms of adrenal insufficiency. Topical formulations are also available for the skin, eyes, lungs, nose and bowels. Corticosteroids are also used supportively to prevent nausea, often in combination with 5-HT3 antagonists.

**ADVERSE EFFECTS:**

Perioral dermatitis:

This is a rash that occurs around the mouth and the eye region that has been associated with topical glucocorticoids.

Ocular effects:

Topical glucocorticoids drops are frequently used after eye surgery but can also raise intra-ocular pressure and increase the risk of glaucoma, cataract, retinopathy as well as systemic adverse effects (8).

Tachyphylaxis:

The acute development of tolerance to the action of a drug after repeated doses. Significant tachyphylaxis can occur by day 4 of therapy. Recovery usually occurs after 3 to 4 days rest (9). This has led to therapies such as 3 days on, 4 days off, or one week on therapy, and one week off therapy.

Other local adverse effects: These include facial hypertrichosis, folliculitis, miliaria, long term use has resulted in Norwegian scabies, Kaposi's sarcoma, and other unusual dermatosis (10).

**CONCLUSION:**

The topical Glucocorticoids still remain one of the most effective and popular forms of treatment of various inflammatory skin disease states. These agents are clearly a complex class of drugs that modulate the activity of several pivotal processes and mediators of inflammation. Modulation of the levels and or compartmentalisation of the Glucocorticoid inducible, anti inflammatory, anti proliferative protein, LC1, following topical Glucocorticoids treatment provides solid evidence supporting the suggestion that this protein plays an important role in the action of topical Glucocorticoids. Exploration of the possibilities of more specific treatment of skin disease with LC1 related products may provide novel more efficient modalities for treatment of inflammatory skin disease.

**REFERENCE:**


