Corticosteroids-An Update

[1]Mr Mahesh Vijay Padala, [2]Dr. Ashutosh Shukla, [3]Dr. Deepali L Jaybhaye

[1]PhD Student, [2]Assistant Professor, [3]Associate Professor
[1,2]IISHLS, [3]Pharma-cology
[1,2]Indus University, Gujrat.
[3]MGM Medical College & Hospital, Aurangabad

Corresponding Author

Name:- Mr Mahesh Vijay Padala

Address:- 5, Vijay Villa, Shabari Chawl, C.P Talav, Rd No:- 27, Wagle Estate, Thane:- 400604, Maharashtra, India.

Total Number of Figures:- 2

Total Number of Tables:- 12

Word Counts:-3795

Abstract:- 51

Text (Including Introduction):- 3660

Funding Source:- This Review received no specific grants from any funding agency in the public, commercial or not-for-profit sectors.

Abstract

Corticosteroids to dermatology helped patients with different skin conditions both as systemic and topical agents. They may cause various reactions mostly if they are taken in higher doses. This article discusses pharmacology, mechanisms of action, treatment guidelines, adverse effects and different ways to minimize the effects of corticosteroids in clinical use.

Keywords:- Corticosteroids-Update, Guidelines, Adverse-Effects.

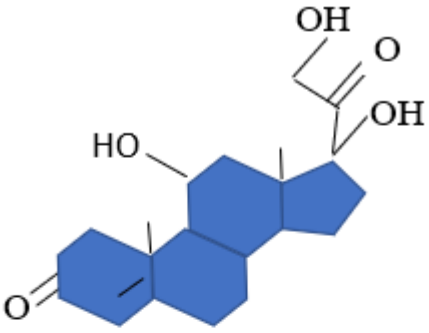
Introduction

No drugs havebeen dominated to such an extent as that of corticosteroids which still remains the mainstay since its discovery in the 1940s. **(1)** In 1948 Edward Kendall and Philip Hench first introduced the curative actions of corticosteroids.**(2)** In clinical practice Corticosteroids were first used in the year 1949 for the treatment of rheumatoid arthritis.**(3)** Improvement in the chemical properties of this primary hormone helped to develop different corticosteroids of various energy, each one of its having their own specific characteristics.**(2)** It is used in almost all the areas of medicine and by every possible routes after its discovery. Corticosteroids are produced by the adrenal cortex which are natural synthetic hormones that include both mineralocorticoids and glucocorticoids activities. Mineralocorticoids has control on water and electrolytes balance while glucocorticoids have immunosuppressive, metabolic, vasoconstrictive and anti-inflammatory effects.**(4)**

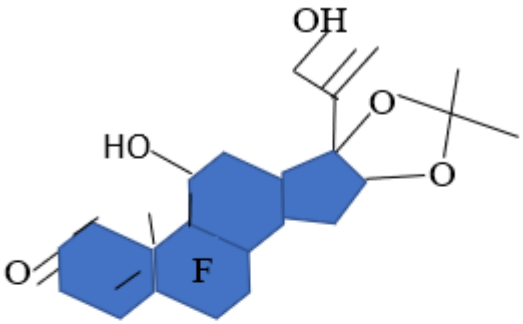
After the introduction of corticosteroids to dermatology half a century ago it is commonly used in patients with different skin conditions both as systemic and topical agents. Corticosteroids are administered through systemic route in lichen planus, psoriasis, seborrheic dermatitis and different types of eczemas such as atopic dermatitis, neurodermatitis and nummular eczema whereas topical steroids are used in various forms of dermatitis, intertrigo, lichen simplex chronicus, etc because of their immunosuppressive, anti-mitogenic and

anti-inflammatory effects.[5,6] Corticosteroids may cause the adverse reactions especially when they are taken in higher doses like sleep disturbance, increased appetite, weight gain, high blood sugar while long term use of it may cause hypertension, infections, diabetes mellitus, necrosis, osteoporosis, glaucoma etc. Topical corticosteroids have many adverse reactions such as hypersensitivity, percutaneous absorption and tachyphylaxis, increase susceptibility to bacterial and fungal infections, skin atrophy and on systemic absorption results into hypothalamic-pituitary adrenal suppression and Cushing syndrome.[7] This article discusses pharmacology, mechanisms of action, treatment guidelines, adverse effects and different ways to minimize the effects of corticosteroids in clinical use.

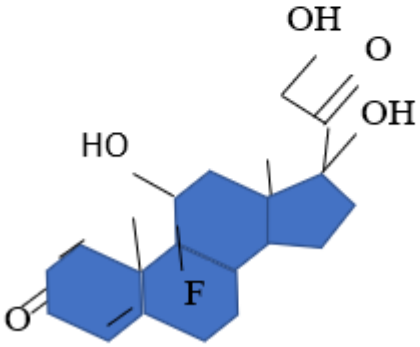
Structural Classification of Corticosteroids, taken from Scheuer and Warshaw et al.[8]



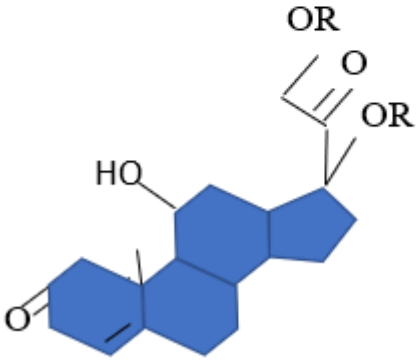
Group A: Hydrocortisone Type



Group B: Triamcinolone Acetonide Type



Group C: Betamethasone Type



Group D: Hydrocortisone-17-Butyrate Type

Classification of Corticosteroids based on the descriptive structural relationships into four groups i.e, A,B, C & D [8]

Group A Corticosteroids			
Sr No	**Topical**	**Sr No**	**Systemic**
01	Cloprednol	01	Cortisone Acetate
02	Dichlorisone Acetate	02	Hydrocortisone-21-Acetate
03	Fludrocortisone Acetate	03	Methylprednisolone Acetate
04	Fluoromethalone	04	Prednisolone Acetate
05	Fluprednisolone Acetate	05	Prednisone
06	Hydrocortisone		
07	Hydrocortisone-21-Sodium-hemisuccinate		

08	Medrysone		
09	Meprednisone		
10	6-α-methylprednisolone acetate		
11	Methylprednisolone		
12	Prednisone Sodium phosphate		
13	Tixocortol pivalate		

Group B Corticosteroids

Sr No	Topical	Sr No	Systemic
01	Amcinonide	01	Triamcinolone
02	Budesonide	02	Triamcinolone benetonide
03	Desonide	03	Triamcinolone diacetate
04	Fluocinolone Acetonide	04	Triamcinolone hexacetonide
05	Fluocinonide		
06	Flumoxonide		
07	Flunisolide		
08	Flurandrenolide		
09	Halcinonide		
10	Triamcinolone Acetonide		

Group C Corticosteroids

Sr No	Topical	Sr No	Systemic
01	Betamethasone-21-Disodium phosphate	01	Betamethasone (not valerate)
02	Desoximetasone	02	Dexamethasone Acetate
03	Dexamethasone- Disodium phosphate	03	Paramethasone Acetate
04	Difluocortolone (pivalate, valerate)		
05	Flumethasone		
06	Fluocortine butyl		
07	Fluocortolone (hexanoate, pivalate, caproate)		
08	Fluprednidene Acetate		
09	Halometasone		

Group D1 Corticosteroids

Sr No	Topical	Sr No	Systemic
01	Aclometasone dipropionate	01	Beclomethasone dipropionate
02	Betamethasone valerate	02	Betamethasone dipropionate
03	Betamethasone dipropionate	03	
04	Clobetasol Propionate		
05	Clobetasone butyrate		
06	Diflorasone Diacetate		
07	Fluticasone propionate		
08	Halobetasol		
09	Mometasone furoate		

Group D2 Corticosteroids

Sr No	Topical
01	Hydrocortisone Aceponate (17-butyrate)

02	Hydrocortisone valerate
03	Prednicarbate
04	Methylprednisolone Aceponate

Classification of Corticosteroids according to its Potency[9]

Sr No	Class	Generic name of Drug	Dosage Form	Dose	Brand Name
01	**Class 1 Superpotent**	Betamethasone dipropionate	Ointment, Cream	0.05%	Diprolene, Diprosone
		Clobetasol propionate	Ointment, Cream	0.05%	Temovate, Dermoxin
		Diflorasone diacetate	Ointment	0.05%	Fluorone, Psorcon
		Halobetasol propionate	Ointment, Cream	0.05%	Ultravate
02	**Class 2 Potent**	Amcinonide	Ointment	0.1%	Cyclocort
		Desoximetasone	Ointment, Cream, Gel	0.25%; 0.05%	Topicort, Ibaril
		Diflorasone diacetate	Ointment	0.05%	Florone, Maxiflor
		Fluocinonide	Ointment, Cream, Gel,	0.05%	Lidex
		Halcinonide	Cream,	0.1%	Halog
		Mometasone furoate	Ointment	0.1%	Elocon, Ecural
03	**Class 3 Potent**	Amcinonide	Cream, Lotion	, 0.1%	Cyclocort
		Betamethasone valerate	Ointment	0.01%	Valisone
		Diflorasone diacetate	Cream	0.05%	Florone, Maxiflor
		Fluticasone propionate	Ointment	0.005 %	Cutivate
		Fluocortolone	Cream	0.25%	Ultralan
		Fluocinonide	Cream	0.05%	Lidex E cream, Topsyn
		Halcinonide	Ointment	0.1%	Halog
		Triamcinolone acetonide	Ointment	0.1%	Aristocort A
		Triamcinolone acetonide	Cream	0.5%	Aristocort-HP
04	**Class 4 Midstrength**	Betamethasone valerate	Lotion	0.01%	Valisone, Luxiq
		Desoximetasone	Cream, Gel	0.05%	Topicort-LP
		Fluocinolone acetonide	Cream	0.2%	Synalar-HP
		Fluocinolone acetonide	Ointment	0.025 %	Synalar
		Flurandrenolide	Ointment	0.05%	Cordran

		Halcinonide	Cream	0.025 %	Halog
		Hydrocortisone valerate	Ointment	0.2%	Westcort
		Mometasone furoate	Cream	0.1%	Elocon Ecural
		Triamcinolone acetonide	Ointment	0.1%	Kenalog
05	**Class 5 Midstrength**	Betamethasone dipropionate	Lotion	0.05%	Diprosone
		Betamethasone valerate	Cream	0.01%	Valisone
		Fluocinolone acetonide	Cream	0.025 %	Synalar
		Fluocinolone acetonide	Oil	0.01%	Dermasmoothe/FS
		Flurandrenolide	Cream	0.05%	Cordran
		Fluticasone propionate	Cream	0.05%	Cutivate
		Hydrocortisone butyrate	Cream	0.1%	Locoid
		Hydrocortisone valerate	Cream	0.2%	Westcort
		Triamcinolone acetonide	Lotion	0.1%	Kenalog
06	**Class 6 Mild**	Alclometasone dipropionate	Ointment, Cream	0.05%	Aclovate
		Betamethasone valerate	Lotion	0.05%	Valisone
		Desonide	Cream	0.05%	Desowen, Tridesilon
		Fluocinolone acetonide	Cream, Solution,	0.01%	Synalar
		Prednicarbate	Cream	0.1%	Dermatop
		Triamcinolone acetonide	Cream	0.1%	Aristocort
07	**Class 7 Least potent**	Dexamethasone	Cream	0.1%	Decadron phosphate
		Hydrocortisone		0.5%, 1%, 2.5%	Hytone, others
		Methylprednisolone		1%	Medrol

Classification of Glucocorticoids according to its Potency[10]

Sr No	Class	Drug
01	Class I	i. Hydrocortisone, ii. hydrocortisone acetate, iii. prednisolone
02	Class II	i. Dexamethasone, ii. hydrocortisone butyrate, iii. methylprednisolone aceponate, iv. prednicarbate, v. triamcinolone acetonide
03	Class III	i. Betamethasone valerate, ii. betamethasone dipropionate, iii. desoximetasone, iv. fluocinoide, v. mometasone furoate
04	Class IV	i. Clobetasol propionate

Pharmacological effects and drug-drug interactions

A group of cyclic natural compounds comprises of Steroids that are formed from the cholesterol that has 17-carbon, 4-ring cholesterol structure. Corticosteroids, bile acids, and sex hormones are natural steroidal hormones that are released from adrenal cortex that function in the body. The use of the term "steroid'' therefore in a clinical medicine is confined to corticosteroid-like synthetic compounds mostly glucocorticoid**.** **(11)**

Drug interaction occurs when there are changes in the effects of a drug by reacting it with the other drug or drugs, with herbs or with a pre-existing comorbidities. This is known as drug interaction. One drug changes the tissue/serum levels and mechanism of action of the other if both the drugs simultaneously comes in contact with each other in the body. Therapeutic effects are produced when the corticosteroids are applied topically to the skin which are localized to the site of application. Even though the topical absorbtion of the drug is less they don't have more of the systemic actions, uptill their use is for longer duration. Thus there may be interactions with other systemic and topical medications when topical application of drugs are done. An example of topical drug-drug interaction is the use of dexamethasone, hydroquionone and tretinoin in Kligman's formula, where dexamethasone helps to minimize skin irritation and tretinoin helps absorption of hydroquinone that may be caused by hydroquinone and tretinoin**.** **(12)**

Another example is use of ketoconazole in immunocompromised patients who are taking prednisone. The activity of some oxidases of the cytochrome P-450 are inhibited by the ketoconazole. Antipyrine or theophylline clearance is not affected but the clearance of chlordiazepoxide is reduced. In the liver due to oxidases activity prednisolone is metabolized. Hence, prednisolone concentrations may be increased by taking ketoconazole with prednisone thereby increasing the biological efficacy of prednisone.**(13)**

Here are some more examples of the drug interaction.[14]

1) Due to drug interaction it is found to have reduced therapeutic effect of corticosteroids with the following. [14]

Sr No	Drugs
01	Rifampicin
02	Phenobarbitone
03	Carbamazepine
04	Aminoglutethimide
05	Primidone
06	Phenytoin

2) Due to drug interaction Corticosteroids also reduce the therapeutic effect of the following drugs:

Sr No	Drugs
01	Hypoglycaemic agents
02	Antihypertensives
03	Diuretics
04	Heparin

3) Corticosteroids increases the hypokalaemic effect of the following:[14]

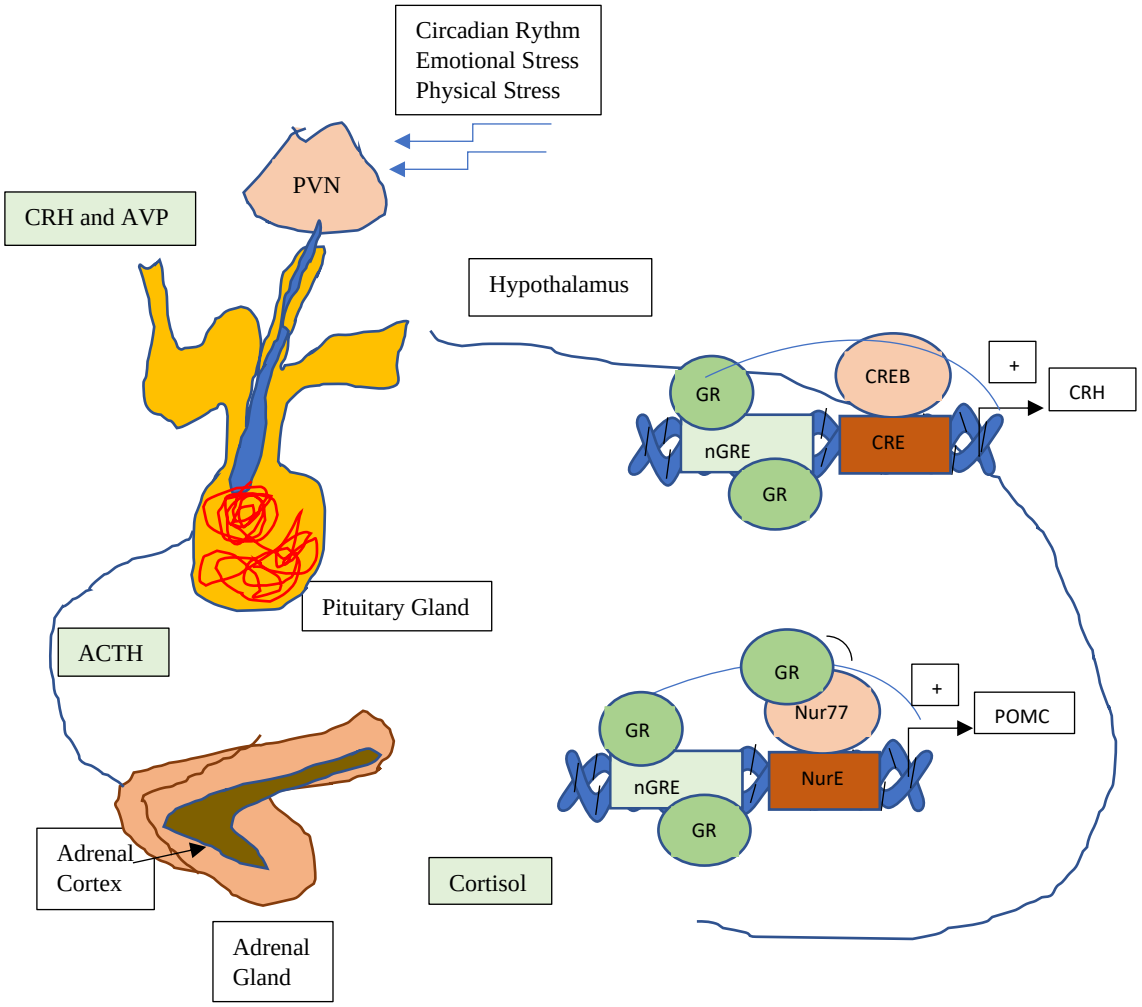
Sr No	Drugs
01	Acetazolamide
02	Diuretics
03	Carbenoxolone

Hypothalamic Pituitary Adrenal (HPA) axis

Corticotrophin-releasing hormone (CRH) is the primary hypothalamic factor that initiates the pituitary secretion of Adreno Cortico Tropic Hormone (ACTH). Then ACTH regulates secretion of Cortisol. Cortisol is the primary negative regulator of hypothalamic-pituitary- adrenal (HPA) axis activity through negative feedback upon the pituitary and the hypothalamus. Thus, both ACTH and CRH creation are inhibited.[15]

The principal target for circulating ACTH is the adrenal cortex, where it stimulates glucocorticoid synthesis and secretion from the zona fasciculata. Glucocorticoids are the downstream effectors of the HPA axis and regulate physiological changes through ubiquitously distributed intracellular receptors. The biological effects of glucocorticoids are usually adaptive; however, inadequate or excessive activation of the HPA axis may contribute to the development of pathologies. [16]

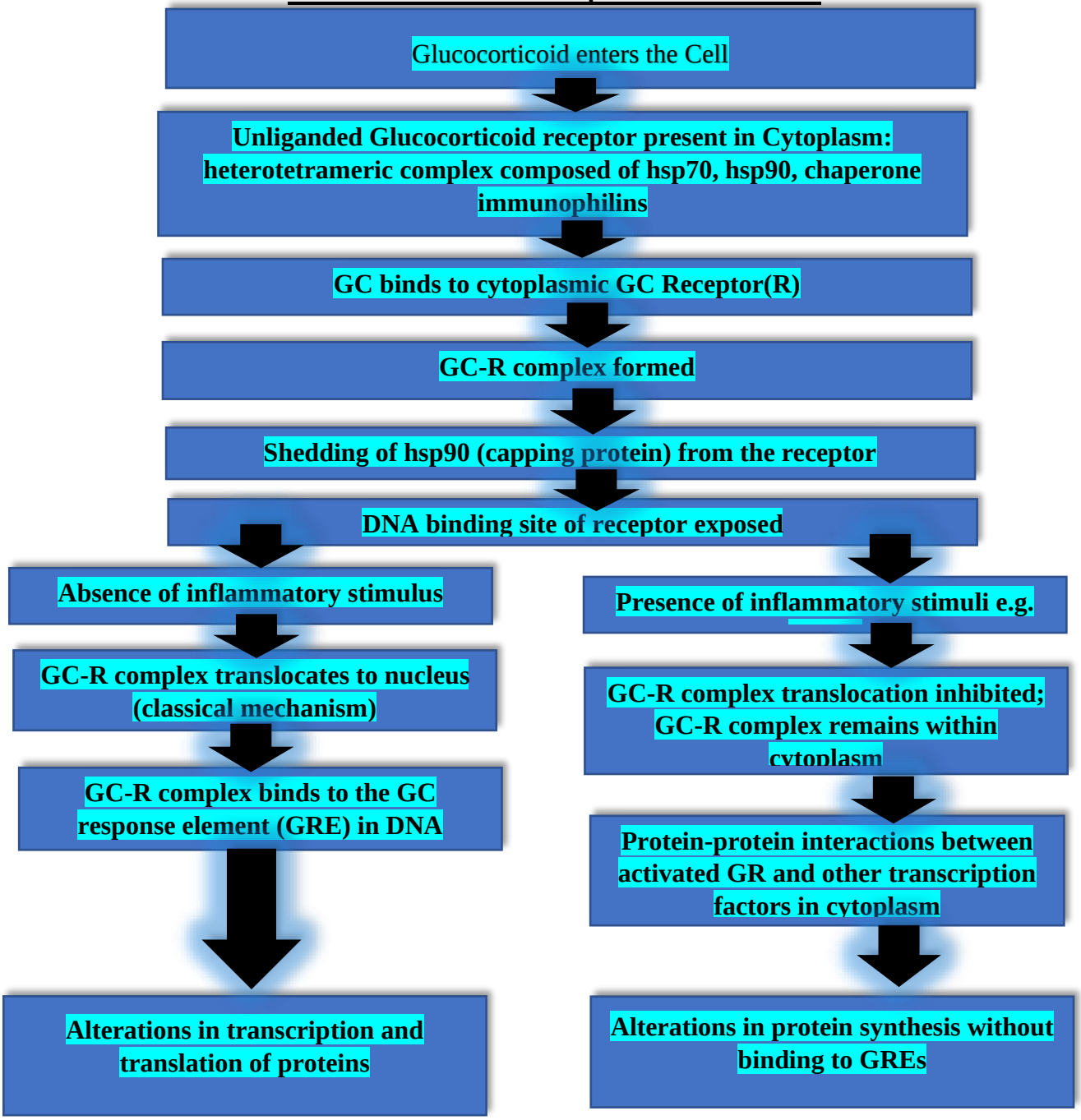
Graph of HPA Axis[17]



Mechanism of action of Corticosteroids

Corticosteroids are either produced by human body or it is manufactured known as steroidal hormones which has their effects through multiple pathways. All the steroidal hormones are made from cholesterol. The physiological functions are regulated when they are secreted into the blood after their synthesis in the adrenal cortex. It has genomic and nongenomic mechanisms of action. Glucocorticoid receptor mediates the genomic one which has immunosuppressive and anti-inflammatory effects. The interactions between the membrane bound glucocorticoid receptor or intracellular glucocorticoid receptor mediates the non genomic mechanism of action. Normally corticosteroids have the following effects, they are immunosuppressive, anti-inflammatory, protein and carbohydrate metabolism, water and electrolyte balance, central nervous system and on blood cells. [18,19]

Mechanism of action of Topical Corticosteroids[20]



Depending upon various factors and the disorders treated administration of corticosteroids can be topical, oral, inhaled, parenteral, injected (intra-articular, intra-muscular, intra-dermal, intra-lesional, etc.) and rectal. While starting the corticosteroid treatment other then the route of administration, dosing, frequency, duration and preparation of treatment are also the factors kept in mind.

In case of emergency and in patients who are unable to tolerate the steroids orally then parenteral administration is often used. Administration of the medication through mouth is used for treating chronic patients. Depending upon the possibilities and to minimize systemic exposure patients should be given non-systemic treatment.[18]

Treatment Guidelines.[21]

1. For the intertriginous areas and face, low-strength preparations should be preferred.
2. In case of more potent steroids short-term use should be done.
3.Very-high strength topical corticosteroids should not be taken for more then 3 weeks.

4. Intermittent therapy may be preferred to continuous therapy even with the use of low-strength topical corticosteroids for long-term management of chronic skin diseases, particularly if large surface areas are being treated.
5.Topical corticosteroids should be discontinued when the skin disease has resolved. If continuous long-term treatment is needed, patients should be monitored for the development of side effects and tachyphylaxis (loss of clinical effect over time).
6. Use the lowest potency corticosteroid that is effective, especially on infants and children.
7. Prolonged use should be avoided in the periorbital area, face, and intertriginous areas.
8. Instruct your patient regarding the proper application technique, specific amount to use, and duration of therapy. Once or twice daily application is often sufficient.
9. For the very potent steroids, even a single daily application is sufficient to decrease the chances of tachyphylaxis.
10. Steroids should be applied lightly and no message is required.
11. Have a look on hypothalamic pituitary axis (HPA) suppression if patient is receiving systemic steroids as well or the requirement of topical steroids is > 50 g.
12. Dilutions and cocktails of steroids with other agents should best be avoided.
13. Patients should not allow the other persons to use their medicine and not to use it themselves for other skin problems at a later time.
14. Topical corticosteroids may be used in pregnancy, as fetal abnormalities have not been documented in human beings.
15. These are also considered safe in lactation but should not be applied to the nipples before nursing.[21]

Adverse Effects

Adverse effects with use of topical corticosteroids are as follows:- [09]

Atrophic changes

1) Steroid atrophy
Use of topical corticosteroids causes preatrophy, atrophy and tachyphylaxis. Atrophy causes burning sensation in the initial use of steroid which further causes vasoconstriction and soothing of the burning.
2) Telangiectasia
Steroid-induced telangiectasia occurs due to stimulation of release of nitric oxide from dermal vessel endothelial cells leading to abnormal dilatation of capillaries.
3) Striae
Cross linking of immature collagen in the dermis causes Striae. Tissue formation and deposition of collagen also causes formation of striae.
4) Purpura
Dermal vessels fragility causes purpura. Face, sides of the neck, forearms, dorsum of the hands and lower legs are the most common affected sites.
5) Stellate pseudoscars
Stellate pseudoscars is found in older patients which is associated with cutaneous atrophy and purpura.[24]
6)Ulceration
Peptic ulcers is caused by the prolonged use of orticosteroids still widely accepted by the clinicians because of the evidences provided by pharmacological and experimental studies.[25]

B) Infections

1) Masked microbial infections (tinea incognito)
Tinea incognito is a cutaneous eruption because of the application of topical corticosteroids on tinea lesions which therefore changes their appearance. ‘‘Mask tinea’’ was been used as a term to elaborate the cases of tinea faciei.[26]

2)Aggravation of cutaneous candidiasis:-

Topical corticosteroids causes suppression of normal cutaneous immune response to dermatophytes which causes fungal infections.[27]

3) Reactivation of Kaposi sarcoma

Infection with the human herpes virus 8 (HHV-8) causes Kaposi's sarcoma. HIV-infected patients increases the clinical progression of Kaposi's sarcoma with the administration of systemic glucocorticoids.[28]

4) Granuloma gluteale infantum

The term granulomata gluteale infantum are coined due to the complication of primary irritant diaper dermatitis. The use of topical steroids for the treatment of diaper dermatitis are said to be the important cause.[2]

Adverse effects with use of other corticosteroids are as follows[28]

1) Osteoporosis and fractures	2) Suppression of the hypothalamic-pituitary-adrenal (HPA) axis	3) Cushingoid features
4) Diabetes	5) Myopathy	6) Glaucoma and cataracts
7) Immunosuppression	8) Cardiovascular disease	9) Gastrointestinal
10) Dermatologic adverse effects		

1) Osteoporosis, fractures, and osteonecrosis:[18]

Corticosteroids have been shown to cause a decrease in bone formation by reducing the activity and lifespan of osteoblasts. Alcoholism, sickle cell disease, human immunodeficiency virus infection and radiation exposure are also associated with osteonecrosis.

2) Adrenal suppression:

Adrenal suppression will often occur after sudden discontinuation of corticosteroid treatment, and therefore, gradual tapering is often part of corticosteroid treatment protocols.

3) Cushingoid features:

Cushing syndrome can occur in patients taking corticosteroids through all routes of administration.

4) Diabetes and hyperglycemia:

Corticosteroids are the most common cause of drug-induced diabetes mellitus.

5) Myopathy:

Corticosteroids are associated with proximal muscle weakness and atrophy. Higher doses can lead to a more rapid onset.

6) Glaucoma and cataracts:

There is a dose-dependent risk for both glaucoma and cataracts for patients on corticosteroids.

7) Psychiatric disturbance:

Corticosteroids can cause a range of psychiatric disorders, including psychosis, agitation, insomnia, irritability, hypomania, anxiety, and mood lability.

8) Immunosuppression:

The desired immune-suppressing and anti-inflammatory effects of corticosteroids can cause infection. Patients on corticosteroids are susceptible to invasive fungal and viral infections.

9) **Cardiovascular adverse effects:**

Use of corticosteroid is associated with higher rates of cardiovascular events, new-onset atrial fibrillation and flutter, ischemic heart disease and heart failure.

10) Gastrointestinal adverse effects:

Multiple gastrointestinal effects correlate with corticosteroid therapy, including gastritis, peptic ulcer disease, abdominal distention and dyspepsia.

11) Dermatologic adverse effects:

Corticosteroid use induces skin atrophy, leading to thinning and fragility of the skin and striae and purpura.

12) Growth suppression:

Oral corticosteroid therapy in children has links with delayed growth and puberty. [18]

Different ways to minimize the effects of corticosteroids in clinical use:- [1]

1) Dermatologist should prescribe lowest effective dose for the shortest duration of time inorder to reduce the adverse effects.

2) Comorbid conditions are necessary to be treated which can reduce the steroids associated AE's .

3) Advise patients to carry a steroid treatment card.

4) If possible every alternate day or intermittent dosing should be considered.

5) If possible one dose in the morning should be administered daily.

6) If there are any behavioural or mood changes, then it has to be informed to the concerned Doctor immediately.

7) Alcohol consumption also need to be reduced while on the steroid therapy.

8) Patients those who have the habbit of smoking should be advised to stop smoking.

9) Avoid things which may increase the risk of weight gain or other AEs while taking the steroid treatment.

10) Along with calcium intake it should be advised to consume a healthy balanced diet.

11) Instant discontinuation of corticosteroid treatment should not be done untill and unless it is advised by the treating Doctor.

12) Avoid contact with the persons who have chickenpox, shingles or measles unless they are treated.

13) Patients need to be motivated for the regular exercise plan.[1]

14) Fluid and electrolyte levels should be monitored in patients on corticosteroids with higher mineralocorticoid activity.

15) The risk of striae can be reduced if patients follow a low-calorie diet along with topical vitamin A cream, pulsed dye lasers, and a non-ablative radiofrequency device.

16) If there is adrenal suppression, then it has be treated with daily physiologic dosing including stress doses as and when required. **(18)**

References:-

1. Liu et al.: A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. Allergy, Asthma & Clinical Immunology 2013 9:30.
2. Onlinelibrary.wiley.com/doi/10.1111/j.1398-9995.2009.02038.x by National Medical Library The Director, Wiley Online Library on [08/12/2022].
3. Roger J. Zoorob, M.D., M.P.H., Dept. of Family Medicine, Louisiana State University Medical Center, 1542 Tulane Ave., Room 122, New Orleans, LA 70112
4. Hodgens A, Sharman T. Corticosteroids. [Updated 2022 Jul 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from https://www.ncbi.nlm.nih.gov/books/NBK554612/
5. Walton RG, Farber EM. Systemic use of corticosteroids in dermatology. Calif Med. 1961 Apr;94(4):209-10. PMID: 13783009; PMCID: PMC1574635.
6. Karekar SR, Marathe PA, Nagarajan VB, Khopkar US, Chikhalkar SB, Desai PK, et al. Use of topical steroids in dermatology: A questionnaire based study. Indian Dermatol Online J 2020;11:725-30.
7. Barneston RS, White AD. The use of corticosteroid in dermatological practice, Med J Aust.1992; 156(6):428-31.
8. Scheuer E, Warshaw E. Allergy to corticosteroids: update and review of epidemiology, clinical characteristics, and structural cross-reactivity. Am J Contact Dermat. 2003 Dec;14(4):179-87. PMID: 14738718.
9. Hengge UR, Ruzicka T, Schwartz RA, Cork MJ. Adverse effects of topical glucocorticosteroids. J Am Acad Dermatol. 2006 Jan;54(1):1-15; quiz 16-8. doi: 10.1016/j.jaad.2005.01.010. PMID: 16384751.
10. Schoepe, S., Schäcke, H., May, E. and Asadullah, K. (2006), Glucocorticoid therapy-induced skin atrophy. Experimental Dermatology, 15: 406-420. https://doi.org/10.1111/j.0906-6705.2006.00435.x
11. Han S. Clinical pharmacology review for primary health care providers: II. Steroids. Transl Clin Pharmacol. 2015 Jun;23(1):15-20. https://doi.org/10.12793/tcp.2015.23.1.15
12. Coondoo A, Chattopadhyay C. Drug interactions in dermatology: What the dermatologist should know.Indian J Dermatol 2013;58:249-254.
13. Zurcher RM, Frey BM, Frey FJ. Impact of ketoconazole on the metabolism of prednisolone. Clin Pharmacol Ther. 1989 Apr;45(4):366-72. doi: 10.1038/clpt.1989.42. PMID: 2639662.
14. STANBURY RM, GRAHAM EM Systemic corticosteroid therapy—side effects and their management *British Journal of Ophthalmology* 1998;**82:**704-708
15. (Deng J, Chalhoub NE, Sherwin CM, Li C, Brunner HI. Glucocorticoids pharmacology and their application in the treatment of childhood-onset systemic lupus erythematosus. Semin Arthritis Rheum. 2019 Oct;49(2):251-259. doi: 10.1016/j.semarthrit.2019.03.010. Epub 2019 Mar 16. PMID: 30987856; PMCID: PMC6744986)
16. Smith SM, Vale WW. The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. Dialogues Clin Neurosci. 2006;8(4):383-95. Doi:10.31887/DCNS.2006.8.4/ssmith. PMID: 17290797; PMCID: PMC3181830.
17. Timmermans S, Souffriau J and Libert C (2019) A General Introduction to Glucocorticoid Biology. Front. Immunol. 10:1545. doi: 10.3389/fimmu.2019.01545
18. Hodgens A, Sharman T. Corticosteroids. [Updated 2022 Jul 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK554612/
19. https://pdfs.semanticscholar.org/bf07/ea2d823456767a4bbbd65e373434fe1c162a.pdf
20. Mehta AB, Nadkarni NJ, Patil SP, Godse KV, Gautam M, Agarwal S. Topical corticosteroids in dermatology. Indian J Dermatol Venereol Leprol 2016;82:371-8

21. Journal of Pakistan Association of Dermatologists 2005; 15: 55-59. https://www.researchgate.net/publication/286217452.
22. 22) Abraham A, Roga G. Topical steroid-damaged skin. Indian J Dermatol. 2014 Sep;59(5):456-9. doi: 10.4103/0019-5154.139872. PMID: 25284849; PMCID: PMC4171912
23. Side Effects of Glucocorticoids http://dx.doi.org/10.5772/intechopen.72019
24. Colomb D. Stellate Spontaneous Pseudoscars: Senile and Presenile Forms: Especially Those Forms Caused by Prolonged Corticoid Therapy. *Arch Dermatol.* 1972;105(4):551–554. doi:10.1001/archderm.1972.01620070023008
25. Guslandi M. Steroid ulcers: Any news? World J Gastrointest Pharmacol Ther. 2013 Aug 6;4(3):39-40. doi: 10.4292/wjgpt.v4.i3.39. PMID: 23919213; PMCID: PMC3729864
26. Russo, R., Trave, I., Cozzani, E. et al. Generalized Tinea Incognito Developing from "Mask Tinea". Mycopathologia (2022). https://doi.org/10.1007/s11046-022-00686-x.
27. Coondoo A, Phiske M, Verma S, Lahiri K. Side-effects of topical steroids: A long overdue revisit. Indian Dermatol Online J. 2014 Oct;5(4):416-25. doi: 10.4103/2229-5178.142483. PMID: 25396122; PMCID: PMC4228634.
28. Fernández-Sánchez M, Iglesias MC, Ablanedo-Terrazas Y, Ormsby CE, Alvarado-de la Barrera C, Reyes-Terán G. Steroids are a risk factor for Kaposi's sarcoma-immune reconstitution inflammatory syndrome and mortality in HIV infection. AIDS. 2016 Mar 27;30(6):909-14. doi: 10.1097/QAD.0000000000000993. PMID: 26636923; PMCID: PMC4794188.