A comprehensive analysis on uses and side effects of steroids with respect to different routes

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INTRODUCTION:

Steroids are a class of chemicals that includes the hormones. There are two types of steroids namely, glucocorticoids & mineralocorticoids. Glucocorticoids such as cortisol, control carbohydrate, fat & protein metabolism and other mechanism. While the mineralocorticoids such as aldosterone control electrolyte and water levels. Most of the uses of corticosteroids in day to day practice have been in the field of Rheumatology, Orthopaedics, dermatology, oncology, respiratory medicine, otorhinolaryngology & ophthalmology.(1) Endocrinology utilizes corticosteroids for hypoadrenalism and tapering regimens in hypothalamic-pituitary-adrenal axis suppression. Glucocorticoids causes the following adverse effects such as osteoporosis, hyperglycemia, cushing syndrome, CVS disease, glaucoma, cataracts, infections. While, mineralocorticoids causes hypernatremia, hypokalemia, arterial hypertension, hyperglycemia, edema as the side effects.(2,3)

The main purpose of this review is to analyse the serious side effects caused by corticosteroids while administering in different routes of administration like topical steroids, intranasal steroids, steroid ear & eye drops, intra-articular steroid injections, oral steroids. Being very powerful anti-inflammatory agents, they were described as impressive drugs as they not only improved certain clinical conditions, but also confered a subjective sense of well-being. So, double headed action of steroids are widely discussed in this paper.

SYSTEM WISE USES AND SIDE EFFECTS OF CORTICOSTEROIDS

Corticosteroids and cardiovascular system:

Studies states that prescribed 7.5mg of prednisolone or more/ day compared to non-steroid prescription in cardio patients causes increased risk of CHF, MI, stroke, transient ischemic attack(Relative risk : 3.72, 3.26,1.73,7.41 respectively)(4).

There was an increased risk of arteriosclerosis in patients with Rheumatoid arthritis receiving long term corticosteroids therapy, shown by 3 fold increase in the incidence of lower limb calcifications.

Corticosteroids and endocrine system:

There is 1.8 fold risk of developing diabetes even at doses lower than 10mg prednisolone per day blood sugar should be monitored before and after commencement of corticosteroids as there is an increased risk of developing hyperglycemia when steroids exceed the dose equivalent to 10mg prednisolone per day.(5-7)

Corticosteroids and bone mineral density:

If steroids are required for prolonged periods, the dose should be limited to 15-20mg prednisolone per day to avert osteonecrosis. Fractures may occur in 30-50 % of patients on chronic corticosteroid therapy. Fracture risk may decrease rapidly after cessation of steroids.(8-10)

Corticosteroids and central nervous system:

At a daily dose prednisolone of 15mg per day, mood disorders have been observed in rheumatoid arthritis patients.High dose of corticosteroids taken for ocular symptoms produced hypomanic symptoms in 30% and depressive symptoms in 10% of patients within 1 week period[36] Partial memory loss was observed in patients receiving steroid doses between 5-40 mg prednisolone per day for one year or more.(11-13)

Corticosteroids and Gastro intestinal system:

Used in inflammatory bowel disease, auto immune hepatitis, severe alcoholic hepatitis.

Oral budesonide is less effective than intravenous because it is an oral non-systemic corticosteroid with only 10% systemic bioavailability.[14]

Corticosteroids and liver disease:

Steroids are used in the treatment of alcoholic hepatitis patient. they are used to suppress the activated immune response but in conditions like renal failure,active infections,gastric bleeding risk may occur.

Steroids when given in combination with NSAID increase the risk of peptic ulcer but when prescribed alone it will not cause any risk.[15-18]

Corticosteroids and hepatitis:

Initial studies had demonstrated the effectiveness of steroids for treating chronic active hepatitis in non hepatitis-B patients. Subsequent studies on patients who are hepatitis –B virus carriers have either shown no added effects or worse outcome in those treated with long term steroids.

There is an increase in hepatitis-B virus DNA levels with the use of steroids and its subsequent cessation can lead to a flare of the condition so it is therefore not advisable to start patients with hepatitis-B virus on long term systemic steroids.

The usage of corticosteroids has neither beneficial nor deleterious effects in patients with Hepatitis – C.[19-22]

Routes of corticosteroids and side effects:

Steroids administered in different routes may cause varied side effects which are discussed below:

TOPICAL ROUTE:

DRUGS	REPORTED ADVERSE EFFECTS	PERCENTAGE
Budesonide	Intra ocular pressure changes	30%
	Irritation,Itching,Bruising	1%
	Contact dermatitis	In 100 out 7238 patients
Hydrocortisone	Pseudotumour , Benign intra cranial hypertension, Cataract glaucoma, Contact dermatitis .	74 out of 7238 patients
Triamcinolone acetonide	Cushing syndrome	

A study report says that misuse of topical steroids out of 6723 patients 379 patients (5.63%) were reported ADR .Out of which 78.89% were females and the remaining were males Most common ADR: acne (37.99%), Telangiectasia(18.99%).[23]

CONDITION	NUMBER	PERCENTAGE
Facial acne	144	37.99%
Plethoric face and telangiectasia	72	18.99%
Facial hypertrichosis	70	18.46%
Hyper hypo pigmentation	60	15.83%
Cutaneous atrophy	38	10.02%
Perioral dermatitis	30	7.91%
Pyoderma	21	5.54%
Tineaincognito	17	4.48%

Side effects topical use of steroids in different age groups :

PATIENTS	**DOSE**	**SIDE EFFECTS**
Infants(210)	89.5g	Telangiectasia is prolonged effect Other effects: Atrophy of the anticubital and popliteal fossae
Children(546)	135g	
Adolescent(515)	304g	
Adult(515)	304g	

INTRANASAL ROUTE:

Used in nasal obstruction, nasal discharge, nasal itching, post nasal drip. It is better than oral histamine.Eg: Budesonide nasal spray administered for 6 weeks which does not cause HPA suppression in children (2-5 years).

Fluticasone propionate administered for one year which does not cause any effect on growth velocity in children(3.5-9 years)

Memetasone furoate administered for one year in children (3-9 years)which does not cause any growth velocity and HPA suppression.

Intranasal corticosteroids causes Osteopenia in male(18%), in female(42%)and it also causes cushing's syndrome[24-26]

INHALATION ROUTE:

The following local adverse effects are caused due to inhalation route of corticosteroids:

- Pharyngitis
- Dysphonia
- Reflex cough
- Bronchospasm
- Oropharyngeal candidiasis
- Reduction in bone markers in adults
- Acute adrenal insufficiency in >500µg / day of fluticasone propionate
- Moderate dose: Aggressiveness,Hyper anxiety, Mood changes and Excitability.
- Skin thining.

In low doses it do not cause neuropsychological and behaviourial changes.[27]

SYSTEMIC SIDE EFFECTS:

It causes the following side effects which includes:

- Suppressed HPA axis function
- Adrenal crisis
- Suppresses growth velocity in children
- Reduced bone mineral density
- Bone fractures
- Osteoporosis
- Skin thining
- Cataract
- Glaucoma

INTRAOCULAR ROUTE:

Steroid induced ocular hypertension (>21mm hg) was reported in some patients. : Total number of patients (156)

NO. OF PATIENTS	CONDITION	PERCENTAGE
36	Steroid induced ocular hypertension	24%
22	Bilateral steroid hypertension	44(eyes)
15	Vernal conjunctivitis	41.6%
16	Withdrawal effects	22(eyes)
7	Needed surgery	10(eyes)

But,It was reported that 80.5% had normal intra ocular pressure even after withdrawing steroids.[28]

ORAL ROUTE:

- It causes HPA axis suppression.
- Oral prednisolone 2 mg /kg / day for 5 days causes behavourial changes(aggression and anxiety)
- It is effective in acute asthma, Polyarticular gout,Ulcerative colitis.[29-31]

PARENTRAL ROUTE:

It is used in early treatment of lateral epicondylitis and medial epicondylitis,De quervian's tenosynovitis, polyarticular gout,adhesive capsulitis,osteoarthritis, ulcerative colitis.

ADR: Subcutaneous necrosis with local skin atophy, post injection pain,local discomfort, flare, bruising, superifical radial nerve neuropraxia and local subcutaneous fat atrophy[32-34]

CONCLUSION:

Steroids are available in different dosage form to explore its potency differently and always there is questions to answer all steroid preparations are same to produce its action and side effects. This review will help us to understand the safety and toxicity profiles of steroids in different route of administration. Selection and use of steroids is like handling double edged sword in a single hand ie., the indication will become a side effect when it is used for a long duration or with wrong therapeutic justification. The practitioner should have a thorough knowledge about the uses and toxicity profile of different steroids in different route before initiating or terminating it.

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