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EVALUATION OF ADVERSE EFFECTS AND UTILIZATION OF GLUCOCORTICOIDS IN A TERITARY CARE HOSPITAL

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ABSTRACT

Introduction: Adverse drug reaction is a noxious unintended effect of a drug which occurs at therapeutic doses normally used in man and Drug utilization is an extent, nature and determinants of drug exposure. The study focuses on the drug use of glucocorticoids and adverse events. **Objective:** To study drug utilization with the special emphasis on the adverse effects of glucocorticoid used in the dermatology department in a tertiary care hospital. Methods and material: A non interventional prospective study was done in dermatology department. 760 inpatient and outpatient prescriptions with glucocorticoids were collected. The data collected was expressed in terms of averages, ratios and proportions. **Results:** Out of 760 patients, 498 females and 262 were male. Highest number of patients were of age group 31-40 years, inpatient were 96 and remaining 664 were outpatient. Prescriptions were analysed of which 59.2% were generic name. Drug betamethasone was the most prescribed glucocorticoid. Common adverse effects observed with glucocorticoids were skin atrophy 27(3.3%), purpura 21(2.6%), striae 21(2.6%) and weight gain 20(2.5%) and betamethasone was the most common causative drug. A few cases of Cushing syndrome were seen with prednisolone and dexamethasone. **Conclusion:** Use of glucocorticoids was found to be appropriate as per standard guidelines. Adverse drug reactions to glucocorticoids are more common and gender difference was significantly seen more in males than female patients.

KEYWORDS: Adverse reactions, Glucocorticoid, Dermatology.

INTRODUCTION

Drug utilization research is an essential part of pharmacoepidemiology as it describes the extent, nature and determinants of drug exposure.[1] Corticosteroids are a class of steroid hormones used for its powerful anti-inflammatory properties. Among the corticosteroids, the topical glucocorticoid preparation are most commonly prescribed agents in the out-patient dermatology department since it was introduced.[2] and they still continues to be one of the largest groups of drugs in the dermatology discipline. But the prevalence of overall adverse effect associated with the use of glucocorticoids even with low dose is high.[3] As a general rule, clinicians should use the weakest possible glucocorticoid to treat the dermatological condition and to be also well apprised of their risks. Topical glucocorticoids are mainly used for non-infective dermatologic disorders associated with inflammation such as psoriasis, atopic dermatitis and contact dermatitis. They do have many adverse effects(AEs) such as hypersensitivity and tachyphylaxis.[4] The potent anti-inflammatory and immunosuppressant actions of oral and sometimes topical corticosteroids increase susceptibility to bacterial and fungal infections. Low dose long term use of glucocorticoids in the treatment of rheumatic arthritis have shown to induce osteoporosis, these risk have heightened the attention of glucocorticoid induced adverse effects.[5] In addition, children may be more vulnerable than adults to systemic effects of topical corticosteroids because percutaneous absorption is greater.[6]

Irrational prescription of drugs is a common occurrence in clinical practice.[7] The cost of such irrational drug use is enormous in developing countries in terms of both scarce resources and the adverse clinical consequences of therapies that may have real risks but no objective benefits.[8]

Hence, the present study was undertaken in the dermatology department, Belagavi institute of medical sciences in patient with glucocorticoid treatment. A detail information on the glucocorticoids prescribed, their prescribing patterns and rational use and to evaluate the adverse effects of glucocorticoids prescribed was analysed.

MATERIALS AND METHODS

A Prospective observational study was done in the department of dermatology, Belagavi Institute of Medical Sciences, Belagavi. A total of 760 outpatient and inpatient prescription records with demographic details, medical history and prescribed with glucocorticoids were collected for a period of one year, after obtaining approval and clearance from the

Institutional Ethics Committee. The patients those who fulfilled inclusion and exclusion criteria were included in our study. Inclusion criteria: All age groups of either sex prescribed with glucocorticoid. Exclusion criteria: Prescriptions which did not contain glucocorticoid, pregnant and lactating mothers.

The relevant data was collected by direct observation and entered in a specially designed proforma containing details such as demographic, disease and drug data and detailed emphasis on adverse effects. These patients were followed up during their hospital stay and on subsequent follow ups and were requested to report if any adverse drug reactions.

Statistical Methods: The present study was analysed by descriptive and inferential stastical analysis. Data was analysed on software using SAS 9.2 and R environment ver.2.11.1. Microsoft word and excel to generate graphs, tables etc. have been used.

RESULTS

The totals of 760 patients were included in our study. In demographic profile, age and sex wise distribution is shown in the "Fig. 1". Total number of female were 498 and male were 262. Highest numbers of patients were of age group of 31-40 year and predominant were males. Prescriptions of 96 inpatients and 664 patients visiting dermatology OPD during the study period prescribed with glucocorticoids were collected is shown in the Table 1.

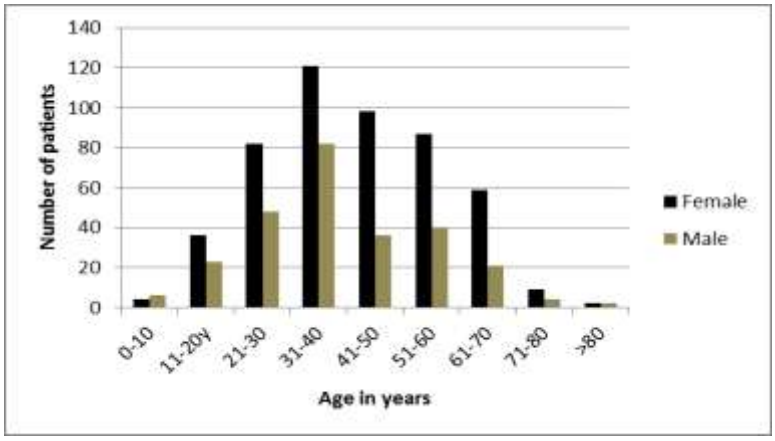

Fig 1: Age and sex wise distribution of patients

Table 1: Inpatient/outpatient studied.

Inpatient/Outpatient	No. of patients	%
Inpatient	96	12.6
Outpatient	664	87.4
Total	760	100

Drug data: In our study population, total of 842 glucocorticoid formulation were prescribed, of which 441(52.4%) consisted of betamethasone which was commonly prescribed, 232(27.5%) was clobetasol and 56 (6.7%) dexamethasone shown in the Table 2.

Table 2: Type of glucocorticoids prescribed to the patients

Corticosteroid	No. of Drugs	%
Betamethasone	441	52.4
Clobetasol	232	27.5
Dexamethasone	56	6.7
Prednisolone	49	5.8
Mometasone	30	3.6
Triamcinolone	28	3.3
Fluticasone	6	0.7
Total	**842**	**100**

Most of the glucocorticoids of different formulation were used in different routes of administration, of which local application was common 731 (86.8%) least used route was intralesion 19(2.3%) shown in the "Fig. 2". 59.2% were generic name dispensed from hospital pharmacy.

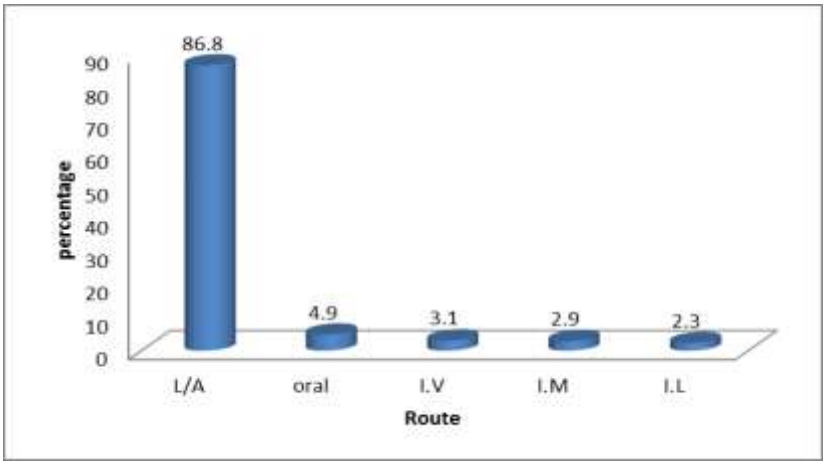

Figure 2: Routes of administration of glucocorticoids

Adverse drug reactions to glucocorticoids: Table 3 shows the various adverse drug reactions among male and female patients. Out of the total 120(14.8%) adverse effects were observed, the most common was skin atrophy 3.3%, Purpura, 2.6%, striae 2.6%. Prevalence of striae, insomnia and weakness was more in males than females.

Betamethasone the long acting glucocorticoid was the commonest to cause adverse reaction of 4.2% when compared with the other glucocorticoids is shown in the Table 4.

Table 3: Sex wise comparison of adverse reaction to glucocorticoids

Adverse reaction	Male	Female	Chi Sq	P value
Skin Atrophy	17	10	1.81	>0.05
Purpura	11	10	0.05	>0.05
Striae	15	6	3.85	<0.05*
Weight gain	9	11	0.2	>0.05
Insomnia	9	1	6.4	<0.05*
Weakness	9	2	4.45	<0.05*
Cushing's Syndrome	4	3	0.14	>0.05
Acne	1	2	0.33	>0.05
Depression	-	1	1	>0.05
Hyperglycemia	1	-	1	>0.05
Hyper pigmentation	1	-	1	>0.05
Osteoporosis	-	1	1	>0.05
Tachyphylaxis	-	1	1	>0.05

**-significance.*

Table 4: Comparison of adverse events to different glucocorticoid.

ADR	Glucocorticoids						Total (%)
	Betamethasone	Clobetasol	Dexamethasone	Prednisolone	Mometasone	Triam- cinolone	
Skin Atrophy	13	4	7	-	2	-	27 (3.3)
Purpura	8	4	6	1	1	1	21(2.6)
Striae	3	9	3	4	1	1	21 (2.6)
Weight gain	1	4	3	12	-	-	20 (2.5)
Insomnia	4	3	2	1	-	-	10 (1.2)
Weakness	2	2	6	1	-	-	11 (1.3)
Cushing Syndrome	-	-	2	5	-	-	7 (0.9)
Acne	3	-	-	-	-	-	3 (0.4)
Depression	-	1	-	-	-	-	1 (0.1)
Hyperglycemia	-	1	-	-	-	-	1 (0.1)
Hyper pigmentation	-	-	-	-	-	1	1 (0.1)
Osteoporosis	-	-	-	1	-	-	1 (0.1)
Tachyphylaxis	-	1	-	-	-	-	1 (0.1)
	34 (4.2%)	29 (3.6%)	29 (3.6%)	26 (3.2%)	4 (0.5%)	2 (0.2%)	120 (15.3)

DISCUSSION

Corticosteroids play an important role in dermatological practice. However, their clinical efficacy is compromised by the metabolic effects of long-term treatment which includes, osteoporosis, hypertension, dyslipidaemia and insulin resistance/type 2 diabetes mellitus.[9] There is also no doubt that misuse of glucocorticoids even with topical preparations can lead to troublesome local effects and potentially serious systemic problems.

In one year study period, Out of total 760 patients 262 (34.5%) were males and 498 (65.5%) were females and patients between the age group of 31-40 years were maximum which were similar when compared with other studies, where males were predominant and middle age group were more.[10, 11]

In a study carried out in North Palestine, topical preparations (51.6%) were prescribed to the outpatient attending dermatology clinic[12] Also studies conducted in India showed 67% & 43%[13,14], our study showed most of the cases were prescribed with topical glucocorticoids(86.8%) to the outpatients and was very high compared to their studies as this route has minimum side effects as compared to systemic routes of drug administration. Prescription also specified the frequency of administration and site of application. But few prescriptions did not specify the dose/strength of topical preparations. This can lead to dispensing error, to avoid this; a rational and appropriate prescription pattern has to be followed for better patient care.

Among the glucocorticoids betamethasone 441 (52.4%) was the most commonly used topical corticosteroid, as it is cost-effective and easily available in our pharmacy. Where it was almost similar to the other study which was 58.8%.[15] In a study by Uppal R et al. clobetasol high potent topical corticosteroids was frequently prescribed.[16] A study done by Ankit P et al intravenous dexamethasone sodium phosphate a longer acting glucocorticoid was highly prescribed drug but it was rationally used with appropriate strength and gradually tapered.[17]
In the current study incidence of dermatological AEs were more in outpatients, higher incidence in males. The same outcome of male preponderance was seen in some studies these high incidences they state that it could be as males are more conscious about dermatological reaction.[18,19] Some studies have also reported female preponderance also.[20-22]

In the present study, the common AEs were Skin atrophy 27 (3.3%) followed by purpura 21(2.6%) and striae 21(2.6%), these skin disorders were more in males than female,

compared to other study women reported more with these disorder.[22] A study conducted by Curtis et al showed greater prevalence of weight gain in 80% of patients treated with corticosteroids, striae and purpura were the next most common reported AEs[23] whereas weight gain was the next common adverse effect in our study.

In our study muscular weakness and insomnia was 11(1.3%) and 10(1.2%) but it was statistically significant in males, comparatively less to other study where it was reported to be 15% and also neuropsychiatric disorder were very less in our study, only one case of depression with clobestol administration was seen, but in Fradet L et al study 52.5% of patient reported with depression, euphoria, irritability, hyperactivity and mania.

Incidence of cushing syndrome in our study was seen with 7 cases it was due to administration of prednisolone to patients with lepra reaction type I and few cases with dexamethasone drug use in pemphigus vulgaris. The abnormal fat deposition cases were also reported in Ankit et al where only 4 cases (4%) was reported and more frequent in females.
In a small clinical trial of patients with rheumatoid arthritis, even with low doses of glucocorticoids AEs of vertebral fractures, weight gain and hyperglycaemia were observed though the incidence rate were low but still corticosteroid should be used cautiously.[24,25]

To limit these adverse effects of corticosteroids selection of individual with few co-morbid illnesses, prescribe for shorter duration with minimum dose necessary to control the disease and frequent followup to detect the AEs has to be followed.

CONCLUSION

Glucocorticoids are one of the most frequently used drugs and the decision with its use is of utmost importance and based on the potential for its serious adverse effects on long term use. Every case treated with corticosteroids should be considered with regard to relative risk and benefits and therefore it should be used rationally and judiciously to minimize the side effects and sufferings of the patients.

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