Global Journal of Pharmacology 6 (1): 19-22, 2012
ISSN 1992-0075

A Study on Monitoring Adverse Effects of Oral and Topical Corticosteroids

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Abstract: AIM:To monitor the adverse effects of oral and topical corticosteroid preparation. Methods: A descriptive study was conducted in outpatients from Rheumatology and Dermatology OPD who were taking corticosteroids for rheumatoid arthritis and chronic eczema for more than 6 months, study was conducted over 6 months period. The WHO definition of an ADR was adopted. Adverse effects were monitored during the study period. The Naranjo algorithm scale was used for causality assessment. Results : Statistical analysis was done by using Microsoft excel. Most common adverse effects observed in oral corticosteroid population were hypertension 46.7%, hyperglycemia 24%, cushingoid feature16%, with causality assessment score 7, 13.3% of peptic ulcer disease with causality assessment score of 6. In topical corticosteroid population adverse effects observed were 60% hyperglycemia, 40% cushingoid feature. Hypertension, peptic ulcer disease were not reported in topical corticosteroid population. This indicates oral and topical corticosteroids were the probable cause of these adverse events. Conclusion : The most common adverse effects observed in oral corticosteroid preparations were hypertension followed by hyperglycemia, cushingoid feature & peptic ulcer disease. For topical corticosteroid preparation the most common adverse effects were hyperglycemia followed by cushingoid feature. In Indian Population the incidence of hypertension and hyperglycemia were more common and the cushingoid feature appears to be less when compared to the studies conducted in Western population.

Key words: OPD · Corticosteroid · Cushingoid Feature · Hyperglycemia · Eczema · Rheumatoid Arthritis

INTRODUCTION

Medicines are important aspect in clinical practice that is designed to improve the health of target population. During the course of treatment drug prescribed to patients produce certain effects other than the desired or expected effects, these issues concern both to the physician and the patient by spiralling costs of medical treatments and also cause a great deal of morbidity and mortality. All medicines carry some risk of harm and it is important to monitor their effects, both intended and unwanted, so that good evidence is available to base an assessment of risk versus effectiveness or risk versus benefit. Adverse drug reactions are noxious, unintended and undesirable effects that occur as a result of drug treatment at doses normally used in man for diagnosis, prophylaxis and treatment. Adverse drug reactions constitute a major clinical problem in terms of human suffering and increased health care costs. It has been reported that the incidence of adverse drug reaction is much more in geriatric, paediatric and female patients. Females are more susceptible to gastrointestinal and cutaneous allergic adverse drug reactions, it has been estimated that 83% of adverse drug reactions in male and 93% of adverse drug reactions in female are dose related [1-5].

Research findings estimate a 6.5% prevalence of adverse drug events. 1% of these adverse drug event resulted in patient death, 12% in life danger, 30% in serious illness, 60% - 70% of adverse drug events are preventable, this calls urgent need to reinforce the monitoring of adverse reactions to drugs, which can lead to reduction in incidence of adverse drug reactions. Early identification of unexpected adverse drug reactions and their risk factor is essential, so that the medicines can be used in an effective manner with the least chance of harm [6].

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Pharmacovigilance is an important tool in the detection, assessment, understanding and prevention of adverse effects or any other possible drug related problems, thereby it improves public health and safety in relation to the use of medicines and communicate the findings in a timely manner. This tool contributes to assessment of benefit, harm, effectiveness and risk of medicines, leading to prevention of harm and maximization of benefit. Aim of the pharmacovigilance is to improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions. It also encourage the safe, rational and more effective (including cost effective) uses of medicines [7].

Corticosteroids are the most common medicaments used to reduce inflammation in inflammatory conditions, suppress the immune system in immunological disorders and replace hormones in the body in hormonal insufficiency conditions. Corticosteroids are proven to be very effective in these conditions which led to popularity and widespread usage of these group of drugs among physicians in different speciality, though corticosteroids have outstanding therapeutic benefits, they may also produce some unwanted or undesirable effects [8].

This is the need of the hour to monitor adverse effects of corticosteroids during the treatment of these different conditions. The present study is intended to investigate adverse drug effects of corticosteroids oral and topical preparation in the Department of Rheumatology and Dermatology in a tertiary care hospital Sri Ramachandra Medical College and Hospital at Chennai.

MATERIAL AND METHODS

The study was conducted at Sri Ramachandra Medical College hospital porur, Chennai, Tamilnadu. A descriptive study was conducted over a period of 6 months from October 2008 to March 2009. Approval of the institutional human ethics committee was obtained.

Total 100 patients aged between 15 - 70 years of age were enrolled in this study, among them 75 patients from rheumatology OPD and 25 patients from dermatology OPD who were taking oral corticosteroid(Tablet. Prednisolone 10mg) for rheumatoid arthritis [9] and for chronic eczema who were taking topical corticosteroid (Oint. Betamethasone dipropionate 0.05%)[10] for more than 6 months were included in this study.

Patients with diabetes mellitus, hypertension, peptic ulcer disease, hormonal disturbances, renal and hepatic insufficiency and pregnant women were excluded from the study. All the out patients were monitored for ADRs during the study period. In the suspected cases past medical or medication history of patients were collected. Patients were interviewed and their medical records were reviewed. The suspected ADRs were carefully analyzed and documented.

All relevant data including all drugs the patients received prior to the onset of the reaction, their respective dosage, route of administration with frequency, date of onset of reaction and the patient allergy status were noted. The causality relationship between the ADR and the suspected drug therapy was assessed using the Naranjo probability scale[11]

Statistical Analysis: Statistical analysis was done by using Microsoft excel.

RESULTS

One hundred patients with ages ranging from 15- 70 years of both sex were evaluated, among them 75 patients taking oral corticosteroid (Tab. Prednisolone 10mg) for rheumatoid arthritis for more than 6 months, 25 patients taking topical corticosteroid (Oin. Betamethasone 0.05%) for chronic eczema for more than six months (Table1 & Fig.1).

Incidence of adverse effects in oral corticosteroid group were 46.7% hypertension, 24% hyperglycemia, 16% cushingoid feature with the causality assessment score (Naranjo score) 7 and the incidence of peptic ulcer disease was 13.3% with the causality assessment score (Naranjo score) 6. (Table2 & Fig.2).

Incidence of adverse effects in topical corticosteroid group were 60% hyperglycemia, 40% cushingoid feature with the causality assessment score (Naranjo score) 7 and there was no incidence of hypertension and peptic ulcer disease (Table 3 & Fig.3).

This indicates oral and topical corticosteroids were the probable cause of these adverse events.

Table1: Distribution of Patients Taking Oral & Topical Corticosteroids

Total Number of Patients N = 100	
Drug	No.of Patients
Oral Corticosteroid	75
Topical Corticosteroids	25

Table 2: Percentage of Adverse Effects in Oral Prednisolone Preparation

Total Number of Subjects N = 75	
Adverse Effects	Percentage
Hypertension	46.7%
Hyperglycemia	24%
Cushingoid Feature	16%
Peptic Ulcer Disease	13.3%

Table 3: Percentage of Adverse Effects in Topical Corticosteroid Preparation

Total Number of Subjects N = 25	
Adverse Events	Percentage
Hyperglycemia	60%
Cushingoid Feature	40%

Table 4: Naranjo Algorithm (Causality) Score on Corticosteroid Induced Adverse Drug Effect

Adverse Effects	Causality Score
Hypertension	7
Hyperglycemia	7
Cushingoid Feature	7
Peptic Ulcer Disease	6

Possible = 1 - 4

Probable = 5 - 8

Definite = > 9

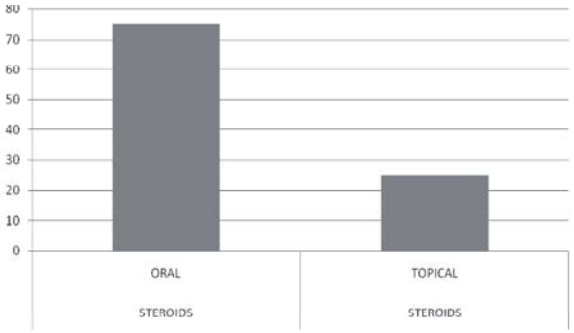

Fig 1: Distribution of Patients Taking Oral & Topical Corticosteroids
Total Number of Patients N = 100
X axis - Number of patients
Y axis - corticosteroid preparation

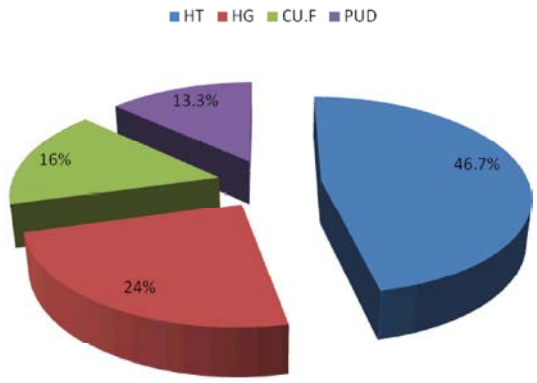

Fig 2: Percentage of Adverse Effects in Oral Prednisolone Preparation
Total Number of Subjects N = 75
HT - Hypertension
HG - Hyperglycemia
CU.F - Cushingoid feature
PUD - Peptic ulcer disease.

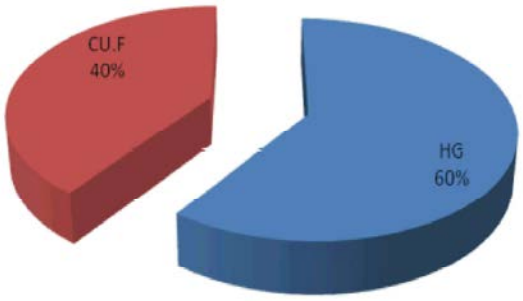

Fig 3: Percentage of Adverse Effects in Topical Corticosteroid Preparation
Total Number of Subjects N = 25
HG - Hyperglycemia
CU.F - Cushingoid feature.

DISCUSSION

Corticosteroid induced adverse events were studied in 100 patients of 15-70 years age group who were suffering from Rheumatoid arthritis and chronic eczematous conditions.

Adverse events like hypertension, hyperglycemia, cushingoid feature & peptic ulcer disease were seen in both oral prednisolone & topical corticosteroid preparations. In our study there was no radiological evidence of osteoporosis in the long term treatment of oral and topical corticosteroids.

Incidence of adverse events in oral prednisolone preparation group was hypertension (46.7%) followed by hyperglycemia (24%), cushingoid feature (16%) then peptic ulcer disease (13.3%). So the more common adverse events observed in oral corticosteroid preparation in descending order were hypertension, hyperglycemia, cushingoid feature and peptic ulcer disease with causality score of seven (Hypertension, hyperglycemia, cushingoid feature) and six for peptic ulcer disease which indicates that the oral steroid preparation were the probable cause for these adverse effects.

Incidence of adverse events in topical corticosteroid (Betamethasone dipropionate 0.05%) were Hyperglycemia (60%) followed by cushingoid feature (40%). So the more common adverse events in topical corticosteroid preparation were Hyperglycemia followed by cushingoid feature with causality score of seven, that is the topical corticosteroids were the probable cause of these adverse effects.

Hypertension is due to corticosteroids directly stimulate cardiac output & potentiate the responses of vascular smooth muscle to the presser effects of catecholamines.

Corticosteroids increases blood glucose level (Hyperglycemia) by increasing the gluconeogenesis.

Cushingoid feature is due to suppression of hypothalamic pituitary adrenal axis by the corticosteroids.

Corticosteroids induces peptic ulcer disease by blocking phospholipase A2 enzyme this leads to inhibition of prostaglandin synthesis (prostaglandin is a protective barrier of gastric mucosa.)

Similar study was conducted by Smyllie and Connolly under 'Incidence of serious complications of corticosteroid therapy in respiratory disease' this is a retrospective survey of patients in the Brompton Hospital. In this study 550 patients treated with corticosteroids. Overall incidence of side effects were cushingoid feature 29% followed by peptic ulcer disease 4.2%, hypertension 4%, hyperglycemia 1.63% [12].

In our study hypertension and hyperglycemia dominates over the other adverse effects and cushingoid feature was comparatively less. This may be due to the differences in the racial, constitutional and other contributory factors in the Indian population.

CONCLUSION

Glucocorticoids are used widely in the treatment of a variety of rheumatic disorders and are the mainstay in the treatment of chronic eczema. In our study the outcome shows that the most common adverse effects of oral and topical corticosteroids, were more for those who take these preparation for more than six months in cases of Rheumatoid Arthritis and Eczema.

The most common adverse effects observed in oral corticosteroid preparations were hypertension followed by hyperglycemia, cushingoid feature & peptic ulcer disease. For topical corticosteroid preparation the most common adverse effects were hyperglycemia followed by cushingoid feature. In Indian Population the incidence of hypertension and hyperglycemia were more common and the cushingoid feature appears to be less when compared to the studies conducted in western population.

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