ISSN: 2279 - 0594

Journal of Biomedical and Pharmaceutical Research

Available Online at www.jbpr.in

CODEN: - JBPRAU (Source: - American Chemical Society)

Index Copernicus Value: 63.24

PubMed (National Library of Medicine): ID: (101671502)

Volume 6, Issue 1: January-February: 2017, 01-08

Research Article

Assessment, Monitoring and Reporting Adverse Drug Reactions of Corticosteroids: A Prospective Observational Study

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Received 20 Nov. 2016; Accepted 02 Jan. 2017

ABSTRACT

Background: Corticosteroids are widely used medication for the treatment of various conditions. Using too little dose of steroids can lead to sub therapeutic response whereas using higher dose of steroids can lead to Adverse drug Reactions (ADRs). These steroids, especially topical preparations are easily available in the pharmacy store and are sold without prescription. This has led to its irrational use and increased ADRs which has become a major concern. **Aim:** To assess, monitor and report suspected ADRs of Corticosteroid.

Method: A prospective observational study was conducted in the department of dermatology and general medicine in a tertiary care teaching hospital for the period of 6 months. All patients receiving any category of Steroid therapy were included. The suspected ADRs were assessed using standard scales and were reported to concerned departments. **Result:** A total of 226 patients were enrolled where 29 ADRs were detected. Around 3.98% of the subjects were found with clinically significant drug interaction. Oral steroids were responsible for most ADRs. Swelling of limbs was the most common ADR (3.09%) followed by joint pain (2.21%). On causality assessment, 31.06% of the ADRs were found to be Unlikely followed by 20.68% of the ADRS were certain via WHO scale whereas 41.4% were Doubtful and 20.68% were Definite via Naranjo scale. Most of the ADRs were probably preventable (72.42%) and moderately severe (62.08%).**Conclusion:** Involvement of pharmacist in patient care can help in prevention of ADRs which can promote drug safety and efficacy.

Keywords: ADR, Corticosteroids, Pharmacist, Pharmacovigilance

INTRODUCTION:

Corticosteroids are preferred for the treatment of wide range of diseases due to their symptomatic relief in a short duration of time[1]. However, these drugs show harmful and unwanted effects when used for a long period of time[2]. In India, most of the corticosteroids, especially topical preparation are sold without prescription and also the patients can easily obtain it from the local drug store. Central Drugs Standard Control Organization (CDSCO) has reported that the off label use of these medication is more commonly practiced in India[3-4]. These medications are used inappropriately for various dermatological disorders like acne, bacterial or fungal infections and rash by non-registered practitioners which are a major concern[5-6]. This leads to increased Adverse Drug Reaction (ADR) and further increases the morbidity and mortality[7].

The study of the ADR is concerned with Pharmacovigilance, an integral part of the drug therapy. However, this is not usually practiced in Indian hospitals. The ADR monitoring reports has been very few in India as ADR monitoring is developing here[8]. The need for efficient Pharmacovigilance programme was felt by CDSCO

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and it mandated monitoring and reporting of ADR. It also focused on creating awareness among health care professionals regarding monitoring and reporting of ADRs[9]. Pharmacist can play a vital role in the development, maintenance and evaluation of the program to reduce the risk of ADRs by assessing, monitoring and reporting of the suspected ADRs. Every suspected ADR can be further scrutinized for its preventability and severity. Pharmacist can aid other Health Care Professionals (HCP) for developing risk reduction strategies along with providing information to HCPs for identifying the ADRs in a better way and encouraging compliance with ADR reporting program[10].

The main objective of our study was to assess and monitor the suspected ADRs related to corticosteroid use among the patients from general medicine and dermatology department of MVJ medical college and research hospital located in Bangalore, South India and reporting the suspected ADRs to the concerned department and to the ADR monitoring authorities.

METHODOLOGY

Study Design and Human Ethical Clearance:

A prospective, observational study was conducted for duration of 6 months from October 2015 to March 2016 in accordance with the ethical principles of declaration of Helsinki and principles of current Good Clinical Practice (GCP). The study protocol was approved by the Institutional Ethical Committee (IEC) with ethical clearance number: Central Research/MVJ MC& RH/08/2016.

Study Population:

Study Site: Department of General Medicine and Department of Dermatology, MVJ Medical College and Research Hospital, Bangalore , South India.

Inclusion criteria: All the patients of various age groups who received any category of steroid therapy in both the departments were included and were monitored for any suspected adverse drug reaction. Patients who had a history of steroid intake and a history of steroid abuse were also included in the study.

Exclusion Criteria: Patients who met all the inclusion criteria but not willing to participate in the study were excluded.

Functional Definitions:

The following functional definitions are defined by the investigators for the study purpose.

Suspected Adverse Drug Reaction was defined as any harmful or unpleasant effects that occur which may or may not be related to corticosteroid use.

Steroid Abuse was defined as inappropriate use of steroids for a period of more than one year.

Method:

All the patients who met the inclusion criteria were enrolled in the study after taking Informed Consent (IC) before commencing the study. The basic demographics, medication related details and laboratory investigation values were collected by the researchers personally using the Case Report Form (CRF). This information was collected from the patient's case sheets. All the patients were monitored for any ADR towards steroid drug usage. The ADRs were suspected through the routine ward rounds, prescription monitoring and reports from health care professionals (doctors, nurses). The suspected ADR were assessed for Causality using WHO[11] and Naranjo scales[12]. They were further assessed for their severity using Hartwig's severity Assessment scale[13]. The preventability criteria were assessed using Schumock and Thornton scale[14]. The results were analyzed using descriptive statistical methods and were reported to the Pharmacovigilance department of MVJ Medical College and Research Hospital which would further be reported to regional pharmacovigilance center.

RESULTS

Demographic data:

A total of 226 patients were enrolled out of which 62 patients were from dermatology department and 164 patients were from general medicine department. Majority of the study subjects who participated in this study were belonging to the age group of >60 years followed by 51-60 years of age. Similarly, more number of males was found to be using corticosteroids as compared to females. Likewise, significant number of patients was found to be smokers and majority of the patients were found to be illiterate. The Patients enrolled were mostly Elderly people who have retired and are not working followed by Housewives and Farmers.

The detailed demographic data is illustrated in Table 1.

Table 1: Demographic Data (N=226)

Gender	**Percentage (%)**
Male	58.4
Female	41.6
Age in Years	
<20	4.87
21-30	8.85
31-40	15
41-50	11.94
51-60	22.12
>60	37.22
Social Habits	
Smoker	38.93
Non Smoker	61.07
Literacy Status	
Illiterate	60.2
Literate	39.8
Occupation	
Business	4.87
Farmer	23.45
Housewife	26.54
Retired (Elderly)	27.79
Student	3.98
Worker	13.37

Suspected Adverse Drug Reactions:

A total of 29 ADRs were suspected from corticosteroid usage in 226 patients. ADRs were suspected through the routine ward rounds, Prescription monitoring and reports from health care professionals (doctors, nurses) as demonstrated in Table 2.

Table 2: Suspected ADRs (N=226)

ADRs	**No of Patients (%)**
Suspected	29 (12.83%)
Not Suspected	197 (87.17%)

Drug Interactions:

In our study, we assessed patients for drug interactions. A total of 44 drug interactions were found out of which majority of them were clinically not significant which means that the drug interactions were found theoretically but not seen in patients clinically, however few were clinically significant. Majority of the patients did not have any drug interactions. This is illustrated in Table 3.

Table 3: Drug Interactions (N=226)

Drug Interaction Found		No of Patients (%)
Found	Clinically Significant	9 (3.98%)
	Clinically Not Significant	35 (15.49%)
Not found		182 (80.53%)

Types of Adverse Drug Reactions Suspected:

In our study, most of the ADRs were associated with oral corticosteroids. The most common ADR associated with steroid use was swelling of limbs which were due to prolonged use of Prednisolone and Dexamethasone followed by moon face, buffalo hump and facial swelling. Skeletal problem like joint pain which may be a symptom of Osteoporosis was seen in few patients. ADRs due to Corticosteroid Injections such as bleeding was not seen any of the patients. Similarly, ADRs of topical steroids such as acne was seen in very few patients. Noisy breathing or trouble in breathing was seen in case of long term use of oral as well as inhaler corticosteroids. The detailed information is illustrated in Table 4.

Table 4: Types of ADRs (N=226)

Types of ADR	Drugs Associated	No. of Patients	Percentage
Weight gain	Prednisolone Dexamethasone	2 1	0.88 0.44
Acne	Clobetasol	2	0.88
Moon face, Buffalo Hump, Facial Swelling	Prednisolone Dexamethasone	4 1	1.76 0.44
Joint pain	Prednisolone Dexamethasone	3 2	1.32 0.88
Noisy Breathing, Troubled breathing	Budesonide Prednisolone Dexamethasone	1 1 1	0.44 0.44 0.44
Swelling of Limbs	Prednisolone Dexamethasone	5 2	2.21 0.88
Decreased Urine	Prednisolone	1	0.44
Decreased Vision	Prednisolone	1	0.44
Hypokalemia	Prednisolone + Furosemide	2	0.88

Causality Assessment:

The Causality Assessment of the suspected ADRs was done using WHO and Naranjo Scale. According to WHO scale, out of 29 ADRs, majority of them were Unlikely followed by certain and Possible. Similarly, when the ADRs were assessed using Naranjo scale, majority were found to be doubtful followed by Definite and Possible which is demonstrated in Table 5.

Table 5: Causality Assessment (N=29)

WHO Scale	Number (%)
Certain	6 (20.68%)
Probable	5 (17.24%)
Possible/Likely	6 (20.68%)
Unlikely	9 (31.06%)
Conditional/Unclassified	3 (10.04%)
Unclassifiable/Unassessable	0

Naranjo Scale	
Definite	6 (20.68%)
Probable	5 (17.24%)
Possible	6 (20.68%)
Doubtful	12 (41.4%)

Preventability Assessment:

The Preventability Assessment was done by using Schumock and Thornton Scale. Out of 29 ADRs, most of them were probably preventable, few were definitely preventable and none of them were Not Preventable. This is shown in Table 6.

Table 6: Preventability Assessment (N=29)

Preventability	No. of Patients (%)
Definitely Preventable	8 (27.58%)
Probably Preventable	21 (72.42%)
Not Preventable	0

Severity Assessment:

The Severity Assessment was done by using Modified Hartwig and Siegel Scale. Out of 29 ADRs, most of them were moderately severe whereas few were of severe and mild in severity as demonstrated in Table 7.

Table 7: Severity Assessment (N=29)

Severity	No. of Patients
Mild	6 (20.68%)
Moderate	18 (62.08%)
Severe	5 (17.24%)

DISCUSSION

Adverse Drug Reaction is a term that describes any harm or unwanted effect associated with the use of a medication at normal dose[15]. It is commanded by the regulatory authorities to track and report ADRs. In order to identify and prevent ADRs, reliable methods which can accurately predict those populations who are at greater risk of getting ADRs must be developed[16]. Also, ADRs decrease the quality of life, increases hospitalization leading to increased cost and may lead to death which makes assessment, monitoring and reporting ADRs very important.

Two hundred twenty six patients were enrolled in the study where 27.5% were enrolled from the department of dermatology and 72.5% were enrolled from the Department of General Medicines. Male patients were 58.4% and 41.6% were female respectively. In our studymajority of corticosteroid received patients belonged to age group >60 years followed by agegroup of 51-60 years. This is supported by study conducted in United Kingdom by *L J Walshet al*[17].Likewise; the social status of our study reported smokers 38.93% and non-smokers 61.07%. This issupported by a study conducted by *Dennis Chen et al* carriedout in south Texas who reported 47.7% of their patients to be smokers[18]. In our study, most of the patients were found to be illiterate. This was one of the reasons for inappropriate use of medication which might have led to drug interactions. Illiterate people may have difficulty in understanding the instructions and may use the medications incorrectly. This makes the role of clinical pharmacist vital as they can participate in proper counseling of the medication and avoid ADRs due to drug or food interaction[10]. In the study, occupational status was noted which showed majority of elderly people using corticosteroids. Elderly population is always at a higher risk of developing ADRs. Many non-

complaint factors like forgetfulness or impaired function of their body make them vulnerable to ADRs. So close monitoring of ADRs in elderly is highly recommended[19]. Similarly Farmers and Housewives were associated with steroidal use. This may be due to type of the work they do on daily basis. On communicating with the patients, it was found that both the population (Famers and Housewives) commonly had diseases associated with skin and respiratory system for which they were using corticosteroids. Normally patients with respiratory illness were using corticosteroids for a longer duration of time that has led to ADRs.

In our Study, we have suspected 29 ADRs in 226 patients. The ADRs were suspected through daily ward rounds with the doctor along with prescription monitoring and reports from health care professionals. Different types of ADRs were suspected. The most common ADR was suspected to be swelling of limbs associated with oral Prednisolone and Dexamethasone. Other ADRs such as moon face, buffalo hump and facial swelling were seen in 2.21% of the cases which is characteristics of Steroid Abuse[20]. On investigation all of these patients were found to be abusing steroids for at least 1 year unknowingly. Similarly, 5 patients also reported to have joint pain and on investigating their medication history, they were found to be taking steroids for a long period of time and the joint pain could be a symptom of Osteoporosis[21]. Likewise, 3 patients, all with respiratory disorders were taking steroids for their treatment and were using drugs like Budesonide (inhaler) and oral prednisolone & dexamethasone for long time. They later developed noisy breathing (hoarseness) and troubled breathing which could be due to pronged use of these medications[20]. Patients were also monitored for weight gain and hyperglycemia. Two patients developed weight gain[20] in duration of 2 months whereas none of the patients were found to be hyperglycemic. Acne was seen in 2 patients, which was due to inappropriate use of Clobetasol[22]. Other reactions like Depression and mood swings were not presented by any patients. On Assessment of Causality by WHO scale, most of them were found to be Unlikely and when done by Naranjo Scale, most of them were found to be Doubtful which was due to lack of concrete information from the patients on their past medical and medication history. These ADRs were still reported because the ADRs were only suspected and further investigations could be done in future. Similarly in Preventability assessment, most of the ADRs were probably preventable. This was because of the symptoms of long term steroid use without tapering along with old age. However, 27.5% of the ADRs were Definitely Preventable. There were no ADRs which were Not Preventable. On Severity assessment, 62.08% of the ADRs were found to be moderately severe whereas 20.68% were found to be of mild severity and required no intervention. Around 17.24% of the patients had severe ADRs and they required hospital stay which increased the cost of their treatment. This indicates that the health care cost increases due to ADR.

Limitations:

The major limitation faced was the short study period which was done only for 6 months and only a few ADRs could be collected. Similarly, the Re-challenge and De-challenge steps were not performed which could confirm the ADRs. Also, our study was restricted to Department of General Medicine and Department of Dermatology only.

Future Outlook:

Active Pharmacovigilance centers can be established or increased for safe and effective use of medicine. Any ADRs which are suspected must be reported so that further researches could be conducted in the future regarding same. Proper prescribing guidelines must be formulated which can help in avoiding many ADRs. Similarly, computerized prescription should be used in all the hospitals in order to avoid medication error which could lead to potential ADRs.

CONCLUSIONS

Very few ADR monitoring centers are active in India, which makes it very difficult to generate the safety of various therapeutically active agents. Mostly, medicines are tested for short term safety and efficacy and on a limited number of cautiously selected patients in clinical trials. This makes it very important to continuously monitor the medication for its safety and efficacy. There is a vital role of clinical pharmacist in monitoring the safety and effectiveness of the medications. They can provide proper counselling on how to use the medication appropriately and avoid ADRs due to

its inappropriate use. Polypharmacy is one of the main reasons for drug-drug interactions leading to ADRs and this should be strictly discouraged for safe and effective use of medication.

AKNOWLEDGEMENT

The authors are thankful to the principal of Krupanidhi College of Pharmacy and MVJ Medical College and Research Hospital for providing the necessary facilities for conduction of the study. The authors are also thankful to the staffs of General Medicine and Dermatology Departments for their valuable services.

CONFLICT OF INTEREST

The authors declare no Conflict of Interest.

ABBREVIATION

ADR: Adverse Drug Reaction

CDSCO: Central Drugs Standard Control Organization

CRF: Case Report Form

GCP: Good Clinical Practice

HCP: Health Care Professionals

IC: Informed Consent

IEC: Institutional Ethical Committee

WHO: World Health Organization

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