

Knowledge of health care workers on corticosteroid adverse drug events in rheumatologic, respiratory and dermatologic clinics in a teaching hospital in Nairobi, Kenya

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Abstract

Background: Corticosteroids form the cornerstone of management for a myriad of rheumatological, dermatological and chronic respiratory tract diseases. Whereas these drugs are crucial in reducing morbidity and mortality, they are not without inherent grave risks. Health Care Workers (HCWs) providing care to patients on long term corticosteroids are required to be well versed with these Adverse Drug Events (ADEs). Kenyatta National Hospital, the teaching hospital of the University of Nairobi, has established rheumatology, respiratory and dermatology clinics. Corticosteroid prescribing and dispensing is provided by the doctors and pharmacy staff respectively with ADEs surveillance and patient education provided by these two cadres as well as the nurses as per standards of practice. As biologic agents are not yet available in these clinics, corticosteroids, as well as other immunosuppressant drugs remain vital in control of immunological diseases.

Materials and Methods: HCWs in these clinics were requested to complete a self-administered questionnaire assessing their knowledge of corticosteroid ADEs. The questions were open ended and the answers given were first analysed into total number of correct answers. Further analysis was done by grouping the correct answers into categories as per the systems affected by corticosteroids. A cut-off point of 6 correct answers was deemed adequate knowledge of ADRs. Correct answers given were calculated as a proportion of all the answers provided by the respondent. Median (interquartile range- IQR) was used to provide the midpoint of correct responses and the spread of the second and third quartiles respectively.

Results: Sixty-two HCWs were recruited, comprising of nurses (21%), pharmacy staff (12.9%) and senior house officers (66.1%). Majority (79%) had been stationed for over 1 year in the study

clinics with 45% of them having worked in more than one of the study clinics.

ADRs of corticosteroids: Median (IQR) number of correct responses was 6.0 (3.0-9.5). Only 61% identified >5 ADRs. Proportion of respondents who documented the various ADRs; Metabolic disorders 89%, cutaneous 61%, mineral bone disease 37%, GIT 36%, neuropsychiatric 32%, adrenal suppression 24%, ophthalmic 21%, myopathy 18%.

Drugs that potentiate the ADRs of corticosteroids: Median (IQR) number of correct responses was 1.0 (1.0-2.0). Proportion of respondents who identified the drugs; Cytotoxics 34%, NSAIDs 35%, anticoagulants 15%, others 10%.

Advice that should be given to patients on corticosteroids: Median (IQR) number of correct responses was 2.0 (2.0-3.0). Surveillance for ADRs- 53% , adherence to duration and dosage 48%, tapering of corticosteroids 32%, drug interactions 16%, drugs to counter corticosteroid ADRs 13%, steroid cards 7%.

Conclusion: Although HCWs routinely administer corticosteroids, the awareness of ADRs and potential drug interactions is low. This needs to be addressed in order to ensure adequate surveillance of ADRs.

Introduction

Immunological and inflammatory diseases, the bulk of which fall under the realm of rheumatology, pulmonology and dermatology, cause a great deal of morbidity and mortality. For decades, corticosteroids have formed the cornerstone in management of these diseases, even in the era of novel immunosuppressants and biological agents. This may be attributed to the fact that corticosteroids are highly effective in addition to being widely available and accessible. This is more so in low to middle income countries where the prohibitive cost of biological immunosuppressant agents limit their adoption.

Corticosteroids have two main effects; mineralocorticoid and glucocorticoid effects. Mineralocorticoid effects, via aldosterone production, regulate salt and water metabolism. Glucocorticoid effects are exerted through glucocorticoid receptor which is widely expressed in the human body, particularly on immune cells. They modulate the immune, cardiovascular, endocrine and metabolic systems^{1,2}.

Synthetic corticosteroids are analogues of endogenous steroids produced by the adrenal gland. Synthetic corticosteroids can be administered in near physiological doses to treat adrenal insufficiency, or in higher (pharmacologic) doses to treat underlying immune disorders. Different synthetic steroids have varying effects; with prednisone, dexamethasone and methylprednisolone having predominantly GC effects while fludrocortisone has mostly mineralocorticoid effects. Cortisone and hydrocortisone have been found to have both GC and MC effects and are therefore preferred in cases of adrenal insufficiency whereas those with GC effects are mostly used for their anti-inflammatory effects¹.

Common conditions treated with pharmacologic synthetic corticosteroids in our setup include Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE), vasculitis; moderate to severe asthma, chronic obstructive pulmonary disease, interstitial lung disease; and dermatitis. Although each route of administration has fewer possibility of ADEs (intravenous, oral, topical and inhalation administration respectively), they can all potentially cause Adverse Drug Events (ADEs). Other routes of administration of corticosteroids are intra-ocular and nasal administration; these will be outside the realm of this study.

Due to their widespread mode of action, corticosteroids exert their effects on a wide array of tissues such as kidneys, cardiovascular system, endocrine organs, immune system and central nervous system as well as regulation of lipids, carbohydrates and proteins. In most instances, the ADEs are an extension of their pharmacologic properties and affect the same organs and tissues¹⁻⁶. The adverse effects of steroids are thought to be related to the dosage and duration of administration, although a dosing threshold is yet to be established for the development of ADEs.

ADEs may also be associated with the fact that release of endogenous steroids has been found to follow a circadian as well as ultradian (highly pulsatile) rhythm. This rhythm cannot be achieved by the continuous release following administration of synthetic steroids. In addition, synthetic steroids have a higher affinity for the GC receptor and a greater bioavailability than endogenous steroids. They are also poorly metabolised in comparison, and therefore tend to persist much longer in plasma.

Well recognized ADEs in adults include hypothalamic-pituitary-adrenal axis suppression; immune suppression and increased infections; impaired glucose tolerance and diabetes mellitus, Cushing's syndrome,

psychiatric disturbances; cardiovascular diseases and dyslipidaemias, osteoporosis; cataracts and glaucoma, dermatological and gastrointestinal disturbances⁶⁻⁸.

At Kenyatta National Hospital, many of these newer and less toxic compounds such as biologic agents are far out of reach for the majority of patients, which translates to an even greater reliance on steroids. This means that corticosteroids are used at higher doses and for longer than in centres where steroid-sparing agents are available. In a retrospective audit carried out in 2011 at the KNH Rheumatology clinic on 394 patients, 54% of them were on corticosteroids. The commonest rheumatologic condition was Rheumatoid Arthritis (RA) which was present in 37% of the patients. Patients with Systemic Lupus Erythematosus (SLE) were only 9% and undifferentiated arthritis comprised 10%⁹. Similar data from the other two clinics was not available.

In most instances, disease activity is high despite immunosuppressive therapy. Studies carried out in RA patients in the rheumatology clinic have shown high disease activity. In 2007, Owino *et al*¹⁰ found that only 12% of the patients were in disease remission using DAS-28 (18% mild, 38% moderate and 32% high disease activity). In 2012, Mbuthia *et al*¹¹ found 11.5% of RA patients were in remission using DAS-28 (9.6% mild, 49% moderate and 29.6% high disease activity). Ganda *et al*¹² in 2012, using RAPID 3 tool found that 62% of the RA patients had moderate to high disease activity.

Data from the Kenya Association for the Prevention of Tuberculosis and Lung Diseases¹³ and WHO¹⁴ estimates that 4 million Kenyans (10-20% of the population) are living with bronchial asthma, majority of whom require inhaled and oral corticosteroids for control of the disease.

Common dermatological conditions encountered in our set-up include atopic dermatitis, contact dermatitis, seborrhoeic dermatitis, psoriasis and vitiligo. In majority of these conditions, topical and systemic steroids are instrumental in management of the conditions. Topical steroid exposure is measured in terms of percentage Body Surface Area (BSA) contact. In an adult patient, 100% BSA application of a topical steroid is approximated as an equivalent on 20mg of oral prednisolone.

Various guidelines exist internationally for evidence based management of corticosteroids ADEs. The European League Against Rheumatism (EULAR)¹⁵, the American College of Rheumatology (ACR)¹⁶, Canadian¹⁷ and South Africa¹⁸ have existing recommendations on glucocorticoid ADEs. Similarly, pharmacovigilance is a well-established tool for the surveillance of ADEs both locally¹⁹ and internationally^{20,21}.

However, these guidelines have not been tailored specifically to address corticosteroid administration in our setting. This makes it imperative that this unique population of patients be assessed for Adverse Drug Events (ADE) and a surveillance protocol be put in place to recognize these complications earlier. Currently, there are no specific guidelines or job aids available in our clinics.

Studies evaluating the Knowledge, Attitudes and Practices (KAP) are useful in evaluating efficacy of a particular intervention. KAP studies in patients have shown less than optimum understanding of medications²² as well as their diseases²³. As self-care is the cornerstone in the management of chronic illnesses, it is imperative; therefore that continued education is carried out for optimization of care. Similarly, the KAP of health care workers has a direct correlation with good clinical outcome of patients^{24,25}. This study set out to establish the adequacy of knowledge among health care providers who were providing care to patients on chronic corticosteroid therapy.

Materials and Methods

This was a cross-sectional study carried out in June 2015 after approval from the University of Nairobi/Kenyatta National Hospital Ethics and Research Committee. Kenyatta National Hospital is the largest hospital in East and Central Africa and is located in Nairobi, Kenya. It serves as the largest teaching, tertiary and referral hospital in Kenya with a bed capacity of 1800 patients with over 6000 workers. Healthcare workers working in the ambulatory rheumatology, respiratory and dermatology clinics were recruited after giving written informed consent.

Study instrument: The questionnaire consisted of four sections and was open ended; the first section compiled demographic information, the second segment looked into knowledge of adverse drug events of steroids. The third section asked about other medications that may interact with corticosteroids to worsen the adverse drug events. The fourth section inquired about the advice patients receive about use of steroids. The questionnaire was distributed in paper formats to the HCWs for self-completion on the spot or to be filled and returned within one week of receiving the questionnaire.

Data analysis: Data collected was cleaned and entered into access data base and exported to SPSS 17.0 (Statistical Package for Social Sciences) for analysis. The answers provided were analysed by the investigators into total number of correct answers. Further analysis was done by grouping the correct answers into categories as per the systems affected by corticosteroids. A cut-off point of 5 correct answers was deemed adequate knowledge of ADRs. Correct answers given were calculated as a proportion of all the answers provided by the respondent. Median (interquartile range- IQR) was used to provide the midpoint of correct responses and the spread of the second and third quartiles respectively.

Results

Sixty two healthcare workers were recruited into the study with 28 (45%) of them having worked in more than one of the target clinics. Pharmacy personnel serving these

three clinics were also recruited. Senior House Officers/ Residents in Internal Medicine comprised of 66.1% of the respondents, with nurses making up 21% and pharmacy staff 12.9%. Majority (79%) had been stationed in the work-station of interest for more than one year.

Table 1: Demographics

Variable	Frequency (%)
Work station	
Dermatology	36 (58.1)
Pharmacy	8 (12.9)
Respiratory	30 (48.4)
Rheumatology	39 (62.9)
Cadre	
Nursing officer	13 (21.0)
Pharmacists	1 (1.6)
Pharmaceutical technologist	7 (11.3)
Senior house officer	41 (66.1)
Years of practice in station	
<1	12 (19.4)
>10	3 (4.8)
>5-10	7 (11.3)
1-5	36 (58.1)
Missing	4 (6.5)

Knowledge on adverse drug events of steroids known: The responses provided were grouped as shown in Table 2. Only 61% of HCWs were able to list 6 or more anticipated ADRs of corticosteroids. The median (IQR) of correct responses was 6.0 (3.0-9.5). Six correct answers were arbitrary used as the cut-off of adequate knowledge.

Table 2: Adverse drug events of steroids known

ADRs	Frequency (%)
Metabolic	55 (88.7)
Skin	38 (61.3)
Other	36 (58.1)
Bone	23 (37.1)
Gastro-intestinal system	22 (35.5)
Central Nervous System	20 (32.3)
Adrenal suppression	15 (24.2)
Myopathy	11 (17.7)
Eye	13 (21.0)

Knowledge on other medications that may interact with corticosteroids to worsen the ADRs: The knowledge of other medications that may interact with corticosteroids to worsen the ADRs was surprisingly low as shown in Table 3 as most answered less than 50%. The commonest drugs identified were NSAIDs (35%), Cytotoxics (34%) and anticoagulants (15%).

Table 3: Other medications that may interact with corticosteroids to worsen the ADRs

Variable	Frequency (%)
NSAIDs	22 (35.5)
Cytotoxic drugs	21 (33.9)
Warfarin	9 (14.5)
Other	6 (9.7)

The median (IQR) for correct responses was 1.0 (1.0-2.0).

Knowledge on advice that should be given to the patients about use of steroids: When asked on instructions given to patients about the use of corticosteroids, 53% of the respondents said they advised on surveillance of ADRs with 48% counselling the patient on adhering to the dosage and duration of the drugs. Only 8% recommended that the patient should inform healthcare workers that they are on corticosteroids when they present to a health facility with only 1 respondent noting the importance on patients carrying a steroid card.

Table 4: What advice should be given to the patients about use of steroids?

Advice	Frequency (%)
Surveillance of ADR	33 (53.2)
Adhere to prescribed dosage & duration	30 (48.4)
Tapering of steroids	20 (32.3)
Avoid over the counter corticosteroids	13 (21.0)
Advice on potential drug interaction with steroids	10 (16.1)
Drugs to prevent ADRs	8 (12.9)
Inform Health Care Worker (HCW) of concurrent steroid use	5 (8.1)
Should have a steroid card/tag	4 (6.5)
Rinse mouth after use of inhalational steroid	1 (1.6)
Others	3 (4.8)

The median (IQR) for correct responses was 2.0 (2.0-3.0)

Discussion

Knowledge and attitude of HCWs on corticosteroids utility, safety and ADRs could greatly influence their behavior and thereby contribute to patient safety. It is important to assess these parameters so as to identify aspects that require actions or interventions from the various regulatory bodies. The present study is the first study of its kind in Kenya that has tried to assess the knowledge of health care workers on corticosteroid adverse drug events. Although the adverse drug events of corticosteroids are well known and should be anticipated and looked for in these patients, the knowledge amongst the healthcare providers working in these clinics and the dispensing pharmacy was low. This is discouraging to note as corticosteroids are commonly used in the departments

surveyed for various conditions. These ADRs have a serious impact on both morbidity and mortality of those affected by them. An example of this is seen in a study by Oyoo *et al*²⁶ where they reported that one in four of the patients with osteoporosis had been on a steroid.

It was discouraging to note that the knowledge on other drugs that could potentiate the ADRs of corticosteroids was low where about one third could identify NSAIDs or cytotoxic medicines. Majority of the patients served in these departments have comorbidities and are on polypharmacy so it is expected that the HCWs would know more about the drug interactions as this would influence their choice of medicines. We however did not inquire as to why the knowledge was low and what steps would the respondents suggest so as to improve their knowledge. This is a potential area for intervention.

More effort needs to be done on communication to the patient on corticosteroids from its usage, tapering, surveillance on potential ADRs etc as the number of positive responses was low. When asked on instructions given to patients about the use of corticosteroids, 53% of the respondents said they advised on surveillance of ADRs with 48% counselling the patient on adhering to the dosage and duration of the drugs. Only 8% recommended that the patient should inform healthcare workers that they are on corticosteroids when they present to a health facility with only one respondent noting the importance on patients carrying a steroid card. This is crucial as the usage of corticosteroids carries with it potential ADRs that can be prevented. Therefore, HCWs need to be actively involved in the surveillance of drug safety issues within the context of their practices. The role of the HCWs in pharmacovigilance may vary from country to country, but the professional responsibility is the same.

Limitations of the study

The results of this study should be considered within the context of its limitations. The sample size was small thus may lack true generalization.

Conclusion

The results of the present study showed that the majority of the HCWs working in the Dermatology, Respiratory and Rheumatology Departments at Kenyatta National Hospital have insufficient knowledge about corticosteroid ADRs. There is a need of pharmacovigilance in the Kenyatta National Hospital Pharmacy, under and postgraduate educational programs about corticosteroids ADR reporting and pharmacovigilance practice need to be included in the curriculum to improve ADR reporting.

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