

# Study on Corticosteroids use Pattern in Dermatological Practice and Investigating Adverse Effect of Corticosteroids Including its Associated Factors

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## ABSTRACT

### Background

Corticosteroids are highly effective drugs with anti-inflammatory and immunosuppressive properties. Due to this, they have become a mainstay of pharmacotherapy in dermatology. However, improper and long term uses are associated with a number of serious adverse effects.

### Objective

To investigate the corticosteroids use pattern, adverse effects and various factors associated with adverse effects in dermatological practice.

### Method

A cross-sectional study was conducted in a dermatology department of tertiary care hospital. All patients using at least one corticosteroids, either topically or systemically or the combination were included in this study. Informed consent was taken from the patients and interviewed using structured questionnaire. Statistical analysis was performed by using SPSS 20. p-value < 0.05 was considered as statistically significant.

### Result

Among the 60 participants under this study, 81.67% of them were females. The mean ( $\pm$ SD) age of the patients was 31.03 years ( $\pm$ 15.0). A majority (58.30%) of the patients was prescribed with topical corticosteroids with low potency (25%). Most of them had used corticosteroids for urticaria. Adverse effects were reported by 33.30% of the patients. The most common adverse effect reported was the shedding of skin. Adverse effects was significantly associated with gender; use of systemic corticosteroids; regular use of corticosteroids; discontinuation of dose abruptly; and missed dose. However, there was no significant association between adverse effects and the duration of use of corticosteroids.

### Conclusion

In conclusion, the present study suggested that the proper counselling and clear instruction regarding the use of corticosteroid should be provided to the patients for avoiding the abrupt discontinuation of the prescribed medication leading to treatment failure.

## KEY WORDS

*Adverse effect, corticosteroid, dermatology, treatment failure.*

## INTRODUCTION

Corticosteroids have been a mainstay of pharmacotherapy because of their anti-inflammatory and immunosuppressive properties in dermatological practice.<sup>1</sup> According to the severity of the underlying condition, anatomic location of application and patient age, corticosteroids of different potencies are prescribed either in topical or systemic routes.<sup>2</sup> They are highly effective, however, their improper and long-term use are associated with a number of serious adverse effects.<sup>3</sup> The amount and potency of corticosteroid which is prescribed, dispensed and applied should be considered carefully because too little steroid can lead to a poor response, and too much can increase the risk of adverse effects.<sup>4</sup> It has now been well established that rational use of these drugs can minimize the adverse effects associated with them.<sup>5</sup> Therefore, in order to achieve the optimum benefit with least adverse effects, safe and effective use of these agents is very crucial.<sup>6</sup> This requires various factors to be considered while prescribing, including the nature of the disease, knowledge of their mechanism of action, age of the patient, site affected, their pharmacology like potency, frequency of use and duration and other potential complicating factors.<sup>6</sup> So, the role of intermittent monitoring of drug use pattern has been emphasized in today's clinical practice.<sup>7</sup> Without a precise knowledge of how drugs are being prescribed and used and different factors associated with them, it is difficult to suggest measures to improve the prescribing as well as drug use habits.<sup>8</sup>

To date, data on corticosteroids use pattern, adverse effects and various factors associated with adverse effects in dermatological practice in Nepal is not reported. Hence by undertaking the present study we sought to study the various parameters related to the use and adverse effects of corticosteroids in the patients. This will help to identify the possible adverse effects associated with their use and the related factors precipitating adverse effects.

## METHODS

A cross sectional study was conducted in Dhulikhel Hospital, Kathmandu University Hospital, Dhulikhel. An ethical approval was taken from Institutional Review Committee, Kathmandu University School of Medical Sciences (IRC/KUSMS). All patients using at least one corticosteroids, either topically or systemically or their combination, who came to dermatology department satisfying inclusion criteria were included in the study. The inclusion criteria were; a) all the patients who were willing to give informed consent, attending dermatology department, b) patients using at least one corticosteroids at the time of data collection and c) patients who, at some point of time had started using corticosteroids but discontinued the medicines on their

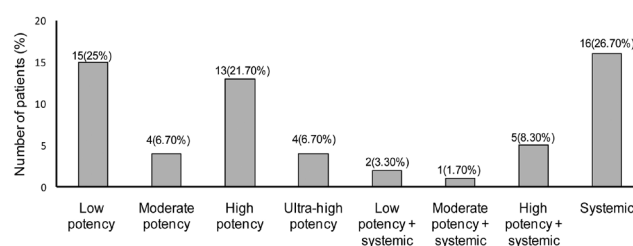
own in spite of the medical recommendations to continue the drugs.

Patients who met the inclusion criteria were informed about the study being done and about their contribution in this study. After taking informed consent from the patients, they were directly interviewed using structured questionnaire. The information regarding age, gender, education, occupation etc were recorded. Further information related to the pattern of use of corticosteroids like name of the drugs, duration of use, routes of administration, purpose of use, frequency of use, missing drug and its frequency, reasons for missing dose, adverse effects, discontinuation and its procedure etc were recorded and filled in the structured questionnaire.

The obtained information was entered into Statistical Package for Social Sciences (spss) Version 20. Statistical analysis was performed by applying Chi-square test using spss 20. p-value < 0.05 was considered as statistically significant.

## RESULTS

A total of 60 patients got enrolled in this study, out of which 49 were female and 11 were male. Mean ( $\pm$ SD) age of the patients was 31.03 years ( $\pm$ 15.0). Majority of the patients (n=35(58.30%)) have used topical corticosteroids, 16 (26.70%) have used corticosteroids by systemic route and 9 (15%) have used corticosteroids by both systemic and topical routes. Among topical corticosteroids users, majority of patients (n=15) have used low potency corticosteroids followed by high potency corticosteroids (n=13). The details of the pattern of use of different corticosteroids are shown in Figure 1.



**Figure 1.** Bar diagram showing different corticosteroids used by 60 patients.

Majority of the patients 35 (58.30%) have used corticosteroids for the first time followed by 15 (25%) patients who were using them regularly and 10 (16.70%) patients used often. Regarding duration of use, 28 (46.70%) patients have used corticosteroids for  $\leq$  2 weeks and 32 (53.30%) patients have used for  $>$  2 weeks. Most of the patients (n=10 (16.70%)) were prescribed with corticosteroids for urticaria. The details are shown in Table 1.

**Table 1. Corticosteroid use pattern among 60 patients.**

Characteristics	No. of Patient (%)
<b>Frequency of use of corticosteroids</b>	
First time	35 (58.30)
Often	10 (16.70)
Regularly	15 (25.00)
<b>Duration of use corticosteroids</b>	
≤	28 (46.70)
>	32 (53.30)
<b>Conditions in which corticosteroids were prescribed</b>	
Urticaria	10 (16.70)
Dermatitis	9 (15.00)
Seborrheic dermatitis	3 (5.00)
Hyperpigmented macules	2 (3.30)
Photosensitivity	8 (13.30)
Psoriasis	2 (3.30)
Lichen Planus	3 (5.00)
Acne	8 (13.30)
Vitiligo	2 (3.30)
Systemic lupus erythematosus	4 (6.70)
Plaque	2 (3.30)
Miscellaneous*	7 (11.70)
<b>Patients who have ever missed corticosteroids</b>	17 (28.34)
<b>Missing Frequency (n=17)</b>	
Rare	15 (88.24)
Often	2 (11.76)
<b>Reasons for missing corticosteroids</b>	
Forgetfulness	15 (88.24)
Carelessness	2 (11.76)
<b>Patients who have ever discontinued corticosteroids</b>	34 (56.67)
<b>Discontinued method (n=34)</b>	
Dose tapering	7 (20.59)
Abruptly	27 (79.41)
<b>Reason of discontinuation of corticosteroids (n=434)</b>	
Relief of symptoms	25 (73.54)
More deterioration of symptoms	2 (5.88)
No benefit	5 (14.70)
Others**	2 (5.88)

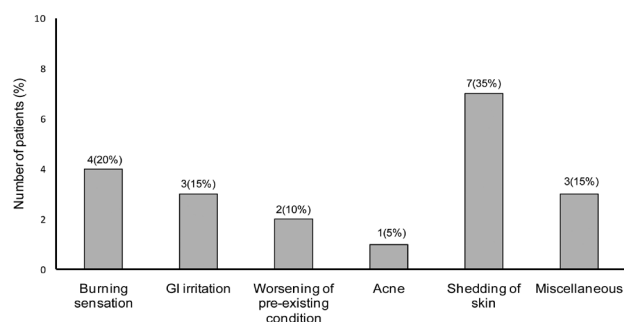
\* Insect bite, Tinea incognito, Alopecia, Hormonal disturbances, Localized scleroderma, keloid and Prurigo Simplex

\*\* Lack of knowledge, unavailability of drugs

Among corticosteroids users in this study, 17 (28.30%) of them have missed the drug, out of which 15 (88.24%) have missed the dose rarely and 2 (11.76%) have missed often. Forgetfulness 15 (88.24%) was the major reason for missing the dose followed by carelessness 2 (11.76%). Out of 34 patients who have discontinued the drug, 7 (20.59%) have followed dose tapering method whereas 27 (79.41%) of patients have discontinued the drug abruptly.

The most common reason 25 (73.54%) for discontinuation of corticosteroids was mentioned as relief of symptoms. The details of the corticosteroids use pattern are shown in Table 1.

Regarding adverse effects of corticosteroids, 20 (33.30%) of patients have reported adverse effects. The most common adverse effect reported by patients was shedding of skin 7 (35%). The details of adverse effects reported are shown in Figure 2.



**Figure 1. Bar diagram showing adverse effects shown by use of corticosteroids. Miscellaneous includes various conditions like Menstruation irregularities, hyperglycemia, swelling of face.**

In the present study, adverse effects were seen in significantly higher number of female patients ( $p < 0.039$ ). Significant association was found between the adverse effects seen in patients with use of systemic corticosteroids ( $p < 0.05$ ). Similarly, adverse effects were reported by significantly higher number of patients who were using corticosteroids on the regular basis ( $p < 0.05$ ) and was less common in those patients who never used to miss dose ( $p < 0.058$ ). Furthermore, our study revealed that significantly higher number of patients who had adverse effects discontinued corticosteroids abruptly ( $p < 0.05$ ). However, no statistical association was found between adverse effects seen in patients with duration of use of corticosteroids (Table 2).

## DISCUSSION

Corticosteroids constitute one of the largest groups of drugs which are being used in dermatological practice as a short term as well as long term therapy that are associated with a number of adverse effects.<sup>7</sup> Their rational use can however, minimize the systemic and cutaneous side effects that occur with corticosteroids.<sup>7</sup> Physicians ought to prescribe the corticosteroid that will treat the dermatological condition with maximum therapeutic benefits and least possible adverse effects.<sup>7</sup>

In the present study, higher number of corticosteroids users was female. In consistence with the findings of our study, previous study has also reported that higher numbers of females were prescribed with corticosteroids along with antimicrobials for different dermatological conditions.<sup>9</sup>

**Table 2. Demographic and other characteristics of 60 patients with reference to adverse effects.**

Variables	Total (n)	Adverse effects (n=20) No. (%)	No adverse effects (n=40) No. (%)	p-value
<b>Gender</b>				
Male	11	1 (9.10)	10 (90.90)	0.039
Female	49	19 (38.77)	30 (61.23)	
<b>Different potences of corticosteroids and combinations used</b>				
Low potency	15	6 (40.00)	9 (60.00)	0.002
Moderate potency	4	0 (0.00)	4 (100.00)	
High potency	13	1 (7.69)	12 (92.31)	
Ultra high potency	4	0 (0.00)	4 (100.00)	
Low potency + systemic	2	2 (100.00)	0 (0.00)	
Moderate potency + systemic	1	0 (0.00)	1 (100.00)	
High potency + systemic	5	1 (20.00)	4 (80.00)	
Systemic	16	10 (62.50)	6 (37.50)	
<b>Frequency of use of corticosteroids</b>				
First time	35	6 (17.14)	29 (82.86)	0.006
Often	10	5 (50.00)	5 (50.00)	
Regularly	15	9 (60.00)	6 (40.00)	
<b>Duration of use of corticosteroids</b>				
≤ 2 weeks	28	6 (21.43)	22 (78.57)	0.067
> 2 weeks	32	14 (33.35)	18 (56.25)	
<b>Missed Dose</b>				
Yes	17	9 (52.94)	8 (47.06)	0.043
No	43	11 (25.58)	32 (74.42)	
<b>Discontinuation procedure</b>				
Not Discontinued	26	4 (15.38)	22 (84.62)	0.016
Dose tapering	7	2 (28.57)	5 (71.43)	
Abruptly	27	14 (51.85)	13 (18.15)	

The high number of females using corticosteroids for dermatological purposes might be due to women being more conscious about the health of their skin. Additionally, women outnumber men in using cosmetics, which might have especially, predisposed them to a number of skin disorders. The present study has revealed that patients in age above 30 years were using corticosteroid which is similar to the previous study showing patients belonging to age below 40 years.<sup>9</sup> This finding strongly supports the fact that people at this age become more conscious about their physical appearance from cosmetic point of view.

A majority of the patients in this study used topical corticosteroids followed by systemic corticosteroids. A very few number of the patients used corticosteroids by both the topical and systemic routes. Our finding is in consistence with several other studies where topical corticosteroids were preferred over systemic corticosteroids for dermatologic disorders.<sup>7,10-12</sup> This might

be due to the effectiveness of topical corticosteroids in many non-infective skin disorders and the fact that they are safer to use for acute skin diseases.<sup>7,13</sup> Although topical corticosteroids are relatively safe, they can more frequently produce local adverse effects and rarely systemic effects when used inappropriately.<sup>13,14</sup> Systemic corticosteroids, however, are required for prolonged periods, as in atopic dermatitis so they have to be tapered or reduced to minimal doses for the long term therapy which makes them less preferred in many other dermatologic disorders.<sup>9</sup>

On the other hand, among the topical corticosteroid users, higher number of patients was prescribed with low potency corticosteroids. It might be because of minimal risk of adverse effects associated with low potency corticosteroids. Furthermore, it has been suggested that low potency corticosteroids are the safest for long term use and can be applied over large surface of the body and on children and elderly as well.<sup>15,16</sup> However, in certain conditions like atopic dermatitis, high potency corticosteroids have been preferred over low and moderately potent corticosteroids as they have shown to reduce the density of *S. aureus* in such condition.<sup>17</sup>

A majority of the patients under this study used corticosteroids for the first time followed by those using it regularly. A study suggests that the optimum dosing schedule of the steroids should have minimum frequency of application and still provide relief.<sup>4</sup> Further, the study suggests that the application of the steroids should be monitored carefully as too little application can lead to a poor response while too much can increase the occurrence of side effects.<sup>4</sup> Additionally, the shortest possible treatment course is recommended for acute skin diseases.<sup>13</sup> Likewise, the study also suggests that treatment for such skin conditions should not last longer than two weeks on the face and three to four weeks on the rest of the body.<sup>13</sup> In contrast, a majority of the patients under the current study had used corticosteroids for more than two weeks. Another study on patients with actinic keratosis suggests that treatment duration exceeding four weeks significantly influences non-adherence.<sup>18</sup> Therefore, for longer treatment periods, intermittent therapy such as every other day, once a week application or a gap of 1-2 weeks in between the cycles has been suggested that might help to reduce the occurrences of adverse effects.<sup>13</sup>

Most of the patients in this study had used corticosteroids for urticaria followed by other conditions such as dermatitis, photosensitivity, acne, and others. Similarly, another study reported that topical corticosteroids were mainly used for treating non-infective dermatologic disorders associated with inflammation such as psoriasis, atopic dermatitis, contact dermatitis and otitis externa.<sup>7</sup> Corticosteroids have been prescribed, most commonly, in psoriasis and also in adult atopic dermatitis and nummular eczema.<sup>13</sup>

The present study showed that about a quarter of patients have missed the dose and majority had never missed the

dose. Consistent with our findings, another study in patients with actinic keratosis reported higher levels of adherence to a once-a-day topical corticosteroid therapy, although rates of adherence declined over the treatment period.<sup>19</sup> On contrary, adherence to topical therapy regimens was found to be low for a range of skin conditions, especially chronic skin disorders such as psoriasis which require a long-term treatment.<sup>20,21</sup> Similarly, another study reported that approximately 40% of the patients with psoriasis did not use treatments as per the direction of physician.<sup>22</sup>

Our study has revealed that the majority of the patients had missed dose due to forgetfulness. Carelessness was another additional reason for missing the prescribed dose in lesser number of patients. Supporting our findings, a previous study has reported that forgetting to take dose accounts for around 40% of non-adherence.<sup>18</sup> Additionally, younger age of the patient, the cosmetic characteristics of treatment, the complexity of treatment regimen, frequency of use, treatment duration, and fear of, or occurrence of adverse effects also contribute to non-adherence to medication in many skin disorders.<sup>18,20</sup> Moreover, the vehicle used in treating skin disorders such as ointment is greasy and difficult to spread, which makes it cosmetically unappealing, leading to patient's poor adherence to treatment.<sup>13</sup>

Among the patients who had discontinued the drug, a majority of them had discontinued the drug abruptly whereas a few patients followed dose tapering method. Similar finding was reported by Shergill et al. where patients with actinic keratosis either forgot to use their treatment or intentionally chose not to apply treatment as per suggestions, and discontinued the medication abruptly.<sup>18</sup> Corticosteroids tapering is essential to avoid persistent dermatological condition, exacerbating the condition and prevent withdrawal symptoms from occurring.<sup>23</sup>

In the present study, a one third of the patients reported adverse effects. The most common adverse effect reported was the shedding of skin followed by burning sensation, GI irritation, worsening of pre-existing condition, acne, and others such as menstrual irregularities, hyperglycaemia, and swelling of face. In consistent with the findings of our study, several other studies have reported various systemic and cutaneous adverse effects with corticosteroids use.<sup>4,7,9,13</sup> Skin atrophy has been reported as the most common adverse effect of topical corticosteroids along with many other reactions such as hypersensitivity, percutaneous absorption and tachyphylaxis.<sup>4,7,9,13</sup> In contrary to the findings of previous studies, in our study, shedding of skin was the most commonly reported adverse effect which might be the consequence of withdrawal from corticosteroids.<sup>24</sup> Topical corticosteroids are known to decrease skin elasticity and bring alterations in its mechanical properties.<sup>25</sup> Burning sensation was the second commonly reported adverse effect in this study which might be due to contact hypersensitivity to topical corticosteroids upon prolonged exposure.<sup>25</sup> However,

contact hypersensitivity to corticosteroids must be differentiated from hypersensitivity to other constituents/excipients in the formulation e.g. lanolin, parabenes, antibiotics.<sup>25</sup> Another adverse effect reported by patients enrolled in this study was gastrointestinal irritation which might be the systemic effect of corticosteroids as suggested by other studies.<sup>26,27</sup> Corticosteroid therapy can even lead to gastrointestinal bleeding and perforation which is more risky when given with non-steroidal anti-inflammatory drugs as reported by other studies.<sup>28,29</sup> Worsening of pre-existing condition has also been reported in this study as reported by several other studies.<sup>30,31</sup> It has been related with either overuse of corticosteroids or aggravation of cutaneous infection depending on their use in various dermatological conditions.<sup>30,31</sup> However, this could not be analysed from the current study as it was a mono-centred study with a limited sample size. Acne is another adverse effect reported by the patients in our study which is consistent to the findings of previous studies in which topical corticosteroids rapidly induced an acneiform eruption.<sup>25,30,31</sup> It has been suggested that the acneogenic effect of topical corticosteroids might be due to the degradation of the follicular epithelium which results in extrusion of the follicular content.<sup>25,30,31</sup> Corticosteroid-induced acne might be due to application of high concentration of drugs, application under occlusion, application to acne-prone areas of face and upper back etc., as proposed by another study.<sup>25</sup> However, these predisposing factors were not assessed by our study as to assess such factors is beyond the scope of the present study and this warrants for further multi-centred study with a large sample size. In the present study, adverse effects were significantly high in females. This might be due to the higher number of females being prescribed with corticosteroids for skin disorders which was consistent to the findings of previous study.<sup>9</sup> Additionally, adverse effects were significantly associated with the use of systemic corticosteroids than topical corticosteroids. In agreement to the finding of our study, even low doses of systemic corticosteroids used for prolonged periods, was associated with significant morbidity and mortality.<sup>23</sup>

Multiple complications such as osteoporosis, delayed wound healing, cutaneous effects including purpura, atrophy, striae, hirsutism, alopecia, hyper/hypopigmentation, facial plethora, and fat redistribution causing the classic "buffalo hump" on the upper back were reported with long-term use of systemic corticosteroids.<sup>23,32</sup> Topical corticosteroids, which are considered relatively safe, are also associated with various adverse effects as discussed above though they are preferred over systemic corticosteroids for dermatologic disorders.<sup>7,10-12</sup> Our study revealed that adverse effects were significantly associated with the regular use of corticosteroids. This finding is in strong agreement with several other studies in which incidence of adverse effects were high with daily and long-term use of corticosteroids like increase in risk of bone fractures, restlessness, insomnia, mania, depression, cognitive defects, weight

gain, thinning of skin etc.<sup>23,32-36</sup> It has been suggested that more frequent administration of steroids does not help improve the condition rather its chronic application can induce tolerance and tachyphylaxis.<sup>4</sup> Additionally, our study found that adverse effects were significantly less common in patients who never missed the prescribed dose. Likewise, another study has suggested that topical corticosteroids when used incorrectly, either missing the prescribed dose or withdrawing abruptly can produce more frequent local adverse effects and an occasional systemic effects.<sup>13</sup> Consistent to our findings, another study has also reported that the risk of osteoporosis, one of the most serious complications in patients receiving long-term corticosteroid therapy, was highly related to the daily corticosteroid dose which worsened upon incomplete medication.<sup>37</sup> Although, the adverse effects encountered with corticosteroids use is bothersome, it is more likely that the patients following the appropriate and prescribed dosage regimen will have less adverse effects as suggested by previous studies.<sup>13,37</sup> Furthermore, our study found that a significantly higher number of patients in whom adverse effects were seen had discontinued corticosteroids abruptly. It might be because of the occurrence of withdrawal symptoms or relapse of underlying disease or aggravation of corticosteroids

induced adverse effects on stopping the drug abruptly as suggested by other studies.<sup>38-40</sup> Such symptoms are seen when topical corticosteroids are used for longer duration, generally > 2 weeks and/or given in high doses and stopped abruptly.<sup>38-40</sup> However, in this study, though higher number of patients in whom adverse effects were seen had used corticosteroids for > 2 weeks, there was no significant association between them. This reinforces for further multi-centred prospective study in a large sample size. Nevertheless, rapid reduction or abrupt withdrawal from corticosteroids therapy should be avoided.

## CONCLUSION

Corticosteroid therapy is of fundamental importance in clinical, especially in dermatological practice. Despite their effectiveness, their inappropriate and prolonged use in various dermatological conditions predisposes a patient to a number of adverse effects, ranging from mild to severe. It is extremely important that patients are correctly educated and instructed for corticosteroid use and properly counselled for the possible adverse effects with their improper use.

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