Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Physiology

Use and Abuse of Glucocorticosteroid: A Study on Hospital Admitting Patients

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DOI: https://doi.org/10.36347/sjams.2025.v13i12.005 | **Received:** 21.10.2025 | **Accepted:** 10.12.2025 | **Published:** 13.12.2025

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Abstract **Original Research Article**

Background: Long-term glucocorticoid abuse is widespread and a substantial public health issue in Third-World countries such as Bangladesh. Unfortunately, there are no substantial research in this field in Bangladesh. ***Aim of the study:*** The purpose of this study was to identify the prevalence of long-term glucocorticosteroid misuse. ***Methods:*** From 1st April 2010 to 30th September 2011, this descriptive cross-sectional study was conducted at Department of Medicine, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh. According to the inclusion and exclusion criteria, 50 instances of long-term glucocorticoid users admitted to the department of medicine at Shaheed Ziaur Rahman Medical College Hospital in Bogra were included. After obtaining informed written consent, data was obtained using a questionnaire, and relevant investigations were conducted. Following that, the acquired data was examined. ***Results:*** Patients with respiratory diseases and arthropathies were the most frequently indication for long-term corticosteroid therapy. Of 50 patients, 12 (24%) were Bronchial asthma, 8 (16%) were Rheumatoid arthritis, osteoarthritis was in 6 (12%). Additionally, 92% (46/50) of patients did not get counseling regarding possible steroid adverse effects. The fact that 34.78% (16/46) of the service providers were qualified is concerning. Almost every patient experienced one or more of the treatment's negative effects. These included osteoporosis (52%), abnormal blood glucose levels (60%), thin skin (96%), weight increase (86%), moon face (92%), and iatrogenic Cushing's disorders (64%). These comprised 20/20 of the group receiving continuous medication (10–20 mg), 25/27 of those receiving intermittent therapy, and 2/3 of those for whom we were unable to determine the dosage and pattern. ***Conclusion:*** The condition of chronic corticosteroid therapy in our country is not adequately represented by the data presented in this study. Therefore, more thorough study is needed to ascertain the entire spectrum of chronic corticosteroid therapy, the true burden of public health problems brought on by these unnecessary chronic corticosteroid prescriptions, and to create management and preventative initiatives.

Keywords: Glucocorticosteroid, therapy, respiratory diseases, arthropathies.

INTRODUCTION

Philip Hench developed glucocorticosteroids in the late 1940s to treat rheumatoid arthritis [1, 2]. The early excitement about their seeming success was quickly subdued as it became clear that their sustained usage came at a high cost in terms of adverse effects [3, 4]. Many disorders are treated with glucocorticoids, frequently at high doses that might cause severe hypercortisolism. The most common type of hypercortisolism seen in clinical practice is iatrogenic hypercortisolism, often known as iatrogenic (exogenous) Cushing's syndrome [5, 6]. Its treatment is still debatable, despite the fact that it frequently produces a severe clinical picture and may manifest after the treatment of many diseases where the anti-inflammatory, immunosuppressive, and apoptosis-inducing effects of glucocorticoids are exploited (such as autoimmune, hematologic, and inflammatory diseases). While many studies on the therapy of other forms of hypercortisolism (spontaneous, endogenous type) have been published in recent years, only a small number of studies address the treatment of the iatrogenic version [7]. Iatrogenic hypercortisolism's clinical presentation is identical to

that of the other types. Weight gain, moon face, plethora, truncal obesity, buffalo hump, myopathy, striae, recurrent easy bruising, unexplained osteoporosis, avascular necrosis of long bones, poor wound healing, increased incidence of infection, decreased carbohydrate tolerance, negative nitrogen balance, renal calculi, and numerous life-threatening conditions like hypertension, cataracts, bleeding peptic ulcers, reactivation or MDR tuberculosis, as well as psychological and cognitive changes. The suppression of the endogenous hypothalamic-pituitary-adrenal (HPA) axis in patients with overt hypercortisolism is an unusual aspect of iatrogenic Cushing's syndrome. Thus, it is possible to think of iatrogenic Cushing's syndrome as a combination of endogenous secondary adrenal insufficiency and exogenous Cushing's syndrome [7]. Therefore, the diagnosis is typically clear from a) the clinical presentation, b) the history of steroid therapy, c) suspected and contaminated homeopathy or kobirazi medications, and d) the laboratory results of the HPA axis suppression, such as low cortisol levels in the morning. The kind of steroids used, how they are administered, how much they are taken, how long they are taken, the patient's age, sex, and other factors all affect how quickly and thoroughly these clinical and biochemical characteristics emerge. Therefore, current conventional rheumatology literature recommends using them in less than 5% of rheumatoid arthritis (RA) cases [8]. "In general, prenisolone doses of less than 5 mg per day or therapy lasting three weeks or less will not cause long-term suppression of the normal adrenal axis. Therefore, long-term (months or years) steroid use, including intra-articular, inhalation, and ointment preparations that may enter the systemic circulation, may also disrupt the endogenous HPA axis and cause iatrogenic Cushing's syndrome [5, 9]. Since the endogenous HPA axis is insufficient and the underlying illness necessitates steroid therapy, it makes sense to treat a side effect or sickness caused by an external substance by avoiding the agent. The underlying illness would reactivate and secondary adrenal insufficiency would manifest if glucocorticoid therapy were abruptly stopped [7]. The most concerning finding is that over one-third of individuals with osteoarthritis of the knee were receiving steroid medication. Long-term steroid use and drug-induced Cushing's syndrome are common in third-world countries, including the United States. Farooqi [10] conducted a study in Pakistan and found that 42.5% (110/256) of patients with arthritis or associated conditions were taking corticosteroids. Approximately 29% of these patients acquired drug-induced Cushing's syndrome, 38.2% of steroid users had no specific diagnosis, and another 38.2% lacked even supporting documentation. The exact prevalence of utilizing the full spectrum of long-term glucocorticoids in our population is unknown. Gross clinical observation indicates that the prevalence is fairly high, posing a substantial public health hazard. Unfortunately, there have been no substantial research in this field in Bangladesh. The goal of this study was to determine the prevalence of long-term glucocorticosteroid abuse.

METHODOLOGY

From 1st April 2010 to 30th September 2011, this descriptive cross-sectional study was conducted at Department of Medicine, Shaheed Ziaur Rahman Medical College Hospital, Bogura, Bangladesh. According to the inclusion and exclusion criteria, 50 instances of long-term glucocorticoid users admitted to the department of medicine at Shaheed Ziaur Rahman Medical College Hospital in Bogra were included. After obtaining informed written consent, data was obtained using a questionnaire, and relevant investigations were conducted. Following that, the acquired data was examined.

Inclusion criteria:

- All adult and adolescent patients on chronic glucocorticosteroid therapy.
- All patients of taking glucocorticosteroid more than weeks.
- All suspected patient of iatrogenic Cushing's syndrome.
- All diagnosed case of Iatrogenic Cushing's syndrome.

Exclusion criteria

- Patients who do not agree to participate into this research work.
- Any patients of spontaneous Cushing's syndrome.
- Any patients of severe form of generalized edema without on chronic glucocorticosteroid therapy.
- All pregnant ladies.

RESULT

Table-1 shows that out of 50 cases; bronchial asthma was the commonest cause of chronic corticosteroid therapy and was found in 12 (24%). The next common, rheumatoid arthritis and osteoarthritis, was found in 8 (16%) and 6 (12%) cases respectively. The less common primary diseases were nonspecific back pain (4%), frozen shoulder (4%), corpulmonale(4%), beautification (4%), minimal change glomerulonephritis (4%) and tuberculous pleural effusion (4%). Table-2 displays that among all causes of chronic corticosteroid therapy, the prescription was rational in chronic bronchial asthma step-v (2 cases), minimal change glomerulonephritis (2 cases), tuberculous pleural effusion (2 cases), IgA nephropathy and ITP (one case each). Together they comprise 16% of the study population. In the remaining 84%, the therapy was avoidable. Table-3 displays that It was observed that the corticosteroid was prescribed by the drug seller (12%), traditional healer (38%), physician followed by self (10%), all together was categorized as nonqualified

service provider and by the physician categorized as qualified in (40%) cases. Table-4 reveals that both the male and the female were victimized 85.5% (29/34) and 81.25% (13/16) respectively by avoidable categories of corticosteroid therapy. Table-5 reveals that the highest use of corticosteroid therapy was by the married people 82% (41/50) and the remaining unmarried people was only 18%. The married are affected by avoidable category of corticosteroid therapy in significant cases (95.12%). Table-6 shows that more than 20 mg equivalent of prednisolone were used absolutely (6/6=100%) in unavoidable cases but 5 to 20 mg equivalent of prednisolone were used mainly (90 to 100%) in avoidable cases. Table-7 shows that the minimum duration of the corticosteroid therapy in the study was for one month with a maximum duration for 360 months (30 years). Table-8 reveals that prednisolone was the most frequently prescribed oral corticosteroid (28/50=56% of all prescriptions). Dexamethasone, triamcinolone and betamethasone were given in 22%, 10% and 8% cases, respectively. Table-9 displays that the thin skin was seen in 94% of patients. Weight gain, muscle weakness and back pain were seen in 86%, 48% and 70%, respectively. Moon face, buffalo hump and central obesity were seen in 92%, 44%, and 52%, respectively. Hypertension was seen in 22%, fungal infection was seen in 12%, cataract was seen in 12% and 16% presented with addisonian crisis. Table-10 displays that Laboratory result revealed that there was abnormal glucose tolerance in 60% cases, fasting lipid abnormality in 36% cases, moderate to severe anaemia in 38% cases and finally low morning cortisol level (< 4.458 micro gram/dl) was found in 64% cases that were confirmed as an iatrogenic Cushing's syndrome.

Table-1: Distribution of primary diseases for taking corticosteroid therapy (N=50)

Disease distribution	Steroid used	Percentage of total
Bronchial asthma	12	24
Rheumatoid arthritis	8	16
Osteoarthritis	6	12
COPD (Chronic obstructive pulmonary disease)	4	8
Nonspecific back pain	2	4
Frozen shoulder	2	4
Corpulmonale	2	4
Beautification/Weight gain	2	4
Spondarthritis	1	2
Eczema,urticaria	1	2
Minimal change glomerulonephritis	2	4
Tuberculous pleural effusion	2	4
PLID (prolapsed intervertebral disc)	1	2
Fibromyalgia	1	2
IGA nephropathy	1	2
ITP (idiopathic thrombocytopenic purpura)	1	2
ICSOL (intra cranial space occupying lesion	1	2
JIA (juvenile idiopathic arthritis)	1	2
Total	**50**	**100**

Table-2: Disease categorization and corticosteroid therapy (N=50)

Avoidable	n =42	Percent	Unavoidable	n=8	Percent
Bronchial asthma (Stage i-iv)	10	20	Chronic persistent asthma (Stage v)	2	4
Rheumatoid arthritis	8	16	Minimal change glomerulonephritis	2	4
Osteoarthritis	6	12	TB. pleural effusion	2	4
Chronic obstructive pulmonary disease	4	8	ITP	1	2
Nonspecific low back pain	2	4	IgA nephropathy	1	2
Frozen shoulder	2	4			
Corpulmonale	2	4			
Beautification	1	2			
Weight gain	1	2			
Spondarthritis	1	2			
Eczema, urticaria	1	2			
Prolapsed lumber inter-vertebral disc	1	2			
Fibromyalgia	1	2			
Intracranial space occupying lesion	1	2			
Juvenile idiopathic arthritis	1	2			
Total	**42**	**84**	**8**		**16**

Table-3: Source of steroid prescriptions

steroid provider	No. of patient N=50
Physician	20
Drug seller	6
Traditional healer	19
Physician followed by self	5
Total	**50**

Table-4: Disease categories of corticosteroid therapy and sex of the patient (N=50)

Sex	Disease categories of corticosteroid therapy (% within the sex of the patient)		Total (100%)
	Unavoidable	Avoidable	
Male	5 (14.70%)	29 (85.29%)	34
Female	3 (18.75%)	13 (81.25%)	16
Total	**8 (16%)**	**42 (84%)**	**50**

Table-5: Marital status of the patient and disease categories of corticosteroid therapy (N=50)

Marital status	Disease categories of corticosteroid therapy (% within the group)		Total (100%)
	Unavoidable	Avoidable	
Married	2 (4.88%)	39 (95.12%)	41
Unmarried	6 (66.67%)	3 (33.33%)	9
Total	**8 (16%)**	**42 (84%)**	**50**

Table-6: Dosages of steroid received and disease categories of corticosteroid therapy (N=50)

Dose (in mg equivalent of prednisolone	Disease categories of corticosteroid therapy (% within the group)		Total (100%)
	Unavoidable	Avoidable	
5 mg or less	0 (0%)	14 (100%)	14
5-10 mg	1 (8.33%)	11 (91.67)	12
10-20 mg	1 (6.67%)	14 (93.33%)	15
20 mg or more	6 (100%)	0 (0%)	6
Indeterminate	0 (0%)	3 (100%)	3
Total	**8 (16%)**	**42 (84%)**	**50**

Table-7: Duration corticosteroid therapy

Duration (in month)	No. of patients	Percentage of total)
Up to 6	14	28
6-12	10	20
12-24	9	18
24-36	9	18
36 & above	8	16
Total	**50**	**100**

Table-8: Formulation used in the corticosteroid therapy

Formulation	No of patient	Percentage of total)
Prednisolone	28	56
Dexamethasone	11	22
Betamethasone	4	8
Triamcinolone	5	10
Methyl predsolone	1	2
Clobetasone prop.	1	2
Total	**50**	**100**

Table-9: Symtoms and signs of corticosteroid abuse and complications

Symtoms and signs	No of patient	Percentage of total)
Weight gain	43	86
Muscle weakness/Malaise	24	48
Back pain	35	70
Moon face	46	92

Thin skin/skin changes	47	94
Buffalo hump	22	44
Central obesity	26	52
Hypertension	11	22
Fungal infection	6	12
Cataract	6	12
Addisonian crisis[2]	8	16
Hirsutism/Hyperpigmentation	0	0
Others[3]	5	10

Table-10: Laboratory findings in chronic corticosteroid therapy (N=50)

Lab. findings	No of patient	Percentage of total)
Abnormal glucose tolerance	30	60
Fasting lipid abnormality	18	36
Moderate to severe anaemia	19	38
Low morning cortisol level	32	64

DISCUSSION

The distribution of chronic corticosteroid therapy in Bangladesh is unknown. The relative details of chronic corticosteroid therapy among 50 individuals in the series with various primary illnesses were investigated. From this observation, a valid inference cannot be drawn about the prevalence or incidence of this chronic corticosteroid therapy in the general population because the relatively severe cases are deliberately admitted to the hospital, whereas the mild and asymptomatic cases are detected in the hospital only by chance, when they attended the hospital for other reasons. The main conditions for which corticosteroid medication was indicated were divided into two categories: preventable and unavoidable. Out of 50 instances, respiratory disease was the most commonly reported condition associated with chronic corticosteroid medication; 24% of patients had bronchial asthma and 8% had COPD. Osteoarthritis and rheumatoid arthritis were found in 12% and 16% of cases, respectively. These findings are largely in line with a large cohort study of the general population in England and Wales [11], which found that musculoskeletal disorders accounted for 15.6% of corticosteroid indications and respiratory disorders for 26.0%. In my research, other explanations were comparatively less common. However, 84% of the time, the therapy was preventable. Patients themselves reported using the medication for the first time (20%), followed by 40% who said they did so on the recommendation of their doctors. It appears that later self-medication may have been based on prior prescriptions. The remaining individuals were classified as non-qualified service providers (60%), including drug dealers (12%) and traditional healers (28%). According to a department survey by Dr. Nguyen Van Doan, [12], chief of the Allergy-Immunity Department at Bach Mai Hospital, 70% of corticosteroid users were prescribed by drug dealers or themselves rather than by doctors, which is nearly in line with my research. Adolescent and adult females are hesitant to seek medical counsel because of shyness and religious views. Instead, they would rather quietly obtain over-the-counter medications from the closest unlicensed traditional healer. In line with a cross-sectional hospital-based study [13] in Basra, Iraq, where 69% of the patients were female, 82% of the chronic corticosteroid users in the current study were married, and the majority were female, including widows and divorced patients. Prednisolone dosages between 5 and 20 mg daily accounted for the majority of prescriptions (82%) in the study. Three patients (6%) who had only visited traditional healers and were using contaminated homeopathic and kobirazi medications had no discernible usage patterns at a study carried out at the department of rheumatology and physical medicine in Islamabad, Pakistan, Farooqi [10] discovered very identical findings. Prednisolone equivalent to more than 20 mg was unavoidably administered in patients that were also treated with decreasing doses. The medication was administered in two or three separate doses per day in the majority of preventable instances. Patients occasionally took it as a single dose, usually when their primary illnesses were getting worse. They occasionally consumed the medication erratically and in a completely chaotic manner. The most commonly administered oral corticosteroid was prednisolone. Patients receiving intermittent or irregular therapy showed comparatively less treatment-related adverse effects. In general, adverse effects were observed in every dosage pattern, particularly in cases where the use was ongoing [14]. Weight gain (86%), back discomfort (70%), and muscle weakness or malaise (48%) were the most commonly reported presenting symptoms in the research. Ninety-six percent of the patients had skin alterations. It should be mentioned that skin changes include striae, echymoses, thinning of the skin, and easy bruising. Moon face (92%), buffalo hump (44%), central obesity (52%), hypertension (22%), fungal infections (12%), cataract (12%), and Addisonian's crisis (16%) were other physical manifestations. In a research conducted in Basra, Iraq, 100% of the patients had thin skin. 36% of long-term corticosteroid users had abnormal fasting lipid levels, and 60% had impaired glucose tolerance (DM and IGT). These findings align with the research conducted by Ross

& Linch and Platz *et al.,* [15]. Lastly, in every instance of chronic corticosteroid therapy, the basal cortisol level in the morning (8.00–9.00) was measured. It was always attempted to send the patient to the laboratory in the morning within the first hour of awakening because the basal levels are well synced to the body's biological clock, peaking within one to two hours of awakening and declining at its nadir at or shortly after midnight [16].

Limitation of the study:

Patients who denied using corticosteroids may have been taking these drugs but had not yet shown any physical symptoms, therefore they were excluded from the study.

CONCLUSION & RECOMMENDATION

The information provided by this study does not fully capture the state of chronic corticosteroid therapy in our nation. Therefore, more extensive research is required to determine the full range of chronic corticosteroid therapy, the actual burden of public health issues caused by these unjustified chronic corticosteroid prescriptions, and to develop management and preventative programs. While we wait for such long-term planning to be developed and put into action, we recognize the urgent need for facilities for accurate diagnosis and for the establishment of an appropriate management program, at least in all university institutions.

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