Corticosteroid Induced Cushing’s Syndrome

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ABSTRACT
Corticosteroids are the drugs that are used commonly now a days as pain relievers, but these corticosteroids can affect the own immune system by suppressing. So, corticosteroids are the one of the reason for occurrence of the life threatening infectious diseases. Chronic use of corticosteroids mainly induces Cushing’s syndrome, osteoporosis, diabetes mellitus, tuberculosis, jaundice etc. In this study we discussed on case studies regarding steroid induced Cushing syndrome who are admitted in the general medicine department at Santhiram Medical College and General Hospital in Nandyal Region. In these cases, the patients had followed the treatment of corticosteroids without any doctor prescription. Prescribing of steroids by RMP’s and community pharmacies is increasing day by day, hence as role of clinical pharmacist it is advisable to create awareness on usage of steroids to the local pharmacies and RMP’s by better training on the management of steroid therapy.

Key words: Corticosteroids, Cushing’s syndrome, RMP, Clinical pharmacist, Management.

INTRODUCTION
Corticosteroids are the steroid hormones that are produced naturally in the adrenal cortex and also available as synthetic analogues. These corticosteroids are mainly two types, they are glucocorticoids and mineralocorticoids. These corticosteroids are available in different types of formulations which includes oral, parenterals, inhalations as well as topical solutions and these formulations are commonly prescribed in health care practices. Corticosteroids are synthesized from cholesterol within the adrenal cortex. Aldosterone and corticosterone are the first part in their biosynthetic pathway and the last part is mediated by aldosterone synthase (for aldosterone) or by 11β-hydroxylase (for corticosterone). Glucocorticoids affects the carbohydrate fat, protein metabolism and have an anti-inflammatory, immunosuppressive, anti-proliferative and vasoconstructive effects. Anti-inflammatory effects are mediated by inhibition of DNA synthesis and epidermal cell turnover and vasoconstrictive effects are mediated by inhibiting the action of inflammatory mediators such as histidine. Mineralocorticosteroids are primarily involved in regulation of electrolyte and water balance by modulating ion transport in the epithelial cells of renal tubules of kidney.1

The chronic use of these corticosteroids causes the Cushing syndrome, osteoporosis, skin infections, diabetes, spine and hip fractures etc. Cushing syndrome may occurred due to the exogenous causes or endogenous causes. The exogenous causes for the occurrence of the Cushing syndrome is due to the administration of the corticosteroids, hence it is called as steroid induced Cushing syndrome or Iatrogenic Cushing syndrome. This steroid induced Cushing syndrome more commonly seen in females than males.2 The endogenous causes are ectopic, ACTH production and the pituitary tumor. The clinical signs of the Cushing syndrome is round red, full moon face, growth retardation in children, fat accumulation on the trunk along with...
weight gain, central obesity, skin infections, purple marks (striae) on the skin of breast, abdomen and thighs, muscle weakness, fractures of the ribs and spine due to thinning of the bones. The diagnosis of the steroid induced Cushing syndrome is done by the laboratory investigations and clinical manifestations. Sudden stoppage of the corticosteroids causes the adrenal crisis, hence the treatment is done by slowly tapering of the dose of the corticosteroids by this adrenal gland atrophy can be reversed. 

CASE STUDY-I

A female patient of age 50 years was admitted in the female general medicine ward with complaints of facial puffiness (Figure 1), back ache and swelling of limbs, muscle weakness since 3 weeks. The patient past medical history reveals that she was suffering with Anaemia since 2 years and she undergone one blood transfusion when the patient haemoglobin level was 4.7g/dl. The past medication history of the patient was taking painkillers (Aceclofenac, Paracetamol and chlorzoxazone combination drug) and a corticosteroid (Prednisolone 5mg) since 2 years daily twice continuously to reduce the pains from the local Pharmacy. Her vitals shows BP 90/70 mm of Hg, pulse rate-65bpm, heart sounds $S_1$ and $S_2$ are present, RS-NVBS present. P/A distension positive. Her laboratory findings show that patient had decreased haemoglobin content 5.7g/dl. Based on these evidences the patient had decreased haemoglobin content 5.7g/dl. Based on these evidences the patient was provisionally diagnosed as Cushing’s syndrome due to chronic use of corticosteroids. Now the patient is treated with the corticosteroid dexamethasone equivalent to the prednisolone dose which is tapered slowly and one packed cell blood transfusion. By this patient was better managed and the withdrawal symptoms are reduced.

CASE STUDY-II

A male patient of age 45 years admitted in the male general medical ward with a complaints of generalized weakness, facial puffiness, fever, tremors of hands present, dry and xerotic, hyper pigmented large macules present on thigh, scaly plaques present on thigh and gluteal region, swelling of both hand, pain in hip and knee region of right leg and loss of appetite (Figure 2-5). The past medication history of the patient was taking injection tramadol and other three drugs (tablet dosage forms) daily from 2 years which are prescribed by the local Rural Medical Practitioner (RMP) to reduce the pains. On laboratory investigations patient had a decreased total proteins (4.2g/dl), increased serum creatinine (1.29mg/dl), borderline level of serum calcium (11.0mg/dl), serum cortisol is 263.41nmol/lit, slight decrease of the blood pressure of admitted 2 days and slight increase of blood pressure after 2 days of admission. On MRI of spine revels lumbar spondylitis. Based on these evidences patient was diagnosed as steroid induced-cushing syndrome with tinea cruris with lumbar spondylitis. Now the patient was treated with the IV fluids of 2. Normal saline @80ml/Hr, Cap. Itraconozole 100 mg, OD; Clotrimazole (Kansel lotion) for local application, BD; Myogen liquid for all over the body, Tab. Hydroxyzine 10 mg, H/s, Tab. Prednisolone 5 mg, Tab. Shelcal, 500 mg, cap. Rabeprazole, cap. Astrymine Forte, Tab. Amoxicillin+ Potassium clavulanate, 625 mg; Tab. Flupirtine+ paracetamol. In this patient the withdrawal symptoms is reduced by tappering of the dose of corticosteroid predisolone 5 mg.
DISCUSSION

Corticosteroids are naturally occurring and synthetic steroid hormones. These steroids affect the humans physiology by affecting the endogenous corticosteroid production and by suppressing the Hypothalamic-pituitary Adrenal axis (HPA). The adrenal cortex consists of 3 layers, they are zone of glomerulosa (aldosterone), zone of fasciculate (cortisol and androgens) zone of reticularis (androgens). Cortisol (hydrocortisone) is the principle glucocorticoids. Glucocorticoid secretion is regulated by Adrencorticotropic Hormone (ACTH) present in the anterior pituitary and it is stimulated by the Corticotrophin Releasing Hormone (CRH) in hypothalamus. By this mechanism adrenal cortex secretes glucocorticoids, mineralocorticoids and androgens. Glucocorticoids help to maintain hemostasis. Mineralocorticoids helps to regulate the fluid and electrolyte balance. Glucocorticoids are classified into three types based on the duration of suppression of ACTH, they are short acting (8-12 hrs)-cortisol, cortisone, prednisolone, prednisone, methylprednisolone; intermediate acting (12-36 hrs)-triamcinolone; long acting (36-72 hrs)-dexamethasone, betamethasone. The drug fludrocortisone is a synthetic mineralocorticoids. The prolonged use of glucocorticoids suppresses the HPA axis. By this there is no endogenous corticosteroid production. If the treatment is >4 weeks, then the doses are tapered/titrated for every 1-2 weeks.

Corticosteroids are widely used for the immunosuppressant, anti-proliferative, vasoconstriction and anti-inflammatory actions. These may be used individually or in combination with other drugs and are prescribed in both short and long courses depending on the condition being treated and response of the patients. The drug prednisolone had more risk for the occurrence of the cushingoids features.

On prolonged use of the corticosteroids, the most commonly seen adverse effects are weight gain, growth retardation and cushingoids features. These adverse effects occurred even with low doses of corticosteroids for long duration of courses. Hypertension (increasing in resistance in the body vascular system, increasing in the intracellular volume, increasing cardiac contractility) and hyperglycemia (insulin resistance) are another side effects associated with long term course of oral corticosteroids. In the short duration of the management of oral corticosteroids the adverse effects we seen includes vomiting, changes in behavior and disturbed sleep.

On intiation of therapy in the patients with long duration, corticosteroids are used with low doses to minimize the adverse effects. The most common adverse effects seen in adults by long term duration includes...
osteoporosis and vertebral fractures (pain problems, disturb the daily activities and profoundly influence the quality of life especially in males), HPA suppression (stress induced acute adrenal crisis/ growth retardation), cushingoid appearance and weight gain (central obesity), hyperglycemia or diabetes, Cardiovascular diseases and dyslipidemia, myopathy, cataracts and glaucoma, psychiatric disturbances, immununsupression (increased in infections) and others include Gastro-intestine (gastritis, ulcer with perforation and hemorrhage, dyspepsisa, abdominal distension, acute pancreatitis) and dermatological events (skin thinning, fragality, red striae and purpura). Impairment of wound healing is a potential adverse effect of the systemic glucocorticoids.2

But low doses are not the sufficient solution to reduce these adverse effects, hence the management of steroid therapy doses should be tapered according to the condition and severity of the disease to minimize the withdrawal affects.6,7

Drug induced-cushing syndrome occurs due to the chronic administration of glucocorticoids and other types of drugs like megestrol acetate and herbal preparations that contain glucocorticoids. In past decades steroid induced-cushing syndrome is seen in health care practices because they are commonly used in the treatment of autoimmune diseases, inflammatory diseases and any allergic reactions for longer duration of course without any tapering of doses. The other reasons for steroid affects include initiation of large doses for longer time, sudden stoppage of drug and lack of awareness on steroid management guidelines. But in the present days they are taking by the people on its own from the pharmacies and from the RMP’s to reduce the symptoms of the back pains, knee pains and body pains without any prescription from the physicians.

CONCLUSION

Now-a-days the usage of the steroids is increasing enormously without any prescriptions, even though it is not an OTC medication. All pharmacies and RMP’s are prescribing steroids as pain killers. On chronic usage of the steroids, people are presenting the withdrawal symptoms. This is the leading cause for occurrences of adverse effects by prolong usage of the steroids. The prevalence of the steroid induced Cushing syndrome is depends upon the frequency of administration, initiation of low doses, tapering of doses and especially counseled the patients regarding the effects of steroid usage.

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CONFLICT OF INTEREST

There is no conflict of interest.

ABBREVIATIONS

RMP: Rural Medical Practitioner; P/A: Per Abdomen; RS: Respiratry System; NVBS: Normal Vesicular Breath Sounds; +ve: Positive; BPM: Beats per Minutes; IV: Intravenous; H/S: Bed Time; OD: Once a Day; BD: Twice a Day; BP: Blood Pressure; MRI: Magnetic Resonance Imaging; ACTH: Adreno Corticotropic Hormone; CRP: Corticotropin Releasing Hormone; HPA: Hypthalamus Pitutary Hormone.

SUMMARY

Corticosteroid drugs usage are enormously increasing by RMP’s and community pharmacies without any physician prescription. Due to prolong use and sudden stoppage, it causes suppression of the ACTH and withdrawal effects, hence these drugs are used based on the severity of the condition and they should be tapered by weekly intervals. Clinical pharmacist had important role in counseling of the patients on usage and effects of the drugs, educate the pharmacists and RMP’s.

REFERENCES