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Deleterious Psychiatric Effects Associated With Corticosteroids

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ABSTRACT:

Corticosteroids are a class of steroidal hormones, which includes glucocorticoids and mineralocorticoids. The term corticosteroid generally refers to glucocorticoids. Glucocorticoids have been widely used for treatment of inflammation, autoimmune diseases, cancer, etc, but can result in troubling psychiatric side-effects. Physicans and other medical professionals should be aware of the potential for these side-effects, possible means of prevention and efficacious treatments.Herein, we review adult case report data published during past quarter century on adverse corticosteroid induced psychiatric disorders.Fifty-five cases and a number of clinical trials investigated the incidence and treatment of these psychiatric symptoms and syndromes were identified.Data on incidence, drug dosage, risk factors, treatment was presented. We conclude that the psychiatric symptoms or complications of corticosteroid treatment are not rare and range from clinically significant anxiety and insomnia, to severe mood and psychotic disorders, delirium and dementia. Psychiatric symptoms associated with glucocorticoids have a rapid onset and usually occur within first two weeks of corticosteroid therapy and seem to be dose related. While tapering or discontinuation of the corticosteroid treatment may remedy these adverse side effects , psycotropic medications are often required either due to medical necessity of the corticosteroid or due to the severity of the psychiatric symptoms. Treatment with antipsychotics or antipsychotics in combination with lithium may be helpful. Further studies are needed to better understand the deleterious psychiatric effects associated with corticosteroids.

OBJECTIVES :

Describe the mechanism of action of corticosteroid induced psychiatric illness. To summarize the potential adverse side-effects associated with corticosteroids. Review toxicity profile of corticosteroids. Explain some interprofessional team statergies for improving care coordination and communication to advance the management of patients on corticosteroids and improve outcomes.

Key Words :

Corticosteroids,inflammation, psychiatric disorder, antipsychotics.

I. INTRODUCTION :

Corticosteroids are synthetic analogs of the natural steroid hormones produced by the adrenal cortex and include glucocorticoids and mineralocorticoids (over here, we mainly discuss about glucocorticoids).

Indications:

Corticosteroids have been used world wide to treat various disorders. These indications can include infectious and inflammatory disorders, allergic and autoimmune diseases, prevention of graft rejection, skin disorders, corticosteroid replacement therapy, systemic lupus erythematosus (SLE) and systemic vasculitis, asthma and chronic obstructive pulmonary disease, cancer, acute and chronic back pain, and in the prevention of postoperative swelling in head and neck surgery.

Adverse Effects :

Despite their significant efficacy, there are many adverse effects limit the utility of corticosteroids. Corticosteroid adverse effects appear to be related to both their average dose and cumulative duration. Corticosteroid adverse effects appear to be related to both their average dose and cumulative duration.Adverse effects are more common at higher doses and with chronic use though they are not limited to these cases. Adverse effects are seen in up to 90% of patients who take them for more than sixty days. The most common adverse effects of corticosteroids include osteoporosis and fractures, suppression of the hypothalamic-pituitary-adrenal (HPA) axis, Cushingoid features, diabetes and hyperglycemia, myopathy, glaucoma and cataracts, psychiatric disturbances, immunosuppression, cardiovascular disease, gastrointestinal and dermatologic adverse effects.

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Psychiatric Disturbances : Corticosteroids can cause a range of psychiatric disorders, including psychosis, agitation, insomnia, irritability, hypomania, anxiety, and mood lability. Short courses of corticosteroids can produce euphoria in many individuals and progress to depressive symptoms with extended course of their use. This review examines data on the nature, severity of psychiatric symptomology and cognitive change.

II. METHODS AND ANALYSIS:

We review the search produced by Heather A. Kenna et al (from wiley online library) .This search produced 55 cases with the following syndromes: hypomania/mania; depression; delirium; subsyndromal symptoms, such as hallucinations and agitation/anxiety, and panic disorder. Of these cases, 34 (61.8%) were psychotic, that is, had hallucinations and/or delusions coupled with impaired reality testing or lack of insight. Suicidal ideation was present in 22 cases (40%), of whom half were psychotic and half not; one patient committed suicide. In addition, the search produced three cases of coticosteroid-induced reversible dementia confirming the 1984 observations of Varney et al., and six cases of psychoses were apparently induced by rapid corticosteroid discontinuation. The dementia cases were atypical, of the corticosteroid cases we identified in that only two patients were younger than age 50 (ages 25 and 44 years), symptoms onset was often not reported until after months of corticosteroid treatment, and recovery, not always complete, often took more than six months after corticosteroid discontinuation.

Our analysis from this article includes 55 non-dementia cases of psychiatric syndromes induced by corticosteroid administration to characterize the patients, the drugs involved, the psychiatric symptoms and treatments. Patients' ages ranged from 18 to 93 years, with a mean of 44.5 ± 17.7 years. As in some of earlier reviews, but not all, more cases involved women (34/55, 61.8%) than men. Symptoms began a mean of 12.2 ± 13.7 days after starting corticosteroids (n = 50), and within one week in 60% (30/50), but onset ranged from 1 to 60days after starting the drug .

Among the 53 cases reviewed, in which the corticosteroid was identified, prednisolone was administered in 20 (mean dose = 46.5 ± 28.5 mg/day, [n = 19]), prednisone in 16 (41.4 ± 24.7 mg/day [n = 15]), methyl prednisone in seven (38.1 ± 44.3 mg/day), dexamethasone in seven (15.3 ± 6.2 mg/day [n = 6], with one outlier at 100 mg/day), betamethasone in two (2 mg/day and 4 mg/day), hydrocortisone in one (50 mg/day), and triamcinolone in one (80 mg/day + prednisone 10 mg/day). The mean (±SD) prednisone-equivalent dose, excluding the dexamethasone outlier, was 63.6 ± 46.2 mg/day, and the range 5–200 mg/day.

MECHANISM OF ACTION:

The pathophysiological mechanisms which give rise to the psychiatric symptoms associated with corticosteroid treatment remain unclear. Speculations regarding these mechanisms are discussed elsewhere and include corticosteroid effects on dopaminergic, cholinergic and serotonergic systems, decrease in serotonin release, and toxic effects on hippocampal neurons or on other regions of brain, and impairment in functions of HPA-axis .

III. RESULTS :

Our review produced 55 cases with the following syndromes: hypomania or mania; depression; delirium; subsyndromal symptoms, such as hallucinations and agitation/anxiety, and panic disorder.

Hypomaina or maina was the most common presentation, and was present in 54.5% (30/55) of cases. Clinical depression was present in 23.6% (13/55). Suicidal ideation was reported in 36.4%(20/55), of whom a little were psychotic. Psychotic mania,psychotic depression or delirium was reported in 64.8% (34/55).The mean (average) prednisone -equivalent dose suggest that psychiatric side -effects are more likely to occur at higher corticosteroid doses.

TREATMENT:

Treatment of corticosteroid-induced psychiatric symptoms should be started whenever possible with dose reduction or tapering of the drug as soon as the disease being treated is under control.

Corticosteroid-induced hypomania, mania and mixed mania have been successfully treated with a typical antipsychotic or mood stabilizer, most often haloperidol, haloperidol with lithium, risperidone, quetiapine, olanzapine with valproate, carbamazepine, lamotrigine. In some of the cases a combination of an antipsychotic and a benzodiazepine has been required to reduce the psychiatric symptoms.

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IV. DISCUSSION :

It has been noted that corticosteroid induced psychiatric Disturbances were related to the dose response relationship i.e high doses of corticosteroids has been shown to develop psychotic symptoms at a higher rate and more earlier.

However,risk of psychiatric complications may be increased by drugs that increase circulating levels of corticosteroids. Clarithromycin, for example, is an inhibitor of the cytochrome P450 enzyme (CYP) 3A4 that metabolizes prednisone's biologically active metabolite, prednisolone, and there by facilitating its action.

V. CONCLUSION :

Psychiatric complications associated with corticosteroid treatment range from anxiety and insomnia to severe mood disorders, delirium and dementia. These psychiatric symptoms typically occur within one or two weeks after starting high-dose corticosteroid treatment and the most common serious adverse event reported is hypomania or mania, though various forms of psychotic syndromes, taken together, are also more common. Hypo-albuminemia appears to be a risk factor worth attending to, as does co-administration of drugs that may slow the metabolism of the corticosteroid or increase its circulating levels, for example, P450 (CYP) 3A4 inhibitors. Although steroid taper or discontinuation can remedy these adverse effects, psychotropic medications are often required, either because of the inability to discontinue the corticosteroid treatment or the severity of the psychiatric symptoms. The psychotropic medication classes that are effective for particular idiopathic psychiatric syndromes and also appear to be effective in cases induced by corticosteroid treatment.

Better understanding of neurodegeneration mediated by corticosteroids could bring new insight into the pathogenesis of mental disorders and stimulate novel diagnostic and therapeutic approaches.

Careful patient monitoring and the use of proper preventative measures are required to reduce the adverse effects of corticosteroids and allow their maximal benefit to the patients.All interprofessional team members should educate their patients about corticosteroids and their potential adverse effects and modifications which can be done to reduce these detrimental effects. This team includes clinicains, nursing staff and pharmacist all working collaboratively with open communication to ensure optimal treatment outcomes of patients with minimal adverse effects.

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