

SOME SYSTEMIC SIDE EFFECTS OF CORTICOSTEROIDS

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Corticosteroids were first used in the 1950s as an anti-inflammatory drug. Over the years, corticosteroids have been used for the management of other clinical conditions including some chronic illnesses. Millions of new corticosteroid prescriptions are written yearly. The affordability and the ease of administration also make corticosteroids the favorite of many doctors in the management of several cases. Initially, much attention was not paid to the potential adverse effects of corticosteroids because it was believed that since they are analogous to natural hormones, they would have a wide safety margin. However, research has shown that corticosteroids have many adverse effects on different body systems that can be manifested during chronic or acute administration. Such systems affected by corticosteroids discussed in this paper include the endocrine system, the integumentary system, the muscular system, the skeletal system, the digestive system, immune system, cardiovascular system, nervous system and the visual system. It is important for healthcare workers to understand and pay attention to possible adverse effects so as to enhance early detection and discontinuation of drug.

The Key Words: Corticosteroids, adverse effects, systems

Introduction

Corticosteroids are drugs that are similar to the natural hormones produced in the cortex of the adrenal gland. Corticosteroids exert effects on different aspects of metabolism including carbohydrate metabolism, protein catabolism and also on physiological processes like immune response and regulation of inflammation, blood electrolyte levels and behaviour. Corticosteroids have found important uses in pharmacology for the treatment of many autoimmune diseases and other chronic illnesses due to their immune-modulating properties. Different generations of corticosteroids have been developed and also "complexing" with fluorine has been used to develop drugs with greater potency and longer durations of action. Drugs have also been developed for different routes of administration in order to reduce systemic side effects. However, since corticosteroids play great roles on different aspects of metabolism and other physiological processes, adverse reactions do occur on different body systems due to acute- or long-term use of corticosteroids. Even with topical preparations designed to cause as few adverse effects as possible by not entering significantly into systemic circulation, such effects still occur because corticosteroids acting like hormones are effective even at little concentrations. Corticosteroids cause adverse reactions on systems including the muscular system where they lead to muscle weakness, in the skeletal system where they can lead to bone loss thereby increasing the propensity to fracture. Corticosteroids have been implicated in glaucoma and cataracts and even in memory loss and behavioural changes. However, millions of new prescriptions continue to be made for corticosteroids yearly around the world. This paper researches available literature for the side effects of corticosteroids on a system-by-system basis.

Adverse Effects of Corticosteroids on the Endocrine System

Corticosteroids being hormones themselves have strong effects on other hormones. Corticosteroids inhibit the secretion of Adrenocorticotrophic hormone by a reverse feedback mechanism.

Corticosteroid-induced inhibition of basal ACTH secretion has been shown to occur within 2 hours in vivo [8]. Cortisol is a natural hormone secreted by the adrenal gland and although corticosteroids do not have the exact effect of natural hormones, they are believed to suppress the hypothalamic-pituitary-adrenal cortex axis. In addition, corticosteroids are believed to have effects on the hypothalamic-pituitary-gonadal axis. Corticosteroids can cause sodium retention through a direct action on the kidney, which leads to fluid retention and hypertension. The primary mineralocorticoid effect is enhancement of Sodium reabsorption in the distal convoluted tubules. Glucocorticoids contribute to water retention by enhancing the secretory activity of the renal tubules. In adrenal insufficiency, the capacity to excrete extra water is reduced so such patients can suffer water intoxication from intravenous infusions.

Adverse Effects of Corticosteroids on the Integumentary System

Topical corticosteroids can cause side effects on the skin depending on the age of the patient, duration of treatment, area of application and potency of the drug. Some of the side effects of corticosteroids include thinning of the skin, easy bruising, acne or perioral dermatitis, muco-cutaneous infections especially, candidiasis which likely appear due to lowered immune response [4].

Corticosteroids are known to lead to the formation of striae or expansion of already existing striae as well. The mechanism of striae formation appears to be due to the action of the steroids on the dermal connective tissue.

When high-dose corticosteroids are combined with an anti-vascular endothelial growth factor therapy like in the treatment of high-grade brain tumors, many significant complications may arise especially in children who are susceptible to abdominal striae. This is thought to happen because vascular endothelial growth factor plays multiple roles in wound healing and stimulating collagen synthesis [5].

It is also reported that chronic systemic steroids may inhibit wound healing in susceptible individuals as some animal studies show a 30% reduction in wound tensile strength with perioperative corticosteroids at 15 to 40 mg/kg/day [15].

Adverse Effects of Corticosteroids on the Muscular System

Steroid myopathy is a disease process that causes weakness mainly to the proximal muscles of the upper and lower limbs and to the neck flexors has been reported in patients with excess exogenous corticosteroids used in treatment [2].

Acute myopathy that is reported in patients with high dose short-term corticosteroid administration results in rhabdomyolysis, diffuse muscle weakness and severe dyspnoea (because of weakness of muscles of the thoracic region, which are involved in breathing). In contrast, chronic

myopathy occurs after prolonged treatment with corticosteroids, and results in proximal muscle weakness and type IIb fibre atrophy. Reports state that steroid myopathy are more frequent with the use of fluorinated corticosteroids than with the use of non-fluorinated ones [14].

Adverse Effects of Corticosteroids on the Skeletal System

Chronic glucocorticoid administration is believed to result in the induction of osteoporosis by a multifaceted process [10]. They influence bone remodelling by influencing osteoblasts, osteoclasts and osteocyte function. In addition, since corticosteroids have effects on calcium metabolism such as increasing renal excretion of Calcium and reducing gastro intestinal absorption of Calcium, total serum Calcium is reduced [6]. Glucocorticoids also increase Parathyroid Hormone sensitivity, which enhances the role of osteoclasts [11]. Considering that more Parathyroid Hormone is synthesized to help maintain Serum Calcium levels, there is increased bone resorption leading to Glucocorticoid-induced osteoporosis (GIO) which is the third most common cause of osteoporosis.

Adverse Effects of corticosteroids on the Digestive system

Corticosteroids have been implicated in adverse effects on the digestive system. It is believed that corticosteroids reduce the absorption of dietary vitamin D from the gut. In addition, corticosteroids are implicated in adverse effects on the teeth. Corticosteroids remove calcium from bones and teeth. In the teeth, the calcium removed causes destruction of the dentin matrix of the teeth. A study reported changes in the teeth in nine out of ten patients where two patients had complete obliteration of the pulp canal [1].

Adverse Effects of Corticosteroids on the Immune System

Corticosteroids are believed to increase the risk of pneumonia in patients with Chronic Obstructive Pulmonary Disease with a significant 69% increase in the risk of serious pneumonia, requiring hospitalization or leading to death [12]. Contact hypersensitivity can also result from use of topical or inhaled glucocorticoids. Inhaled corticosteroids are believed to predispose patients to oral Candidiasis.

Adverse Effects of Corticosteroids on the Cardiovascular System

The major adverse effects of corticosteroids on the cardiovascular system include dyslipidemia and hypertension. These effects may predispose patients to coronary artery disease if high doses and prolonged courses are used. The elevation of various lipid sub-fractions is thought to be caused by increased plasma insulin levels, impaired lipid catabolism and increased lipid production in the liver. In addition, researchers report an increase in the incidence of acute myocardial infarction. Hypertension may probably be due to activation of mineralocorticoid receptor by the drugs [13].

Adverse Effects of Corticosteroids on the Nervous System

Corticosteroids have been associated with neurotoxic and neurodamaging potentials. There are cognitive deficits that have been reported during both long- and short-term corticosteroid therapy. These changes include mania, depression, psychotic or mixed affective states, cognitive deficits, and minor psychiatric disturbances (irritability, insomnia, anxiety, labile mood) and in children, these disturbances could manifest as behavioural changes. Corticosteroids are believed to cause steroid induced memory loss [17].

Adverse Effects of Corticosteroids on the Visual System

Long-term administration of corticosteroids has been implicated in the development of cataracts and/or glaucoma [16]. A rise in intraocular pressure (IOP) can occur as an adverse effect of corticosteroid therapy and can lead to damage of the optic nerve causing Steroid-induced glaucoma.

Due to difficulty in establishing different models, there is limited research in this area so the mechanism of cataracts remains unknown [7]. One of the proposed mechanisms suggests that glucocorticoids may be capable of inducing changes to the transcription of genes in lens epithelial cells that are related to many cellular processes [3]. A novel mechanism has been proposed, in which steroids do not directly act on the lens but rather affect the balance of ocular cytokines and growth factors.

Glaucoma is caused by increase in the intra-ocular pressure and such increase has been shown to occur with various methods of steroid administration although it is most commonly a complication of topical corticosteroid application with drugs such as dexamethasone or prednisolone [9].

Conclusion

Corticosteroids are the favourite treatment by many doctors for many autoimmune diseases and chronic diseases due to their efficacy, ease of use and affordability. Millions of many new corticosteroids are prescribed every year on an in-patient and an out-patient bases. In addition, corticosteroids are available over the counter and can be easily abused by patients. Researches however show that corticosteroids have many potential side effects on different body systems. It is important that doctors and patients pay attention to these side effects, because the propensity of corticosteroids affecting different systems of the body might make them dangerous especially in chronic use. In addition, with increased knowledge about adverse effects due to the use of corticosteroids, physicians can become more cautious about prescribing them. Physicians can be encouraged to stop unsafe use of corticosteroids such as its use in the treatment of fever if they are made to pay more attention to potential adverse effects.

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