



Impact of Steroids on Long Term Use: A Review

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ABSTRACT

This review provides an overview of the impact of long-term use of steroids. Steroids are natural substances with many different effects in the human body, which begin over several days, as even birth control pills are a form of steroids. Natural steroids can be used to increase certain enzymes which a person's body may have trouble creating naturally, such as testosterone, which is vital in the growth and development. The therapeutic advantages of steroids have not always been clearly distinguished from their undesirable side effects, especially when used for lengthy periods of time. Physicians may believe that short term steroids are safe and do not have the well-known long term side effects of steroids; however even short courses of systemic corticosteroids can cause hyperglycaemia, elevated blood pressure, mood, sleep disturbances, sepsis, fracture and venous thromboembolism. For children with persistent asthma, inhaled corticosteroids (ICS) are the most effective treatment. However, ICS's adverse effects on the hypothalamo pituitary adrenal (HPA) axis, growth and bone metabolism are reason for concern. As a result, the major goal of this study was to compare the effects of long term inhaled corticosteroid therapy (ICS) on adrenal function, growth and bone health in children with asthma to a group of children with asthma who were not on ICS. This review summarizes the basic pharmacology of steroids its classification, types and uses. While corticosteroids are relatively inexpensive and commonly used as treatment for a variety of conditions, long term use is known to be associated with certain toxicities. The objective of this study was to conduct a systematic literature review of certain publications on the burden of long-term corticosteroid use and to reveal data gaps for additional research.

Keywords: Steroids, Hormones, Inflammation, Testosterone, Prednisone, Anti-cholinergic, Bronchodilator.

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INTRODUCTION

Steroids

A steroid is an organic molecule with four rings organised in a certain chemical configuration that is physiologically active. Steroids serve two main biological functions: they are key components of cell membranes that affect membrane fluidity, and they are signalling chemicals. Natural steroids are formed in the body by using protein to develop muscle tissue; natural steroids are produced in the body through.

Steroids, commonly known as corticosteroids, are anti-inflammatory drugs that are used to treat a variety of ailments. Steroids are a group of hormones that are very significant. Hormones are chemical molecules secreted into the circulatory system by particular cells in the body. These chemicals interact with hormone receptor proteins and cause unique physiological responses when they reach their target cells. The physiological response is achieved in the case of steroid hormones by controlling the expression

of certain genes¹. Cortisol is a natural steroid hormone produced by the adrenal gland in response to stress, and it is one of the most often used steroids. This hormone raises blood pressure and blood sugar levels while also reducing inflammation in the target tissues. Cortisol is very valuable in medicine because of its anti-inflammatory effects. Cortisol is found in skin ointments and asthma inhalers. It's also used in injections to lessen the inflammation linked with arthritis and regulate swelling caused by traumas. Progesterone (a progestin steroid) and estradiol are two more steroid hormones widely employed (an oestrogen steroid). Estradiol influences feminine traits and progesterone controls events during pregnancy. Both of these steroid hormones work to suppress ovulation and are used in birth control pills.

Steroid Classification

The following are some of the most prevalent steroid categories:

- *Animal
- *Insect
- *Ecdysteroids, such as ecdysterone
- *Vertebrate
- * Steroid hormones



*Sex steroids are a subset of sex hormones that cause or support sex differences reproduction. Androgens, oestrogens, and progestogens are among them.

* Glucocorticoids and mineralocorticoids are two types of corticosteroids. Glucocorticoids

*Mineralocorticoids assist maintain blood volume and regulate many aspects of metabolism and immunological function and regulate electrolyte excretion in the kidneys

Most medical 'steroid' drugs are corticosteroids.

- Anabolic steroid hormones are a class of steroids that interact with androgen receptors to enhance muscle and bone integration. There are natural and synthetic anabolic steroid hormones.

The term "steroids" is commonly used to refer to anabolic steroids.

*Cholesterol is a lipid that regulates the fluidity of cell membranes and is a major component of atherosclerotic plaques.

* plant

*Phytosterols

Beta-Sitosterol and Stigmasterol are examples of phytosterols.

*Brassinosteroids

Campesterol is an example of a Brassinosteroids.

*Fungus

*Ergosterols

Yeast is an example

Types of steroids

The main types are:

- Tablets, syrups and liquids- such as prednisolone
- Inhalers-such as beclomethasone and fluticasone
- Nasal sprays-such as beclomethasone and fluticasone
- Injection(given into joints muscle or blood vessels)-such as methylprednisolone.

Side effects of steroids

When administered for a short period of time or at a low dose, steroids rarely cause significant side effect. However, they can sometimes have adverse effects include increased appetite, mood swings, and difficulty sleeping. When it comes to steroid tablets, this is the most prevalent occurrence .The side effects will normally go away once you've completed your therapy, but don't stop taking your drug without consulting your doctor first. Stopping a prescription medication can result in even more unpleasant side effects (withdrawal symptoms).

Uses of steroids

Steroids can be used to treat a variety of conditions, including:

- Asthma and chronic obstructive pulmonary disease (COPD)
- Hay fever
- Hives and eczema
- Painful joints or muscles-such as arthritis, tennis elbow and frozen shoulder
- Pain caused by an irritated or trapped nerve-such as sciatica
- Inflammatory bowel disease-such as Crohn's disease
- Lupus
- Multiple sclerosis (MS)

How steroids work

Steroids are synthetic versions of hormones produced naturally by the adrenal glands, which are two tiny glands located above the kidneys. Steroids reduce redness and swelling when taken in higher doses than your body generates naturally (inflammation). Inflammatory disorders like asthma and eczema can benefit from this. Steroids also lower the immune system's functioning, which is the body's natural defence against disease and infection. This can aid in the treatment of autoimmune diseases such as rheumatoid arthritis and lupus, which are caused by the immune system attacking the body incorrectly².

Effects on long term use

Adrenal suppression is caused by long-term use of corticosteroids, which can blunt or inhibit the natural adrenal response to physiologic stress. Many cancer patients may get occasional doses of steroids as an antiemetic to prevent hypersensitive reactions or as adjuvants for pain control in order to avoid this impact. In 14 patients receiving high-dose prednisone for emesis prophylaxis prior to chemotherapy, Spiegel and colleagues performed Adreno Corticotropic Hormone (ACTH) stimulation assays. At 24 hours, 13 patients' adrenal function was suppressed, and 5 patients' adrenal function remained suppressed for more than a week. ACTH stimulation tests were done in nine women with ovarian cancer before and during chemotherapy in which dexamethasone was used as a pre-medication. A total of 523 medications were used. They observed effects on the hypothalamic-pituitary axis for up to eight days, but no long-term suppression was documented. Although adrenal suppression should be considered when patients who have had such treatment appear with hypotension and severe sickness, tapering steroids is probably not essential when they are given in brief, intermittent doses. Lefor, recently studied the use of replacement-dose steroids in cancer



patients who are having surgery. The dangers of corticosteroid use in advanced cancer patients have been thoroughly investigated. Dyspepsia, peptic ulcer disease, sleeplessness, oral and vaginal candidiasis, anxiety, and glucose intolerance are among the acute adverse effects. Cushingoid look, weight gain, oedema, cataracts, osteoporosis, proximal myopathy, thinning of the skin, infection, and delayed wound healing are among side

effects of long-term use. Corticosteroids can cause depression, agitation, and psychosis, among other neuropsychiatric side effects. As a result, it's critical to carefully assess the possible benefits of corticosteroid medication against the risks of side effects, as well as to continuously monitor the drug's efficacy. If there is no progress, the treatment should be changed or stopped⁷.

Table 1: Side Effects of Long-Term High-Dose Steroid Therapy

Steroid side effect	Monitor	Potential treatment options
Weight gain and obesity	Dietary advice should be provided to families before starting a steroid regimen to avoid weight gain. Steroids often increase your appetite	It is important that the whole family eat sensibly in order to prevent excess weight gain. Heathy eating plans can be found at ³
Cushingoid features (“moon face”)	You may notice fullness in the face and cheeks becomes more noticeable over time	Maintaining a healthy diet and minimizing sugar and junk food can help minimize these features. It may be advised by a doctor to restrict salt intake
Excessive growth of hair on the body (hirsutism)	You or your child may notice more hair on the body	This is not usually severe enough to warrant a change in medication
Acne, fungal infections of the skin(tinea), warts	More noticeable in teenagers	Use specific treatments (topical prescription) and do not rush to change the steroid regimen unless there is emotional distress.
Short stature	Ensure height is measured every 6 months as part of general care to track growth.	If you feel growth has slowed or stopped, discuss with your neuromuscular specialist, they may refer you to an endocrinologist.
Delayed puberty	Monitor your pubertal development at home. Identify any family history of delayed sexual maturation (i.e., explore ages parents went through pubertal changes)	If you or your child are concerned about his pubertal development or if puberty has not started by age 14, ask your neuromuscular specialist for an endocrine evaluation. Testosterone replacement therapy is generally recommended for boys who have not started puberty by age 14
Adverse behavioral changes	Identify any baseline mood, temperament, and ADHD issues (even before starting steroids). Be aware that these often temporarily worsen in the initial six weeks on steroid therapy	Baseline behavior issues should be treated prior to starting steroid therapy, e.g., ADHD counselling or prescription. It may help to change the timing of steroid medication to later in the day (avoiding the school/work day) - discuss this with your doctor, who may also consider a behavioral health referral
Immune suppression	Taking steroids can reduce immunity (the ability to fight infections). Be aware of risk of serious infection and the need to promptly address minor infections	Avoid “live” vaccinations if possible or talk to your primary care doctor about getting them before you start steroids
Adrenal suppression *This is a potential life-threatening medical emergency that can happen if steroids are stopped suddenly and the body produces insufficient levels of cortisol, or “stress hormone”	If you need to go to a new doctor, an emergency room, or urgent care, let them know you are on steroids, and carry a steroid alert card. It is very important that steroids doses are not missed for more than 24 hours for any reason.	Ask your doctor for a “Stress Dose Steroid Plan” that explains: <ul style="list-style-type: none"> • What to do in the case of a missed steroid dose >24 hours (because of fasting, illness, or prescription unavailability). • When to give stress dose steroids, at what dose, and in what form (by mouth, by intramuscular injection or by IV); consult the

	<p>Know when stress dose steroids should be given (severe illness, major trauma or surgery) to prevent adrenal crisis.</p> <p>Know the signs and symptoms of adrenal crisis (stomach pain, vomiting, lethargy).</p> <p>Have a vial/kit containing hydrocortisone for intramuscular injection at home and know how to administer in case of adrenal crisis (prescribed by an NMS)</p>	<p>“PJ Nicholoff Steroid Protocol” for an example⁴• If your child is going to stop taking steroid medications, ask your doctor for tapering plan, for an example plan⁵</p>
Hypertension	<p>Monitor blood pressure (BP) at each clinic visit</p>	<p>If BP is elevated, reducing salt intake and weight reduction may be useful first steps (under supervision of your cardiologist). Your cardiologist may prescribe blood pressure medication</p>
Glucose intolerance (high blood glucose levels)	<p>Test urine for glucose with dipstick test at clinic visits. Inquire about increased urination or increased thirst. Blood test once a year to monitor for development of type II diabetes and other complications of steroid induced weight gain</p>	<p>Further blood tests may be needed if urine tests or symptoms are positive</p>
Gastritis/ gastroesophageal reflux	<p>Look out for reflux symptoms (heartburn)</p>	<p>Avoid non-steroidal anti-inflammatory drugs (NSAIDs) - such as aspirin, ibuprofen, naproxen. Antacid can be used for symptoms</p>
Peptic Ulcer Disease	<p>Report symptoms of stomach pain as this can be a sign of damage to the lining of the stomach. Stool can be checked for blood if anaemic or if there is suggestive history</p>	<p>Avoid NSAIDs (aspirin, ibuprofen, naproxen). Drugs and antacid can be used if symptomatic Seek gastrointestinal consultation</p>
Cataracts	<p>Annual eye exam to look for cataracts</p>	<p>Consider switching from deflazacort to prednisone if cataracts evolve that affect vision. Seek ophthalmology consultation. Cataracts will only need to be treated if they interfere with vision</p>
Osteoporosis	<p>Take careful fracture history and ask about back pain at all visits. Spine x-rays every 1-2 years to monitor for vertebral compression. DEXA every 2-3 years to monitor bone density. Yearly vitamin D blood level (ideally late winter in seasonal climates) and supplement with vitamin D3 if levels are low. Yearly assessment of calcium intake by a dietician</p>	<p>Vitamin D supplements may be needed depending on level in blood Check 25. O-H vitamin D levels annually; supplement as needed. Make sure that dietary calcium intake meets recommendations for age. Calcium supplements may be needed if unable to meet. Weight-bearing activities can be helpful for bone health Discuss with your NMS/PT before starting an exercise/weight bearing program</p>
Myoglobinuria (Urine looks reddish brown coloured because it contains breakdown products of muscle proteins. This needs to be tested for in a hospital lab.)	<p>Report any reddish-brown urine to your child’s doctor. Urine can be tested for myoglobin</p>	<p>Avoid vigorous exercise and eccentric exercises, such as running downhill or jumping on a trampoline. Good fluid intake is important. Kidney exams and tests are needed if it persists⁶</p>

Effect of short steroid course

The beneficial effects of oral steroids are observable after a few hours. Breathing gets easier, and symptoms such as wheezing, coughing, mucus production, and chest tightness fade over time. The anti-inflammatory activity of oral steroids is likely to aid with other allergic conditions such as eczema and nasal congestion and drip. Oral steroids, regardless of their effect on breathing, provide a substantial surge of energy for a short period of time for many people. Steroids, such as prednisone, are anti-inflammatory medications that can be used to treat asthma and other lung illnesses. In asthma, prednisone and other steroids (inhaled, oral, or injectable) help to reduce airway inflammation. If you've ever had a severe asthma attack, you may have received heavy dosages of steroids delivered intravenously in the hospital. Prednisone is a steroid that is taken orally. If you suffer a severe worsening of asthma symptoms (an asthma attack), your doctor may prescribe oral steroids like prednisone for a short period of time. Oral steroids may also be prescribed when your asthma symptoms worsen but you do not require hospitalization⁸. Prednisone is a systemic steroid that is taken orally. This means that, unlike inhaled steroids (anti-inflammatory asthma inhalers), prednisone is absorbed directly into the bloodstream after being taken by mouth (orally). Prednisone and other systemic steroids may be used to treat asthma episodes and improve asthma control in people. Steroids are used in combination with other asthma drugs to treat long-term, difficult-to-control asthma or to control sudden and severe asthma attacks. Prednisone and other systemic steroids are sometimes given at high doses for a few days. This is referred to as a steroid burst. For long-term asthma management, they can also be taken at a modest dose daily or every other day. While a two-week course or "short burst" of oral steroids like prednisone is relatively safe, long-term use is not recommended due to the risk of major adverse effects. Taking calcium supplements can help prevent osteoporosis, or bone weakening, which is a side effect of long-term steroid treatment. If you need steroids for "rescue" therapy repeatedly, it could be a sign of poor airway inflammation control or ongoing exposure to an unknown allergen. In this scenario, discuss inhaling anti-inflammatory drugs with your healthcare physician. Anti-inflammatory asthma inhalers are the first-line treatment for asthma and may also help with other respiratory conditions. In fact, new research suggests that anti-inflammatory asthma inhalers should be used early in the disease's progression. The requirement for oral steroids like prednisone may reduce after the introduction of inhaled steroids. Unlike the major adverse effects of oral steroids, hoarseness and thrush are the most prevalent side effects of anti-inflammatory asthma inhalers, especially in the elderly. After using your asthma inhaler, you should rinse your mouth well, as you should with all asthma inhalers. After inhalation, gargle with water to help prevent oral thrush⁹.

The role of OCS in severe asthma

Corticosteroids are a very effective treatment for asthma, which is a chronic inflammatory airway condition. As a result, inhaled corticosteroids (ICS) are suggested for all asthma patients and are required for those who have more than simply occasional symptoms (more than twice a week)¹⁰. Bronchodilation is required in the majority of cases. As a result, long-acting β -agonists (LABA) are added, usually in a fixed combination with ICS for inhalation, for compliance concerns. The corticosteroids are delivered to the bronchial and lung tissue by inhalation as an aerosol or powder, maximising local anti-inflammatory effects while minimising unwanted systemic effects. Severe asthma, according to GINA, is asthma that requires step 4 or 5 medication to maintain control, such as high-dose ICS+LABA with or without a third controller, or asthma that remains uncontrolled despite this treatment¹¹. It's critical to separate severe asthma from asthma that isn't well-controlled due to poor treatment, poor adherence to medication, psychosocial problems, or poorly managed comorbidities. This definition is consistent with the European Respiratory Society's/American Thoracic Society's international guidelines¹². guidelines on severe asthma. The majority of patients with severe asthma who do not respond to ICS, LABA, and additional anti-inflammatory medicines (e.g., leukotriene antagonists) and bronchodilators (e.g., anticholinergics such as tiotropium) will be moved to systemic corticosteroids treatment¹³. Systemic corticosteroids increase the beneficial anti-inflammatory impact while also causing the characteristic undesirable side effects of systemic corticosteroids, which vary based on dose, duration of treatment, and individual susceptibility. There are two main uses of OCS in asthma: as a "controller alternative" for severe asthma and as a short-term exacerbation therapy. The use of OCS as a controller therapy in individuals with severe asthma is the subject of this article.¹⁰⁻¹²

CONCLUSION

Our research underlined the need for greater information on patients who are on long-term corticosteroid medication. Patients have expressed a desire for more dependable, accessible, recurrent, individually-adapted, and unbiased information in their own words. Various tools have been offered, with a similar emphasis on the relevance of the physician's oral information. Written information with unfettered access is offered as a tool, even if it is geographically remote. Educational brochures or a web page (the most commonly utilised information media) were proposed in this scenario. To ensure its reliability and neutrality, this information should also be supplied in a medical structure. Finally, a treatment support group could complement the information provided by physicians by allowing patients to discuss about their difficulties with others who have similar experiences with corticosteroid therapy and providing a forum for the exchange of practical tools that improve quality of life.



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