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REVIEW

Long-term side effects of glucocorticoids

Merih Oray[a,b,c], Khawla Abu Samra[a,b], Nazanin Ebrahimiadib[a,b], Halea Meese[a,b] and C. Stephen Foster[a,b,d]

[a]Massachusetts Eye Research and Surgery Institution (MERSI), Waltham, MA, USA; [b]Ocular Immunology and Uveitis Foundation, Waltham, MA, USA; [c]Istanbul Faculty of Medicine, Department of Ophthalmology, Istanbul University, Istanbul, Turkey; [d]Department of Ophthalmology, Harvard Medical School, Boston, MA, USA

ABSTRACT

Introduction: Glucocorticoids represent the standard therapy for reducing inflammation and immune activation in various diseases. However, as with any potent medication, they are not without side effects. Glucocorticoid-associated side effects may involve most major organ systems. Musculoskeletal, gastrointestinal, cardiovascular, endocrine, neuropsychiatric, dermatologic, ocular, and immunologic side effects are all possible.

Areas Covered: This article analyzes English-language literature and provides an update on the most recent literature regarding side effects of systemic glucocorticoid treatment.

Expert Opinion: The risk/benefit ratio of glucocorticoid therapy can be improved by proper use. Careful monitoring and using appropriate preventive strategies can potentially minimize side effects.

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glucocorticoids; immunosuppression; side effects; corticosteroids

1. Introduction

The isolation of cortisone in 1953 by Edward C Kendall and the clinical demonstration of the beneficial effects of cortisone and of adrenocorticotropic hormone in the treatment of acute rheumatoid arthritis by Hench and colleagues in 1950 revealed a revolution in modern medical therapeutics, and since then corticosteroids have infiltrated nearly every branch of medicine.[1,2]

Corticosteroids, including glucocorticoids and mineralocorticoids, are a class of chemicals encompassing both laboratory-synthesized and naturally produced hormones. They produce a myriad of important biochemical and physiologic effects on various tissues throughout the body. Glucocorticoids, in general, regulate metabolism and inflammation; mineralocorticoids regulate sodium and water levels.[3,4] Today, glucocorticoids represent the standard therapy for reducing inflammation and immune activation in various diseases including asthma, as well as allergic, rheumatoid, collagen, vascular, dermatological, inflammatory bowel and other systemic diseases, and in ocular inflammatory diseases. These agents have anti-inflammatory and immunosuppressive actions, as well as the potentially undesirable side effects.[3,4]

Side effects of glucocorticoid therapy are common and may be problematic, ranging from a minor case of acne to Cushing syndrome that may result in diabetes mellitus or potentially life-threatening heart disease if untreated. Glucocorticoid-associated side effects may be endocrine, neuropsychiatric, gastrointestinal, musculoskeletal, cardiovascular, dermatologic, ocular, or immunologic in nature (Table 1). Different side effects may occur in up to 90% of patients who take glucocorticoids for more than 60 days.[5,6] Side effects can occur at a wide range of doses and vary depending on the route of administration. Some of these side effects may occur even in patients taking low (≤7.5 mg/d) dosages.[5,6]

A recent literature search has shown that data on monitoring corticosteroid-associated adverse effects were scarce, because most articles focused on the therapeutic effects of glucocorticoids, not on the occurrence and monitoring of side effects.[54] Hence, the purpose of this review is to provide an update on the most recent literature regarding the side effects of systemic glucocorticoid treatment. Search of the peer-reviewed English literature about the side effects of glucocorticoids was conducted using Medline. The following databases were also searched: Cumulative Index to Nursing and Allied Health Literature, Cochrane Library, Global Health and MD Consult. Time frame was open, as we did not want to miss historical documentation of diseases like the original article published on Cushing disease.

CONTACT C. Stephen Foster sfoster@mersi.com Massachusetts Eye Research and Surgery Institution, 1440 Main Street, Waltham, MA 02142, USA

Article highlights

- Glucocorticoid-associated side effects may be musculoskeletal, endocrine, gastrointestinal, neuropsychiatric, cardiovascular, dermatologic, ocular or immunologic in nature.
- The risk of osteonecrosis and osteoporosis usually occurs with high doses and prolonged treatment duration; however, they may also develop with short-term exposure.
- Glucocorticoid-induced myopathy is the most common type of drug-induced myopathy and is characterized by painless muscle weakness, atrophy and fatigue.
- Endocrine and metabolic side effects of glucocorticoids include glucocorticoid-induced hyperglycemia, dyslipidemia, weight gain, cushingoid features, adrenal suppression and growth suppression.
- Cardiovascular side effects include hypertension, coronary heart disease, ischemic heart disease, heart failure and even sudden death.
- Dermatologic side effects include skin atrophy, ecchymosis, erosions, striae, delayed wound healing, purpura, easy bruising, acne, hirsutism and hair loss.
- The most common ophthalmologic side effects are cataract and glaucoma.
- Neuropsychiatric symptoms such as minor mood changes, depression, euphoria, mood lability, irritability, akathisia and anxiety as well as cognitive impairment such as attention, concentration and memory deficit have been reported after treatment with corticosteroids. In rare cases, psychosis, dementia and delirium may occur.
- The risk/benefit ratio of corticosteroid therapy can be improved by proper use of corticosteroids.

This box summarizes key points contained in the article.

Table 1. Long-term side effects of glucocorticoids.

System affected	Side-effects
Musculoskeletal	Osteoporosis,[7–13] Avascular necrosis of bone, [14,15] Myopathy [16,17]
Endocrine and Metabolic	Hyperglycemia,[18,19] Diabetes mellitus,[18,19] Dyslipidemia [20,21] Weight gain, Cushingoid features,[22] Growth suppression,[23] Adrenal suppression [24]
Gastrointestinal	Gastritis, Peptic ulcer, Gastrointestinal bleeding [25,26] Visceral perforation, Hepatic steatosis, Pancreatitis [26–29]
Cardiovascular	Hypertension [30–32] Coronary heart disease, Ischemic heart disease, Heart failure [32–37]
Dermatologic	Dermatoprosis,[22,38,39] Skin atrophy, Ecchymosis, Purpura, Erosions, Striae, Delayed wound healing, Easy bruising, Acne, Hirsutism, Hair loss [22]
Neuropsychiatric	Mood changes, Depression, Euphoria, Mood lability, Irritability Akathisia, Anxiety, Cognitive impairment, Psychosis, Dementia Delirium [40–45]
Ophthalmologic	Cataract,[30,46,47] Glaucoma,[22,48–50] Ptosis, Mydriasis, Opportunistic ocular infections, Central serous chorioretinopathy [49,50]
Immunologic	Suppression of cell-mediated immunity, Predisposition to infections, Reactivation of latent infections [51–53]

2. Musculoskeletal side effects

2.1. Osteoporosis

As defined by the National Osteoporosis Foundation, osteoporosis is a chronic and progressive disease characterized by low bone mass, microarchitecture deterioration of bone tissue, bone fragility and a consequent increase in fracture risk.[55] Osteoporosis is either primary – related to aging and loss of gonadal function – or secondary to medical illnesses and systemic drug use – mainly corticosteroid.[56]

Secondary osteoporosis, as one of the most debilitating complications of glucocorticoid therapy, has been recognized since 1940. Both the cumulative dose and duration of glucocorticoid exposure are determinants of the risk of fractures and it has been shown that the prolonged exposure to doses of prednisolone as low as 2.5–5 mg daily may be associated with an increased risk of hip and vertebral fractures.[7,8] Inhibition of osteoblast function is the main effect of glucocorticoid on bone metabolism leading to a decrease in bone formation. Bone loss starts promptly after the initiation of glucocorticoid therapy and is mainly taking place in the first six months of treatment. Bone loss is predominantly found in bone with high trabecular content, like the vertebrae.[9] In addition to causing bone loss, glucocorticoid therapy may result in changes in the architectural integrity of the bone.[10]

In a major population-based study of limb fractures, Hooyman et al. reported that the risks of hip, distal forearm and proximal humeral fractures were approximately doubled in a group of patients with rheumatoid arthritis who were exposed to glucocorticoids when compared to patients with rheumatoid arthritis alone.[11] According to the data of Russia's large-scale GLUCOST survey, Baranova et al. found that every four patients with chronic inflammatory disease who are on long-term glucocorticoid therapy have one low-energy fracture or more.[12]

Although no conclusive evidence exists for a safe minimum dose or duration of glucocorticoid exposure, effective prevention and treatment options are available and can result in reduction of the significant morbidity and mortality associated with the corticosteroid-induced osteoporosis.[13]

Bone mineral density should be measured at baseline if glucocorticoid therapy will be given for more than 3 months, and then repeated yearly. Measures to prevent secondary osteoporosis include the use of the minimal effective dose of glucocorticoids, calcium and vitamin D supplementation in addition to appropriate physical activity. Treatment of active osteoporosis is usually with anti-resorptive drugs, among which bisphosphonates are currently the first-line therapy.[13]

The American College of Rheumatology provides the following specific treatment guidelines for patients treated with at least 5 mg of corticosteroids daily for >3 months: calcium 1500 mg/day and vitamin D 800 U/day; bisphosphonate therapy; replacement of gonadal steroids. Substitution of calcitonin should be

considered for patients intolerant to bisphosphonates and hydrochlorothiazide should be used in instances of hypercalciuria.[57]

2.2. Avascular necrosis of bone (osteonecrosis)

Glucocorticoids are the leading cause of non-traumatic osteonecrosis and up to 40% of patients can present with osteonecrosis after long-term use of glucocorticoids. Like osteoporosis, the risk of osteonecrosis occurs with high doses and prolonged treatment duration, but may also occur with short-term exposure.[14] The mechanism by which glucocorticoids induce osteonecrosis includes the induction of osteocyte apoptosis, thus affecting bone remodeling and starting the sequence of events leading to bone collapse.[14,15]

Patients with osteonecrosis can be either symptomatic or asymptomatic. Symptoms include persistent joint pain and decreased range of motion. Treatments include surgery to replace the joint and bisphosphonates, which is indicated to reduce pain, increase ambulation and delay bone collapse in patients with osteonecrosis.[14,15]

2.3. Myopathy

Glucocorticoid-induced myopathy was first described by Harvey Cushing in 1932 [16] and is the most common type of drug-induced myopathy. It is characterized by painless muscle weakness, atrophy and fatigue.[17] The effect of glucocorticoids on muscle includes decreasing protein synthesis and increasing the rate of protein catabolism leading to muscle atrophy.[17]

The clinical manifestations of glucocorticoid-induced myopathy include an acute and a chronic form. The acute form occurs frequently in the intensive care unit setting and is characterized by rapidly progressive weakening of the proximal and distal muscle with possible involvement of the respiratory muscles.[17] The chronic form of the myopathy is characterized by painless or mildly painful muscle weakness that affects the proximal muscles, particularly the pelvic girdle muscles, and progresses very slowly.[17]

It has been shown in previous studies that glucocorticoid-induced myopathy is more common with the use of fluorinated glucocorticoids such as dexamethasone, betamethasone and triamcinolone, than with the use of non-fluorinated preparations, such as prednisone and prednisolone.[17]

The glucocorticoid dose that is associated with myopathy varies greatly between patients. Some patients develop muscle weakness with low dose of glucocorticoids, while others might not develop weakness even with high doses of glucocorticoids for months or years.[17]

The management of glucocorticoid-induced myopathy involves the discontinuation of the drug with an increase in muscle strength being observed within 3–4 weeks. In the treatment regimen of such patients, fluorinated glucocorticoids such as dexamethasone should be replaced with non-fluorinated glucocorticoids such as prednisone, and the lowest recommended dose should be used.[17]

3. Endocrine and metabolic side effects

3.1. Effect on glucose metabolism

It has been previously shown that the effect of glucocorticoids on glucose metabolism is dose-dependent and causes a mild increase in fasting blood glucose levels and a larger increase in postprandial blood glucose in patients without preexisting diabetes mellitus. The development of de novo diabetes in a patient with previously normal glucose tolerance is uncommon.[18] Patients with a history of diabetes or glucose intolerance who are on glucocorticoid treatment suffer higher blood glucose levels, resulting in an increased difficulty with glycemic control.[18]

Glucocorticoid-induced hyperglycemia is multifactorial in origin and may be explained by the augmentation of hepatic gluconeogenesis, the inhibition of glucose uptake in adipose tissue and the alteration of receptor and post-receptor functions induced by glucocorticoids.[18,19] Risk factors for developing hyperglycemia in the setting of glucocorticoid therapy are the same as those for other patients, including a family history of diabetes, increased age, obesity and a history of gestational diabetes.[19]

Glucocorticoid-induced hyperglycemia improves with reduction in the dose of glucocorticoid and usually reverses when the medication is stopped, although some patients may develop persistent hyperglycemia.[19]

3.2. Dyslipidemia

Glucocorticoid-induced dyslipidemia is multifactorial in origin and involves the induction of lipolysis, an increase in the synthesis of very low-density lipoprotein (VLDL), production of free fatty acids and their accumulation in the liver.[20]

Although the data available on glucocorticoid-induced dyslipidemia is scarce, all forms of abnormal lipid profile have been previously reported with glucocorticoid use. Studies or guidelines on how to manage

glucocorticoid-induced dyslipidemia are lacking and patients should be managed and treated based on general clinical practice.[20,21]

3.3. Weight gain and Cushingoid features

Both Cushingoid features and weight gain are quite troubling adverse events associated with glucocorticoids. Cushingoid features result from the redistribution of body fat with characteristic truncal obesity, buffalo hump and moon face secondary to long-term glucocorticoid therapy. The risk of these complications is dependent on both the dose and the duration of the treatment. In patients with rheumatoid arthritis, it has been shown that the use of 5–10 mg/day of prednisone or equivalent over two years was associated with an increase of mean body weight of 4–8%.[22]

Factors that may contribute to weight gain include increased appetite associated with glucocorticoid therapy, and an increase in food intake for symptomatic relief in patients with gastropathy or peptic ulcer disease.[22]

3.4. Growth suppression

Suppression of growth is an important and well-recognized adverse effect of glucocorticoid therapy in children. The mechanism of growth suppression includes the effect of glucocorticoids on the essential components of anabolism and growth including bone metabolism, as explained previously, nitrogen retention and the effect on collagen formation.[23]

It also has been shown that glucocorticoids, even at moderate doses, result in inhibition of growth hormone release and insulin-like growth factor-1 bioavailability. The effect of glucocorticoids on growth suppression can be inhibited by using growth hormone replacement therapy in the form of injections.[23]

It is very important to remember that glucocorticoid-induced growth defects may not always be fully compensated for after steroid withdrawal, especially if corticosteroid treatment has lasted for more than 18 months.[23]

3.5. Adrenal suppression

Administration of exogenous glucocorticoids can suppress the hypothalamic-pituitary-adrenal axis (HPA) and it has been shown that long-term glucocorticoid use is associated with adrenal gland suppression with significant individual variation in response. Patients who are using glucocorticoid chronically may suffer hypotension and cardiovascular collapse if the steroids are suddenly withdrawn or tapered too quickly as a result of the adrenal gland suppression. Although it may take up to 9 months for normalization of the adrenal gland function after glucocorticoid withdrawal, approximately 70% of patients will have normal function within a month depending on the duration and dosage of corticosteroids and speed of taper.[24]

4. Gastrointestinal side effects

Glucocorticoids are considered as an independent risk factor for a number of gastrointestinal adverse events including gastritis, peptic ulcer formation and gastrointestinal bleeding.[25] The risk of peptic ulcer disease due to glucocorticoids rises significantly when they are used in combination with non-steroidal anti-inflammatory drugs (NSAIDs).[25]

In an interesting study by Gabriel and colleagues, the authors showed that the use of glucocorticoids is associated with a twofold increase in the risk of gastrointestinal adverse reaction among patients also taking NSAIDs when compared with those who use NSAIDs alone.[26] In addition, it has been shown by Piper and colleagues that the use of both NSAIDs and glucocorticoids is associated with a fourfold increase in the risk of a gastrointestinal side effects compared with the nonuse of either drug.[25]

Other serious gastrointestinal complications that can occur with glucocorticoid use include visceral perforation, hepatic steatosis (fatty liver) and pancreatitis.[26,27] The etiology of glucocorticoid-induced hepatic steatosis is unknown, but may be related to hyperglycemia. A single case describing a fat embolism that was thought to have originated from the liver was previously reported in the literature.[27]

While there is some evidence suggesting an etiologic role for glucocorticoids in causing pancreatitis, the exact role of these drugs in causing acute pancreatitis is still uncertain.[28] In a large population-based case-control study, it was found that there is an increased risk for acute pancreatitis among patients who use oral glucocorticoids compared with nonusers.[28,29]

The risk of pancreatitis in patients receiving long-term glucocorticoids also remains uncertain, reflecting the need for large prospective studies in order to more clearly define the relationship of newly started glucocorticoid therapy with the onset of pancreatitis.[28,29]

5. Cardiovascular side effects

5.1. Hypertension

Risk of hypertension is increased by about twofold in patients treated with corticosteroids regardless of the duration of treatment. The risk is associated with

cumulative dosage of corticosteroids.[30] The incidence of hypertension induced by high-dose corticosteroid for more than 3 months was reported to be 9%; however, it increased to 37% in patients older than 65 years.[31] Two forms of hypertension may develop; the first form is early onset and occurs in the absence of known risk factors of hypertension, presumably mediated by some vasoactive substances that cause imbalance between vasoconstriction and vasodilation. The second develops as a result of weight gain secondary to corticosteroid effects on fat metabolism.[32]

In contrast to other forms of hypertension, sodium intake has no effect on corticosteroid-mediated hypertension, as mineralocorticoids seem not to be involved.[32]

5.2. Cardiac side effects

The risk of coronary heart disease, ischemic heart disease, heart failure and even sudden death has been reported to be increased 2–4-fold by using 7.5 mg or more of prednisolone.[33] This is an indirect side effect of hypertension, hyperglycemia and hypertriglyceridemia.[32] Moreover, accumulation of triglycerides in the myocardium can lead to impaired left ventricular filling dynamics.[34] Systemic glucocorticoids may induce atrial fibrillation and flutter as well.[35] Cardiac risks are dose dependent and the risk decreases with stopping the medication.[36]

During pulse therapy, sudden death may occur in rare cases possibly due to an electrolyte shift due to rapid infusion. Reports are mostly from patients with preexisting kidney or heart diseases. So, it is recommended to infuse slowly over 2–3 hours with cardiac monitoring in high-risk patients.[37]

6. Dermatologic side effects

Corticosteroids affect keratinocytes and prevent the secretion of collagen and hyaluronic acid by fibroblasts in dermis. This interferes with cell proliferation, and with chronic glucocorticoid usage, skin thinning ensues.[22]

Chronic skin insufficiency and fragility is called dermatoporosis, comparable to osteoporosis in the elderly.[38] Corticosteroid administration precipitates the occurrence of dermatoporosis, which is characterized by thinning, telangiectasia and hematoma of the skin that becomes lacerated with poor healing in advanced stages.[39] In the end stage, loss of barrier function of the skin is life threatening and requires hospitalization with skin grafting.

Systemic glucocorticoid usage for more than one year, even at low dosage (equivalent to less than 5 mg/day prednisone), induces skin atrophy, ecchymosis and erosions in about 5% of patients. Catabolic effects of corticosteroids cause atrophy, striae and delayed wound healing, whereas decreased vascular structure integrity leads to purpura and easy bruising. With higher dosage, steroid acne, hirsutism and hair loss can been seen.[22]

7. Neuropsychiatric side effects

Neuropsychiatric symptoms such as minor mood changes, depression, euphoria, mood lability, irritability, akathisia and anxiety as well as cognitive impairments such as attention, concentration and memory deficit have been reported after treatment with corticosteroids. In rare cases, psychosis, dementia and delirium may occur.[40]

A cohort study by Fardet et al. showed that neuropsychiatric disorders in addition to lipodystrophy are the most common and most disturbing side effects in patients treating with more than 20 mg a day of prednisone for more than 3 months.[41] Memory loss and cognitive impairment may be overlooked by physicians and even patients. As a brain area with a high number of corticosteroid receptors, the hippocampus plays a particularly significant role in corticosteroid-induced cognitive dysfunction.[42]

The frequency of neuropsychiatric symptoms reported by Fardet et al. was 52%.[41] In a prospective longitudinal study over 12 months on patients with chronic skin disease needing long-term corticosteroid therapy, depression and anxiety were reported to be 16 and 11%, respectively.[43] Symptoms start within a short period after the introduction of corticosteroids and become milder with the continuation of therapy. Early in the course of treatment, patients experience optimism and improved concentration, which is replaced by depression later in the course of treatment. With short-course high-dose steroid, mania and hypomania can be seen more predominantly than depression.[43]

The Boston Collaborative Drug Study demonstrated that the incidence of side effects is associated with cumulative steroid dosage.[44] Associated risk factors for developing neuropsychiatric side effects include female gender, psychiatric background and age above 40 years.[43]

Lewis and Smith demonstrated that in over 90% of patients, symptoms resolved within 6 weeks of cessation of therapy. Recovery was faster for delirium (5.4 days) than for other symptoms such as depression, mania or psychosis (19.3 days).[45]

8. Ophthalmologic side effects

Cataract (11–15%) and glaucoma (12.8%) are the two most common ophthalmologic side effects of glucocorticoids.[46] The risk increases with dose and length of treatment.[47]

8.1. Cataract

Posterior subcapsular (PSC) and cortical cataract have been reported even in doses less than 5 mg/day.[30] Change in gene transcription in lens epithelial cells in addition to alterations in the level of intraocular growth factors have been hypothesized to be involved in the mechanism of corticosteroid-induced PSC formation.[47]

8.2. Glaucoma

Systemic glucocorticoids can lead to increased intraocular pressure (IOP) in 18–36% of the population. It seems that a genetic predisposition exists for developing glaucoma.[22] In addition, known cases of glaucoma are more susceptible to elevations in IOP; 46–92% of open-angle and 65% of closed-angle glaucomatous patients experienced such exacerbations with corticosteroid therapy. In most cases, IOP will return to normal within 2–4 weeks after cessation of corticosteroids.[22]

The mechanism of corticosteroid-induced glaucoma is similar to primary open-angle glaucoma. It reduces the function of trabecular meshwork, which normally drains approximately 90% of aqueous humor.[48]

Other ocular side effects secondary to corticosteroid treatment include ptosis, mydriasis and, with high doses, opportunistic infections such as herpetic keratitis and cytomegalovirus retinitis.[49] In addition, central serous chorioretinopathy, a disorder characterized by neurosensory retinal detachment, retinal pigment epithelium detachment and choroidal hyperpermeability can be triggered by corticosteroids. Presentation may be atypical when induced by corticosteroids.[50]

9. Immunologic side effects

Treatment with long-term systemic steroids suppresses cell-mediated immunity and predisposes patients to intracellular infections. It alters monocyte function as well, which resolves rapidly with stopping medication. [51] Effects of corticosteroids on the immune system are dose related and with short-term or alternate-day treatment, the risk of infection remains unchanged. A meta-analysis showed that with daily usage of prednisone less than 10 mg or a cumulative dose of less than 700 mg, the chance of infection does not increase.[52]

High-dose corticosteroid treatment makes patients vulnerable to virus, bacteria, fungus and parasite infection, and increases the risk of reactivation of latent infection such as tuberculosis. Unusual organisms may be involved and also the classic manifestations of infection may be masked and make the diagnosis challenging. Patients should undertake the necessary precautions to prevent contact with varicella zoster and measles and live vaccines should also be avoided.[53]

10. Conclusion

Although glucocorticoid treatment may have various side effects, careful monitoring and using appropriate preventive strategies can potentially minimize these side effects. Physicians should make patients aware of these data and help them decide which prevention and/or treatment options are best for them.

11. Expert opinion

Corticosteroid treatment is an important component of therapy for a variety of diseases. However, as with any potent medication, they are not without side effects. Practitioners should be aware that corticosteroid therapy could possibly exacerbate a preexisting condition or present a new medical condition. Knowledge of the clinical implications of prescribing these agents is critical. For proper use of systemic corticosteroids, a basic knowledge of the pharmacology, clinical usage guidelines and adverse reactions of these agents is essential. Both short- and long-term side effects should be well known by the physicians. Practitioners should also educate patients about the prevalence of various adverse effects prior to the initiation of corticosteroid therapy and patients should be closely monitored for the development of potential side effects.

The risk/benefit ratio of corticosteroid therapy can be improved by the proper use of corticosteroids and prior to initiation of therapy, a thorough patient history is important to anticipate any potential problems. In 2007 European League Against Rheumatism (EULAR) evidence-based recommendations on the management of systemic glucocorticoid therapy in rheumatic diseases were published and they provide a useful tool for the improved use and management of glucocorticoid therapy.[58] The 10 propositions include patient education, dosing, comorbidities and risk factors,

monitoring of adverse effects, concomitant therapy and special safety advice.[58]

Most published studies on glucocorticoid-associated side effects are retrospective and observational. Randomized controlled clinical trials are needed to better understand possible safe glucocorticoid thresholds for certain side effects, ascertain the independent effects of glucocorticoids on various outcomes and identify improved ways to administer glucocorticoids more effectively and safely.

In addition, unnecessary corticosteroid exposure should be avoided via the introduction of corticosteroid-sparing therapies and tapering of corticosteroids to a minimal effective dose. When long-term therapy with systemic corticosteroids is anticipated, additional steroid-sparing immunomodulatory therapy should be considered. However, still new biological therapies have not replaced glucocorticoids, and probably will not replace them in the near future. Therefore, more studies on the mechanisms causing beneficial and harmful effects and on the predictive factors for the effects of glucocorticoids are needed. New glucocorticoids without potential to cause side effects, such as selective glucocorticoid receptor agonists, are being developed to minimize the adverse effects. Further research on this topic is ongoing; however, the application of a new agent in clinical practice will probably not occur within the next few years.[59,60] In addition, there are also studies in the field of nanotechnology to provide targeted local treatment, decrease systemic absorption and minimize first-pass metabolism.[61,62]

In summary, a good doctor–patient relationship is essential in managing the patient on long-term glucocorticoids. Patients should be informed of what to expect from this therapy, advised to return for regular visits and be encouraged to promptly report any side effects to the physician. Adverse effects of glucocorticoids are partially avoidable. To avoid adverse events as much as possible, several measures can be taken. If the strategies noted previously are followed, problems from long-term glucocorticoid therapy may be minimized.

Declaration of Interest

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