GRUSZKA, Marta, POLAŃSKA, Paulina, KUBICKA, Maria, ZAKROCKA, Martyna and FICK, Jakub. Adverse effects of oral glucocorticoid therapy - a brief review of literature. Journal of Education, Health and Sport. 2025;78:57512eISSN 2391-8306.
https://doi.org/10.12775/JEHS.2025.78.57512
https://apcz.umk.pl/JEHS/article/view/57512

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 02.01.2025. Revised: 27.01.2025. Accepted: 9.02.2025. Published: 17.02.2025.

Adverse effects of oral glucocorticoid therapy - a brief review of literature

MD Marta Gruszka[1], MD Paulina Polańska[2], MD Maria Kubicka[3], MD Martyna Zakrocka[4], MD Jakub Fick[5]

[1] 4th Military Clinical Hospital in Wrocław, Weigla 5, 53-114 Wrocław, Poland;
kulacz.marta@gmail.com
ORCID: 0009-0003-0775-3451

[2] 4th Military Clinical Hospital in Wrocław, Weigla 5, 53-114 Wrocław, Poland;
polanska.paulina@gmail.com
ORCID: 0009-0004-2365-7977

[3] Faculty of Medicine, Wroclaw Medical University, Wybrzeże L. Pasteura 1, 50-367 Wroclaw, Poland;
maria.kubicka@student.umw.edu.pl
ORCID 0000-0001-6913-9914

[4] Lower Silesian Oncology, Pulmonology and Hematology Center, pl. Ludwika Hirszfelda 12, 53-413 Wroclaw, Poland;
zakrockamartyna@gmail.com
ORCID: 0009-0004-5091-5919

[5] Municipal Hospital Complex in Chorzów, Strzelców Bytomskich 11, 41-500 Chorzów, Poland;
fick.jakub@gmail.com
ORCID: 0009-0006-2822-9423

ABSTRACT

Introduction and Objective: Glucocorticoids (GCs) are among the most commonly prescribed pharmaceuticals across various medical specialties. The purpose of this article is to provide an overview of the most common side effects of oral glucocorticoid therapy and to underline the importance of educating healthcare professionals and patients on this topic.

State of knowledge: Glucocorticoids are commonly used in a wide range of patients because of their anti-inflammatory and immunosuppressive properties. Oral glucocorticoids can lead to a greater number of side effects in comparison with other routes of administration due to their systemic action. Adverse effects of glucocorticoid therapy involve endocrine, cardiovascular, musculoskeletal and central nervous systems. Patients often present with elevated serum glucose levels caused by reduced insulin sensitivity and amplified hepatic glucose production. Moreover, hyperglycemia and hypertension increase the risk of ischemic heart disease and heart failure. GCs impede bone formation and escalate bone resorption, resulting in bone mass reduction and osteoporosis. Myopathy may occur as a result of intensified catabolic processes. Glucocorticoid therapy impacts the production of cortisol by the adrenal glands and can lead to adrenal insufficiency and even adrenal crisis. Characteristic changes in external appearance aggravate self-esteem and mental health of patients resulting in decreased quality of life. Another adverse effect described in literature is substantial cognitive decline.

Summary: Despite their multiple positive applications, glucocorticoids are associated with numerous side effects. It is imperative for medical professionals to ascertain that the disadvantages do not outweigh the advantages of glucocorticoid therapy. Further research is needed to ensure that patients are provided with the best possible care.

Keywords: glucocorticoid therapy, side effects, excess glucocorticoids, adverse effects

INTRODUCTION

Since the implementation of glucocorticoid therapy in the 1950s, when it was first used to treat a patient with rheumatic arthritis [1], glucocorticoids (GCs) have been introduced in a multitude of medical fields. Due to their anti-inflammatory and immunosuppressive properties GCs are one of the most widely employed types of drugs used. Another reason for their widespread use is the possibility of multiple routes of administration. GCs can be administered via injection, oral ingestion, inhalation, or topical application.

Steroid therapy has become an integral part of modern medicine. In the United States between 2009 and 2018 average annual prevalence of oral glucocorticoids was 6,8% with an annual growth rate of around 1,5% [2]. Long-term oral GCs prescriptions in the UK have increased by 34% over the past 20 years [3]. The global market for glucocorticoids has reached a value of almost 5 billion dollars and is expected to continue growing [4].

According to a recent cohort study, upper respiratory tract infections, intervertebral disc disorders, spinal conditions, allergies and bronchitis were the most common indications for short-term oral corticosteroid use [5].

The downside of this “miracle” drug is a multitude of adverse effects, especially related to oral glucocorticoids as their systemic bioavailability ranges from 76% up to 99% [6].

METABOLISM

Hyperglycemia was one of the first reported side effects of oral steroid therapy, appearing in the literature as early as the 1950s [7]. In a recent study, after 30-day observation period of 2424 patients on glucocorticoid therapy, overall frequency of glucocorticoid-induced hyperglycemia (GIH) was 33.5% [8].

Glucocorticoids have the opposite metabolic effect of insulin, promoting gluconeogenesis in the liver by upregulating gluconeogenic enzyme expression, including phosphoenolpyruvate carboxykinase and glucose-6-phosphatase [9]. Glucocorticoids also reduce insulin sensitivity by increasing visceral adiposity and leptin secretion, leading to

impaired glucose uptake in peripheral tissues. These metabolic disruptions impair pancreatic islets function by causing β-cell dysfunction which further exacerbates hyperglycemia [10].
Oral glucocorticoids are associated with the highest risk of hyperglycemia compared to other routes of administration. There is a clear correlation between GIH prevalence and administered dose of medication [11]. Among other factors associated with GIH and diabetes mellitius are abdominal obesity, hypertriglyceridemia, BMI over >25 kg/m2 or glycated haemoglobin (HbA1c) values over 6.0% [12,13]. Patients over the age of 60 are also at higher risk due to the decline in pancreatic beta-cell function and the increase in glucose intolerance with age [12].

CARDIOVASCULAR SYSTEM

Glucocorticoid therapy displays a significant impact on the cardiovascular system. The risk of hypertension in patients taking glucocorticoid drugs increased twofold in comparison with the placebo receiving control group [14]. The pathophysiology of steroid-induced hypertension lays in an imbalance between vasodilation and vasoconstriction. Various vasoactive agents activation, such as catecholamines or nitric oxide, are not without significance [15]. Moreover, obesity and dyslipidemia, among others adverse effects of excess GCs, are additional independent risk factors of hypertension [14].
A recent study found that individuals who had been prescribed systemic glucocorticoids exhibited a six-fold elevated risk of developing atrial fibrillation in comparison with the control group [16]. In another study prolonged use of glucocorticoids was connected to increased risk of coronary disease, heart failure and stroke [17].

OSTEOPOROSIS

Osteoporosis is a progressive disease where gradual decrease of bone density increases fragility and the risk of fractures [18].

GCs are the main culprit of drug-induced osteoporosis. Pathomechanism of glucocorticoid-induced osteoporosis (GIOP) consists of exacerbation of osteoclast activity as well as disrupted osteoblast precursors differentiation that leads to limited osteoblast formation. Stem cells in bone marrow are also affected and the osteoblast lineage decreases at the expense of the adipocyte lineage [19]. Studies show that up to 50% of patients with prolonged glucocorticoid therapy experience bone fractures. They can occur as soon as 3 months after the first dose of medication was administered [20]. Trabecular bones such as vertebral bodies

are especially susceptible to the detrimental impact of GCs. As only 30% of vertebral fractures are symptomatic, clinicians should pay particular attention to the follow-up care of their patients [21].

MUSCLE ATROPHY

Muscle weakness, especially the pelvic girdle muscles, is a result of fast-twitch type II muscle fibres damage. Glucocorticoid therapy impacts catabolic processes, particularly the ubiquitin-proteasome and autophagy-lysosomal pathways, which result in myofibril degeneration. In addition, GCs limit muscle protein synthesis by decreasing the concentration of insulin-like growth factor-I (IGF-I), a beneficial mediator of muscle development. Moreover, GCs upregulate myostatin concentration causing increased proteolysis. Prevalence of myopathy is higher in the elderly and in patients with other comorbidities, such as cancer or respiratory distress syndrome [22,23].

Glucocorticoid-induced skeletal muscle atrophy has a tremendous effect on patients' everyday lives. Easily fatigued after climbing stairs or marching, patients become unable to perform everyday physical activity unassisted and their quality of life reduces. In result, this independence turnover often leads to further socio-economic issues [22].

HYPOTHALAMIC-PITUITARY-ADRENAL AXIS

The hypothalamic-pituitary-adrenal axis balances endogenous cortisol levels through a negative feedback mechanism. Endogenous cortisol suppresses the release of corticotrophin-releasing hormone (CTH) from the hypothalamus and adrenocorticotropic hormone (ACTH) from the anterior pituitary. Excess glucocorticoids disrupt the homeostasis and can cause secondary and tertiary adrenal insufficiency which may continue even after the corticosteroid therapy has been ceased [24,25]. Adrenal insufficiency is a particularly perilous adverse effect of corticosteroid therapy as it can unfold in adrenal crisis, a life-threatening condition. In circumstances where the concentration of cortisol in the blood is insufficient, an excess of pro-inflammatory cytokines may result in the onset of uncontrolled inflammation, vasodilation and cardiac dysfunction. In clinical practice the patient would present with hypotension, hypoglycemia and shock [26,27].

Broersen and colleagues have found that endogenous glucocorticoids deficiency occurred in 48% of patients after oral steroid use and showed association with cumulative

glucocorticoid exposure. However, due to distinct individual variability neither treatment duration nor dose can accurately predict the risk of adrenal insufficiency [28]. Taking into consideration the lack of unambiguous risk factors and non-specific onset symptoms (e.g. fatigue or abdominal pain) the hypothalamic-pituitary-adrenal axis function should be closely monitored in patients during and after glucocorticoid therapy [27].

INFECTIONS

GCs use affects the immune response through intracellular glucocorticoid receptors, which when activated, modulate gene transcription and protein synthesis [29]. Glucocorticoids inhibit inflammatory cytokines production, such as tumor necrosis factor (TNF), IL-1, IL-3, or interferon (IFN). They reduce the number of eosinophils and basophils, impair the elimination of opsonized bacteria and inhibit mast cell proliferation. The adaptive immune system is also affected. As a result of glucocorticoid administration, T-cell activation and response are limited. Moreover, B-cell activating factor (BAFF) is substantially reduced resulting in lower concentration of immunoglobulins, especially IgG. In result, the number of immune cells at the site of infection and their ability to eliminate pathogens is scarce [30,31]. Thereupon increased risk of not only bacterial, viral and fungal infections but also opportunistic and latent infections is well recognised and have been confirmed by many studies.

Among rheumatic arthritis patients on DMARD therapy the rate of infection-related hospitalisations ranged from 5.2-17.7% in patients receiving glucocorticoids compared to 4,0-8,7% in patients not receiving GCs. The percentage of hospital admissions was in direct proportion to the cumulative and average daily glucocorticoid doses received. Pneumonia, UTIs and skin infections were the most common cause of hospitalisation [32,33].

CUSHINGOID FEATURES AND SKIN

Numerous hormonal and metabolic changes caused by excessive levels of GCs can manifest themselves in the external appearance of patients and are referred to as cushingoid features. A recent systematic review indicated cushingoid features as the third most common adverse effect of oral GCs in children, with a prevalence rate of 18.1% [34]. Due to fat tissue redistribution and fluid retention patients on glucocorticoid therapy can present with a moon face and a buffalo hump. A moon face is a term used in literature to describe a round, puffy, and swollen appearance of the face, whereas buffalo hump stands for accumulation of fat tissue

at the back of the neck and upper back. Another characteristic features of appearance are facial plethora, an exaggerated blood flow to the face, and hirsutism stemming from hormonal imbalance [35].

Impaired collagen synthesis results in excessively thin and fragile “parchment-like” skin. Another side effects of excessive corticosteroids are striae, elongated red or purple streaks arising from rapid skin stretching. Striae most commonly appear on the stomach, back and bottom. Moreover, due to weakened skin tissue, more frequent and easier bruising can occur. Because of the immune system suppression, the ability of the skin to regenerate and repair is compromised which leads to delayed wound healing [36].

DIGESTIVE TRACT

Gastritis, peptic ulceration, and gastrointestinal bleeding are among the most significant gastrointestinal complications of oral glucocorticoids therapy. Interestingly, studies have showed that adding glucocorticoids to non-steroidal anti-inflammatory therapy doubled the risk of these adverse effects [37]. Regarding peptic ulcers formation, duration of therapy, as opposed to dose, was of greater impact [38].

Although other potential variables cannot be excluded, it is estimated that 3% of drug-related pancreatitis is glucocorticoid-induced [39]. It was also found that patients on oral GCs therapy had higher risk of acute pancreatitis compared with non-users [37].

MENTAL HEALTH

Although psychiatric and cognitive side effects of oral glucocorticoid medications are uncommon and less known, they cannot be excluded. Exposure to exogenous glucocorticoids has been linked with higher risk of psychosis, depression and anxiety. Cognitive decline in the form of impaired memory, concentration and mental processing speed can also occur and are referred to as the “steroid dementia syndrome” in literature [6,40,41]. There is a clear correlation between these adverse psychiatric and cognitive side effects and the dose of administered glucocorticoids. The reversibility of these impairments is still a matter of debate [42].

FETUS DEVELOPMENT

The range of pharmacotherapy options for pregnant women is severely restricted due to the potential impact of many drugs on embryogenesis. However, in cases where the patient's clinical condition necessitates it and the benefits outweigh the risks, drugs such as glucocorticoids may be considered.

Studies show that exposure to GCs during fetal life causes upregulation of GLUT1 transporters. As GLUT1 is a glycoprotein responsible for the transport of glucose into the heart cells, it results in disrupted cardiac glucose metabolism in fetus. Moreover, GCs exposure can cause decreased ventricular weight and hypertrophy of the myocardium [43].

The hypothalamic-pituitary-adrenal axis is particularly sensitive to glucocorticoid levels. Fetuses of mothers taking GCs were shown to have lower concentration of hormones such as cortisol, ACTH and DHEA than controls. Hormone levels were measured in cord blood and amniotic fluid [44]. However, basal cortisol levels determined in heel-prick blood draw in infants exposed to glucocorticoids in uteru showed normal values as soon as in the first week of neonatal life [45,46].

CONCLUSIONS

Although there are numerous indications for glucocorticoid therapy, there are instances in which this treatment can exacerbate a patient's condition and result in adverse outcomes. Thereupon it is crucial to inform patients not only about the benefits of GCs therapy but also about the risks and side effects associated with it. In addition, more attention should be paid to deepen the knowledge of medical personnel on the incidence and severity of various adverse effects of GCs so that they can plan treatments accordingly. In conclusion, further research is needed to better understand the mechanisms and interrelations of glucocorticoid therapy as valid reliable data is still scarce.

Author contributions

Conceptualization, MG and PP; methodology, MK and MG; software, not applicable; check, MK, MZ and PP; formal analysis, MG, PP, JF; investigation, MG and MZ; resources, not applicable; data curation, MG; writing- rough preparation, MG; writing - review and editing, MG, MZ and MK; visualization, MK, MZ; supervision, JF; project administration, PP;

receiving funding, not applicable. All authors have read and agreed with the published version of the manuscript.

Funding Statement

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

Not applicable.

Acknowledgments

Not applicable.

Conflicts of Interest

The authors declare no conflict of interest.

BIBLIOGRAPHY:

[1] Kirwan JR, Balint G, Szebenyi B. Anniversary: 50 years of glucocorticoid treatment in rheumatoid arthritis. Rheumatology 1999;38:100–2. https://doi.org/10.1093/RHEUMATOLOGY/38.2.100.

[2] Wallace BI, Tsai HJ, Lin P, Aasbjerg K, Wu AC, Tsai YF, et al. Prevalence and prescribing patterns of oral corticosteroids in the United States, Taiwan, and Denmark, 2009–2018. Clin Transl Sci 2023;16:2565–76. https://doi.org/10.1111/CTS.13649.

[3] Fardet L, Petersen I, Nazareth I. Prevalence of long-term oral glucocorticoid prescriptions in the UK over the past 20 years. Rheumatology (Oxford) 2011;50:1982–90. https://doi.org/10.1093/RHEUMATOLOGY/KER017.

[4] Steroid-Corticosteroids - Market, Report Size, Worth, Revenue, Growth, Industry Value, Share 2024 n.d. https://reports.valuates.com/market-reports/QYRE-Auto-1C374/global-steroid-corticosteroids (accessed December 29, 2024).

[5] Waljee AK, Rogers MAM, Lin P, Singal AG, Stein JD, Marks RM, et al. Short term use of oral corticosteroids and related harms among adults in the United States: population based cohort study. The BMJ 2017;357:j1415. https://doi.org/10.1136/BMJ.J1415.

[6] Pofi R, Caratti G, Ray DW, Tomlinson JW. Treating the Side Effects of Exogenous Glucocorticoids; Can We Separate the Good From the Bad? Endocr Rev 2023;44:975. https://doi.org/10.1210/ENDREV/BNAD016.

[7] INGLE DJ, BEARY DF, PURMALIS A. Some further observations on steroid diabetes in the rat. Acta Endocrinol (Copenh) 1954;15:129–32. https://doi.org/10.1530/ACTA.0.0150129.

[8] Delfs N, Struja T, Gafner S, Muri T, Baechli C, Schuetz P, et al. Outcomes of Hospitalized Patients with Glucocorticoid-Induced Hyperglycemia—A Retrospective Analysis. J Clin Med 2020;9:4079. https://doi.org/10.3390/JCM9124079.

[9] Van Raalte DH, Diamant M. Steroid diabetes: from mechanism to treatment? Neth J Med. 2014 Feb;72(2):62-72. PMID: 24659588.

[10] Cho JH, Suh S. Glucocorticoid-Induced Hyperglycemia: A Neglected Problem. Endocrinology and Metabolism 2024;39:222. https://doi.org/10.3803/ENM.2024.1951.

[11] Blackburn D, Hux J, Mamdani M. Quantification of the Risk of Corticosteroid-induced Diabetes Mellitus Among the Elderly. J Gen Intern Med 2002;17:717. https://doi.org/10.1046/J.1525-1497.2002.10649.X.

[12] Nakamura H, Fujieda Y, Nakamura A, Atsumi T. How should rheumatologists manage glucocorticoid-induced hyperglycemia? Mod Rheumatol 2021;31:519–28. https://doi.org/10.1080/14397595.2020.1823060.

[13] Katsuyama T, Sada KE, Namba S, Watanabe H, Katsuyama E, Yamanari T, et al. Risk factors for the development of glucocorticoid-induced diabetes mellitus. Diabetes Res Clin Pract 2015;108:273–9. https://doi.org/10.1016/J.DIABRES.2015.02.010.

[14] Fardet L, Fève B. Systemic glucocorticoid therapy: A review of its metabolic and cardiovascular adverse events. Drugs 2014;74:1731–45. https://doi.org/10.1007/S40265-014-0282-9/METRICS.

[15] Ong SLH, Whitworth JA. How do glucocorticoids cause hypertension: role of nitric oxide deficiency, oxidative stress, and eicosanoids. Endocrinol Metab Clin North Am 2011;40:393–407. https://doi.org/10.1016/J.ECL.2011.01.010.

[16] Van Der Hooft CS, Heeringa J, Brusselle GG, Hofman A, Witteman JCM, Kingma JH, et al. Corticosteroids and the risk of atrial fibrillation. Arch Intern Med 2006;166:1016–20. https://doi.org/10.1001/ARCHINTE.166.9.1016.

[17] Wei L, MacDonald TM, Walker BR. Taking glucocorticoids by prescription is associated with subsequent cardiovascular disease. Ann Intern Med 2004;141. https://doi.org/10.7326/0003-4819-141-10-200411160-00007.

[18] Kuai J, Zheng J, Kumar A, Gao H. Anti-inflammatory, antiosteoporotic, and bone protective effect of hydroxysafflor yellow A against glucocorticoid-induced osteoporosis in rats. J Biochem Mol Toxicol 2024;38. https://doi.org/10.1002/JBT.23797.

[19] Gado M, Baschant U, Hofbauer LC, Henneicke H. Bad to the Bone: The Effects of Therapeutic Glucocorticoids on Osteoblasts and Osteocytes. Front Endocrinol (Lausanne) 2022;13:835720. https://doi.org/10.3389/FENDO.2022.835720/BIBTEX.

[20] Ziambaras K, Civitelli R. Epidemiology of glucocorticoid-induced osteoporosis. J Endocrinol Invest 2008;7:2–6. PMID: 18791344.

[21] Berris KK, Repp AL, Kleerekoper M. Glucocorticoid-induced osteoporosis. Curr Opin Endocrinol Diabetes Obes 2007;14:446–50. https://doi.org/10.1097/MED.0B013E3282F15407.

[22] Bodine SC, Furlow JD. Glucocorticoids and Skeletal Muscle. Adv Exp Med Biol 2015;872:145–76. https://doi.org/10.1007/978-1-4939-2895-8_7.

[23] Lee MK, Jeong HH, Kim MJ, Ryu HY, Baek JW, Lee BG. Nutrients against Glucocorticoid-Induced Muscle Atrophy. Foods 2022;11:687. https://doi.org/10.3390/FOODS11050687.

[24] Martin-Grace J, Dineen R, Sherlock M, Thompson CJ. Adrenal insufficiency: Physiology, clinical presentation and diagnostic challenges. Clin Chim Acta 2020;505:78–91. https://doi.org/10.1016/J.CCA.2020.01.029.

[25] Arlt W, Allolio B. Adrenal insufficiency. Lancet 2003;361:1881–93. https://doi.org/10.1016/S0140-6736(03)13492-7.

[26] Kesari S, Barron C, Cohen LE, Regelmann MO, Baer TG. Dexamethasone swish and spit: A cause of iatrogenic adrenal insufficiency. Pediatr Blood Cancer 2024;71:e31138. https://doi.org/10.1002/PBC.31138.

[27] Dinsen S, Baslund B, Klose M, Rasmussen AK, Friis-Hansen L, Hilsted L, et al. Why glucocorticoid withdrawal may sometimes be as dangerous as the treatment itself. Eur J Intern Med 2013;24:714–20. https://doi.org/10.1016/J.EJIM.2013.05.014.

[28] Broersen LHA, Pereira AM, Jørgensen JOL, Dekkers OM. Adrenal Insufficiency in Corticosteroids Use: Systematic Review and Meta-Analysis. J Clin Endocrinol Metab 2015;100:2171–80. https://doi.org/10.1210/JC.2015-1218.

[29] J. M. Schaaf M, Meijer OC. Immune Modulations by Glucocorticoids: From Molecular Biology to Clinical Research. Cells 2022, Vol 11, Page 4032 2022;11:4032. https://doi.org/10.3390/CELLS11244032.

[30] Chastain DB, Spradlin M, Ahmad H, Henao-Martínez AF. Unintended Consequences: Risk of Opportunistic Infections Associated With Long-term Glucocorticoid Therapies in Adults. Clinical Infectious Diseases 2024;78:e37–56. https://doi.org/10.1093/CID/CIAD474.

[31] Franco LM, Gadkari M, Howe KN, Sun J, Kardava L, Kumar P, et al. Immune regulation by glucocorticoids can be linked to cell type-dependent transcriptional responses. J Exp Med 2019;216:384–406. https://doi.org/10.1084/JEM.20180595.

[32] George MD, Baker JF, Winthrop K, Hsu JY, Wu Q, Chen L, et al. Risk for Serious Infection With Low-Dose Glucocorticoids in Patients With Rheumatoid Arthritis A Cohort Study. Ann Intern Med 2020;173:870. https://doi.org/10.7326/M20-1594.

[33] Wilson JC, Sarsour K, Gale S, Pethö-Schramm A, Jick SS, Meier CR. Incidence and Risk of Glucocorticoid-Associated Adverse Effects in Patients With Rheumatoid Arthritis. Arthritis Care Res (Hoboken) 2019;71:498–511. https://doi.org/10.1002/ACR.23611.

[34] Aljebab F, Choonara I, Conroy S. Systematic Review of the Toxicity of Long-Course Oral Corticosteroids in Children. PLoS One 2017;12:e0170259. https://doi.org/10.1371/JOURNAL.PONE.0170259.

[35] Newell-Price J, Bertagna X, Grossman AB, Nieman LK. Cushing's syndrome. Lancet 2006;367:1605–17. https://doi.org/10.1016/S0140-6736(06)68699-6.

[36] Castinetti F, Morange I, Conte-Devolx B, Brue T. Cushing's disease. Orphanet J Rare Dis 2012;7:41. https://doi.org/10.1186/1750-1172-7-41.

[37] Oray M, Abu Samra K, Ebrahimiadib N, Meese H, Foster CS. Long-term side effects of glucocorticoids. Expert Opin Drug Saf 2016;15:457–65. https://doi.org/10.1517/14740338.2016.1140743.

[38] Filaretova L, Podvigina T, Yarushkina N. Physiological and Pharmacological Effects of Glucocorticoids on the Gastrointestinal Tract. Curr Pharm Des 2020;26:2962–70. https://doi.org/10.2174/1381612826666200521142746.

[39] Wolfe D, Kanji S, Yazdi F, Barbeau P, Rice D, Beck A, et al. Drug induced pancreatitis: A systematic review of case reports to determine potential drug associations. PLoS One 2020;15:e0231883. https://doi.org/10.1371/JOURNAL.PONE.0231883.

[40] Pivonello R, Simeoli C, De Martino MC, Cozzolino A, De Leo M, Iacuaniello D, et al. Neuropsychiatric disorders in Cushing's syndrome. Front Neurosci 2015;9. https://doi.org/10.3389/FNINS.2015.00129.

[41] Wolkowitz OM, Lupien SJ, Bigler ED. The "steroid dementia syndrome": a possible model of human glucocorticoid neurotoxicity. Neurocase 2007;13:189–200. https://doi.org/10.1080/13554790701475468.

[42] De Alcubierre D, Ferrari D, Mauro G, Isidori AM, Tomlinson JW, Pofi R. Glucocorticoids and cognitive function: a walkthrough in endogenous and exogenous alterations. J Endocrinol Invest 2023;46:1961. https://doi.org/10.1007/S40618-023-02091-7.

[43] Zhao C, He L, Li L, Deng F, Zhang M, Wang C, et al. Prenatal glucocorticoids exposure and adverse cardiovascular effects in offspring. Front Endocrinol (Lausanne) 2024;15:1430334. https://doi.org/10.3389/FENDO.2024.1430334.

[44] Tegethoff M, Pryce C, Meinlschmidt G. Effects of Intrauterine Exposure to Synthetic Glucocorticoids on Fetal, Newborn, and Infant Hypothalamic-Pituitary-Adrenal Axis Function in Humans: A Systematic Review. Endocr Rev 2009;30:753–89. https://doi.org/10.1210/ER.2008-0014.

[45] Braun T, Challis JR, Newnham JP, Sloboda DM. Early-life glucocorticoid exposure: the hypothalamic-pituitary-adrenal axis, placental function, and long-term disease risk. Endocr Rev 2013;34:885–916. https://doi.org/10.1210/ER.2013-1012.

[46] Matthews SG, Owen D, Kalabis G, Banjanin S, Setiawan EB, Dunn EA, et al. Fetal Glucocorticoid Exposure and Hypothalamo-Pituitary-Adrenal (HPA) Function After Birth. Endocr Res 2004;30:827–36. https://doi.org/10.1081/ERC-200044091.