THE NEW ARMENIAN MEDICAL JOURNAL
Vol.16 (2022), No 1 p. 94-100
DOI: https://doi.org/10.56936/18290825-2022.16.1-94

ORTHODONTIC TREATMENT ALGORITHM FOR PATIENTS WITH POSITIVE DRUG ANAMNESIS. GLUCOCORTICOIDS

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Received 20.11.2021; accepted for printing 18.01.2022

Abstract

Glucocorticoids are the most prescribed drugs for the treatment of inflammatory, allergic and autoimmune diseases. However, a wide range of side effects can negatively affect the process of active orthodontic treatment and the stability of results.

The study aimed to identify the side effects of glucocorticoids that negatively affect orthodontic treatment and retention period, to develop an orthodontic treatment algorithm for patients taking glucocorticoids on regular basis in different drug release forms (intra-articular injections, tablets, inhalations, sprays, ointments/creams), to test the algorithm in clinical practice.

An electronic search of published meta-analyzes and systematic reviews included in databases (Cochrane Library, EMBASE and MEDLINE, Web of Science) was used. In clinical part of our own research 348 patients were included with any type of orthodontic pathology (patients age 5-53 years).

The total number of articles found was 23. The algorithm contains clinical recommendations during active treatment and retention period for patients taking glucocorticoids in various drug release forms. Among 348 patients, 27 patients (7.8%) aged 6 to 53 years, used glucocorticoids on regular basis. From them 8 patients (29.6%) used glucocorticoids nasal sprays (beclomethasone, budesonide), 8 patients (29.6%) – ointments/creams (betamethasone, methylprednisolone), 9 patients (33.3%) used corticosteroids by inhalation (budesonide, beclomethasone) and 2 patients (7.4%) – per os 3 patients (11.1%) simultaneously used glucocorticoids in 2 different forms (nasal sprays + inhalations, inhalations + ointments).

1. Decreased bone mineral density, a possible skeletal growth retardation in children, increased risk of caries, candidiasis and xerostomia are the most common side effects, which could affect orthodontic treatment negatively.

2. For 27 patients (7.8%) treatment plan and orthodontic procedures were carried out in accordance with medical and positive drug anamnesis.

Keywords: *glucocorticoids, orthodontic treatment, anamnesis.*

Introduction

Glucocorticoids (GCS) are traditionally used for a wide range of inflammatory, allergic, autoimmune diseases, as well as immunosuppressive therapy.

Over the past decade in dermatological practice, there has been an increasing number of patients with skin and subcutaneous tissue diseases. 6.4-6.9 millions of new cases such diseases are registered annually [*Belousova T, Kail M, 2020*]. Topical steroids (ointments/creams) are successfully used in dermatology for the treatment of eczema, allergic skin diseases, atopic and contact dermatitis in children and adults [*Levina Y et al., 2019*].

Modern treatment plan of allergic rhinitis, adenoiditis, acute and chronic rhinosinusitis, as well as the management of the postoperative period during intervention in the nasal cavity and paranasal sinuses include the use of topical GCS in the form of sprays and inhalations [*Garashchenko T,*

Cite This Article as:

Tsvetkova M.A., Sohov S.T. (2022); Orthodontic treatment algorithm for patients with positive drug anamnesis. Glucocorticoids.; NAMJ v.16 (2022) No.1, p. 94-100;
DOI: https://doi.org/10.56936/18290825-2022.16.1-94

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Tarasova G, 2020].

Inhaled forms of corticosteroids are one of the fundamental method of basic therapy for chronic obstructive pulmonary disease, asthma and interstitial lung diseases, and in case of exacerbations, systemic corticosteroids are also used [*Gavrisyuk V, Gumenyuk G, 2015*].

There is no rheumatic disease in which GCS would not be used in certain regimes. For systemic connective tissue diseases and vasculitis, GCS are first-line drugs. Without using GCS, it is impossible to achieve clinical and laboratory remission [*Kovalenko V et al., 2018*].

In addition to the various therapeutic effects, corticosteroids have side effects that directly depend on the dosage used and the duration of treatment. Some authors highlight the minimum dangerous doses, below which side effect development is unlikely [*Ruiz-Irastorza G et al., 2012*]. However, according to other authors, there is no lower dose limit for most of the side effects, and, for example, treatment with GCS for more than 6 months will lead to bone mineral density loss regardless of dosage used [*Kavanaugh A, Wells A, 2014*].

Due to the widespread distribution of GCS and a wide range of side effects that can negatively affect the active orthodontic treatment and stability of the result, the orthodontist should develop treatment plan according to systemic manifestations of GCS and patient's anamnesis.

The study aimed to investigate the results of systematic reviews and meta-analyzes conducted on the effect of GCS on bone metabolism and to determine the side effects of GCS that negatively affect orthodontic treatment and retention period;

2. To develop an orthodontic treatment algorithm for patients taking GCS on regular basis in different clinical forms (injections, tablets, inhalations, sprays, ointments/creams);

3. To test the algorithm in clinical practice.

Material and methods

An electronic search of published meta-analyzes and systematic reviews included in databases (Cochrane Library, EMBASE and MEDLINE, Web of Science) was using the following search terms in titles and abstracts: "orthodontic treatment"; "orthodontic tooth movement"; "GCS and bone metabolism"; "GCS side effects"; "GCS osteoporosis"; "GCS/oral health".

The search depth was 10 years. References from the found articles were scanned for additional relevant publications.

The selection criteria for published articles were:

- clinical or experimental animal studies with the presence of an experimental and a control group;
- systemic or local use of corticosteroids, capable of influencing the physiological bone remodeling within the framework of both its mechanism of action and as a result of side effects;
- a detailed description of dosages and methods of administration;
- a detailed description of used orthodontic appliances, indication of force levels and activation mode, a description of the method for calculating the speed of teeth movement.

The analysis of this scientific literature served as the evidence base for the development of orthodontic treatment algorithm.

General information on the medications and their effects derived from the following web sites: https://www.vidal.ru, https://www.rlsnet.ru.

In clinical part of our own research 348 patients were included with any type of orthodontic pathology (patients age from 5 to 53 years).

Results

The total number of articles found was 23.

The algorithm contains clinical recommendations during active treatment and retention period for patients taking GCS in various drug releasing forms (intra-articular injections, tablets, inhalations, sprays, ointments/creams) (Fig. 1).

Among 348 patients who came for consultation and orthodontic treatment, 27 patients (7.8%) aged 6 to 53 years, used GCS on regular basis. From them, 8 patients (29.6%) used GCS nasal sprays (beclomethasone, budesonide), 8 patients (29.6%) - ointments/creams (betamethasone, methylprednisolone), 9 patients (33.3%)

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

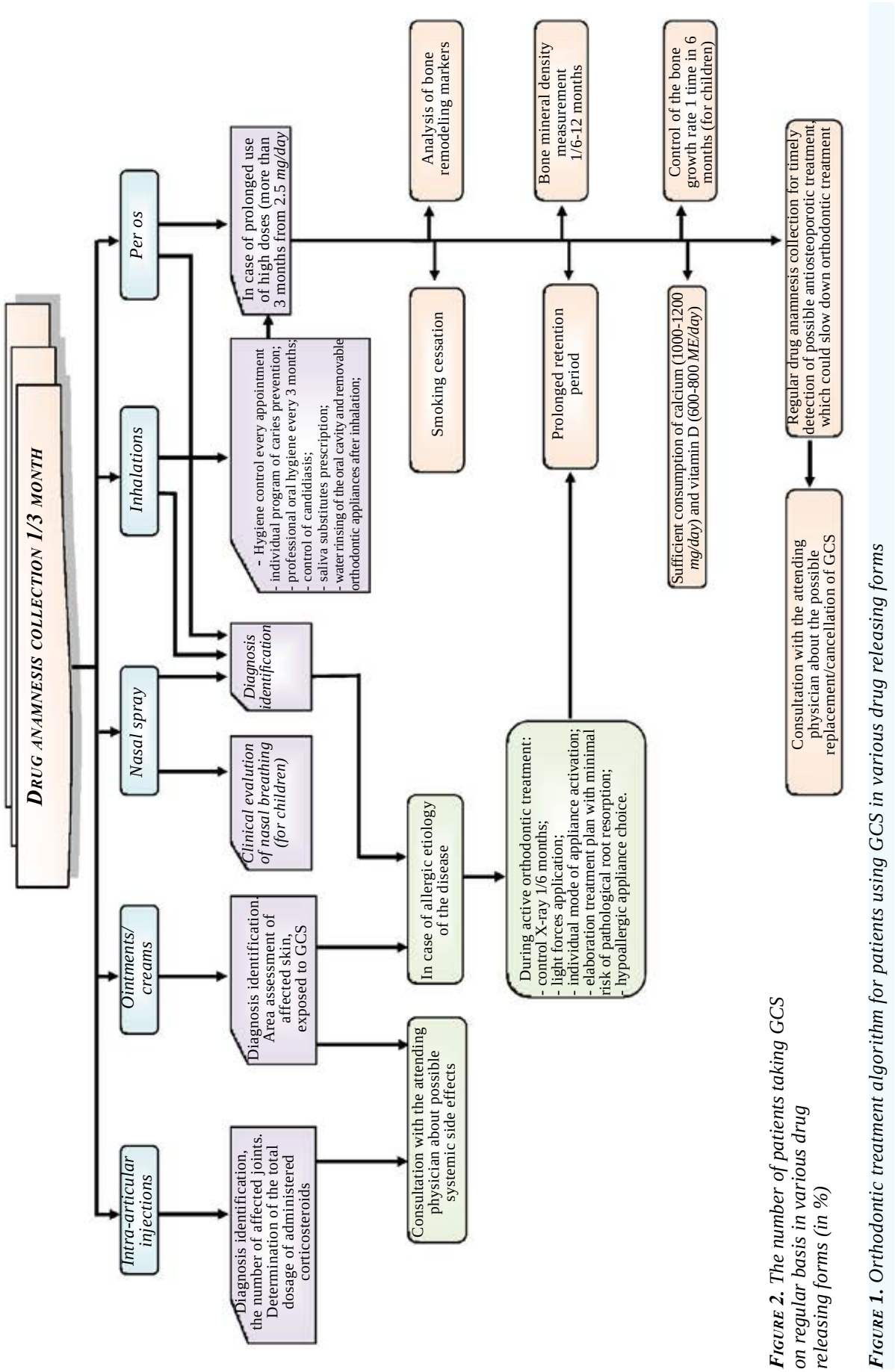

Figure 1. *Orthodontic treatment algorithm for patients using GCS in various drug releasing forms*

Figure 2. *The number of patients taking GCS on regular basis in various drug releasing forms (in %)*

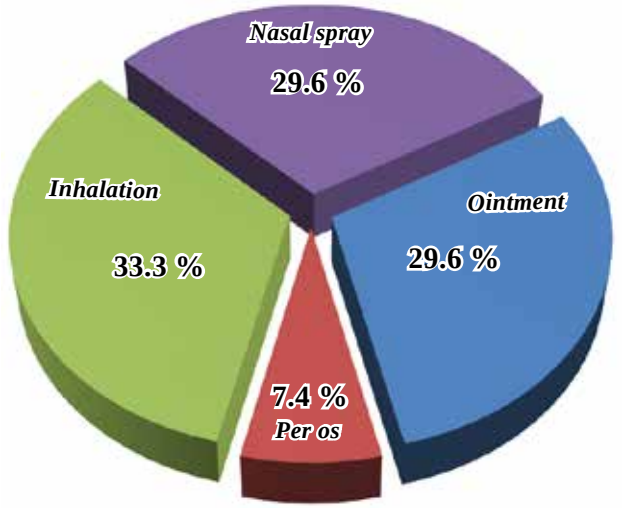

Figure 2. *The number of patients taking GCS on regular basis in various drug releasing forms (in %)*

used corticosteroids by inhalation (budesonide, beclomethasone) and 2 patients (7.4%) - per os 3 patients (11.1%) simultaneously used GCS in 2 different forms (nasal sprays + inhalations, inhalations + ointments) (Fig. 2).

Our study identified 8 patients from 6 to 14 years old with a diagnosis of atopic dermatitis. All patients used GCS locally as prescribed by a dermatologist. The consultation with the treating dermatologists made it possible to assess the area of the affected skin exposed to GCS, the bioavailability of the active components of ointments/creams in order to predict the probable systemic side effects occurrence. Since atopic dermatitis is an allergic disease, for patients treated with fixed appliances, an orthodontic treatment plan was developed with a minimal risk of root resorption (shortening of active treatment duration, using light forces, choosing a treatment plan that does not involve intrusion and movement of teeth over a long distance). In addition, patients were referred for control panoramic x-ray once every 6 months. A consultation with a allergologist revealed the absence of allergic reactions to nickel, latex, polymers, composites, etc., which determined the absence of contraindications to the choice of appliances.

Among patients using GCS-based nasal sprays, 5 patients (from 6 to 10 years old) reported the presence of adenoiditis, 3 patients (from 9 to 38 years old) - presence of chronic allergic rhinitis/sinusitis. All patients underwent a clinical assessment of nasal breathing, according to the results of which 2 patients were referred to an otorhinolaryngologist in order to improve respiratory function of the upper airways. The orthodontic treatment plan was developed also taking into account the allergic anamnesis.

Nine patients with obstructive bronchitis (7 people) and asthma (2 people) from 6 to 53 years old used inhaled GCS. When drawing up a plan of orthodontic treatment, the allergic status of each patient was taken into account. Since the inhalation use of GCS can contribute to the development of xerostomia, candidiasis and dental caries progression, we assessed level of hygiene at each appointment, gave recommendations on caries prevention, prevented opportunistic diseases, and prescribed saliva substitutes.

Two patients with diagnoses of systemic lupus erythematosus in remission and elevated cortisol levels, respectively, regularly took oral corticosteroids.

For all patients in the study, the doses of corticosteroids used did not exceed 2.5 *mg/day* in prednisolone equivalent. However, regardless of the dosage, all patients were recommended a prolonged retention period, smoking cessation, a balanced diet with a sufficient content of calcium and vitamin D3, as well as consultation with the attending physician about the possible replacement/cancellation of GCS.

For all children skeletal growth parameters were compared with age norms once every 6 months. No deviations in the rate of skeletal development were found.

Discussion

The bioavailability of GCS is the amount of active substance entering the systemic circulation, as a percentage of the administered dose [*Emelyanov A, 2018*]. Plenty of drugs related to GCS can differ significantly in terms of systemic bioavailability. This parameter largely determines the risk of side effects [*Kryukov A et al., 2016*].

An orthodontist during active treatment and planning of the retention period should take into account that the simultaneous combination of various forms of GCS, the duration of use, dosage and bioavailability of a particular drug can lead to an increase in the total concentration of GCS and the development of systemic complications.

The frequency of side effect occurrence and their severity during treatment with oral and topical corticosteroids differ significantly, since topical corticosteroids act locally, and their overall effect is due only to that part of the dose that enters the systemic circulation. Thus, when using GCS per os, the likelihood of developing systemic side effects is maximum due to the high concentration of the drug reaching the bloodstream [*Knyazheskaya N, 2012*].

One of the general complications of GCS usage is the development of osteoporosis. Corticosteroids interfere with the physiological interaction of resorption and bone formation, promoting excessive resorption. Even low doses of corticosteroids can directly affect osteoblast cells (by reducing the ratio of osteoprotegerin and increasing receptor activator of nuclear factor kappa-B ligand), disrupting their differentiation and slowing down collagen synthesis, keeping the rate of bone resorption by osteoclasts at the same level, which ultimately leads to the development of osteoporosis [*Briot K, 2018*]. Hsu E. (2017) said that prednisolone at a dosage of 2.5 *mg/d* for more than 3 months is an indication for measuring bone mineral density (BMD). However, in some patients, even lower doses of drugs can negatively affect this parameter. Thus, the severity of osteoporosis increases with a combination of GCS with other concomitant diseases that contribute to a decrease BMD, with a family history of osteoporosis, smoking, postmenopausal period [*Waljee A et al., 2017*].

In case of a decreased BMD during active treatment, the orthodontist is recommended to use light forces, to shorten the interval between activations of the appliance, as well as to increase the duration of the retention period. Regular analysis of the drug anamnesis and communication with a general doctor are necessary for the timely detection of antiosteoporotic drugs prescription, which can negatively affect the overall duration and results of orthodontic treatment.

Complete cancellation of GCS or a significant reduction in dosage agreed with the attending physician, as well as an improvement in BMD due to a diet rich in calcium and vitamin D3, smoking cessation and/or drug treatment of osteoporosis will have a favorable effect on the teeth position stability in retention period [*Huang J et al., 2019*].

Long-term use of corticosteroids in children can slow down skeletal growth. This must be taken into account when planning an orthodontic treatment, based on jaw growth stimulation.

Despite the low likelihood of developing systemic side effects, topical corticosteroids can cause local side effects that negatively affect orthodontic treatment. Local complications caused by inhalation of corticosteroids occur in 55-58% of cases. One of the most common complication in the oral cavity is candidiasis, the incidence of which ranges from 5 to 25% of patients [*Gavrisyuk V, Gumenyuk G, 2015*]. In addition, long-term use of corticosteroids in the form of inhalation is associated with an increased risk of multiple caries in children [*Wogelius P et al., 2004*]. Rinsing with water oral cavity and removable orthodontic appliances after inhalation, as well as hygiene control and caries prevention procedures will reduce the concentration of GCS in the oral cavity and reduce the likelihood of local side effects. In case of xerostomia, the prescription of saliva substitutes is indicated.

With the local use of GCS, the development of systemic complications is also possible. Komerik N. and co-authors (2005) found that the BMD of the mandible was significantly lower in patients taking inhaled corticosteroids for a long time, compared with healthy people who made up the control group.

Clinical evaluation of nasal breathing is an important part of comprehensive orthodontic diagnostics. Ear, nose, and throat pathology and, as a consequence, unfavorable change in myodynamic balance, lead to pronounced deformities of facial skeleton. Patients using intranasal corticosteroids have a low risk of developing systemic side effects [*Tae Y, Young H, 2016*]. However, with the use of nasal sprays for a long time and in high dosage, the likelihood of systemic side effects increases [*Gulliver T, Eid N, 2005*]. Thus, according to Allen D.B. (2000), a decrease in rate of skeletal growth can be observed with frequent intranasal use of certain corticosteroids (2 times a day) for a long time. The communication of the orthodontist with the otorhinolaryngologist should be focused on the possibility of complete restoration of nasal breathing and the rejection of GCS.

The use of corticosteroids in the form of oint-

ments, due to their ability to have an anti-inflammatory and proliferative effect, has become the main treatment of many dermatological diseases [*Ghosh A, Coondoo A, 2018*]. The absorption of ointments containing GCS increases when applied to damaged skin or mucous membranes. Patients with large erosive or atrophic foci, with open blood vessels on the ulcerated surface have an increased risk of side effects. Children are more susceptible to the development of systemic side effects with topical application of corticosteroids due to the greater ratio of the total surface area of the skin to body weight, due to the high absorption capacity of children's skin and the slow metabolism of drugs in children compared to adults [*Jinagal J et al., 2019*].

Intra-articular injections of GCS rarely cause systemic complications unless it used frequently, in many joints and in high dosage [*Baid S, Nieman L, 2006*]. During anamnesis collection, an orthodontist should verify the diagnosis and consult with the attending physician about possible systemic complications.

One of the most common reasons for prescribing GCS in any drug releasing forms is allergic reactions. In case of positive allergoanamnesis, an orthodontist should develop treatment plan with a minimal risk of root resorption, use light forces, choose hypoallergenic appliances and make control X-rays once every 6 months.

Conclusion

The research of published scientific studies revealed a wide range of systemic and local side effects caused by GCS, and can negatively affect orthodontic treatment and stability in the retention period (decreased BMD, a possible skeletal growth retardation in children, increased risk of caries, candidiasis and xerostomia).

Orthodontic treatment algorithm for patients using GCS in various drug releasing forms is a practical guide for treatment plan definition, additional diagnostic and therapeutic procedures and consultations with other medical specialists.

Using algorithm, for 27 patients (7.8%) orthodontic treatment plan and the appliance activation mode were elaborate in accordance with medical and positive drug anamnesis. Among them, 13 patients (48.1%) were referred for the consultations with allergologist, 2 patients (7.4%) - with otorhinolaryngologist. All patients taking corticosteroids in any drug releasing forms were advised to consult with their attending physician about the degree of underlying disease compensation, to determine of contraindications to orthodontic treatment and possible replacement of corticosteroids with an analog without a negative effect on bone metabolism.

Constant contact with other medical specialists and regular analysis of the medical and drug anamnesis are necessary for successful orthodontic treatment.

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Vol.16 (2022). No 1

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THE NEW ARMENIAN MEDICAL JOURNAL

Vol.16 (2022). No 1

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