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Family Physicians' Awareness of the Burden of Oral Corticosteroids in Asthma Patients

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Abstract

Objective. The objective of this study was to identify when family physicians decide to prescribe oral corticosteroids (OCS) to treat asthma, to establish the factors affecting their decision, and how familiar family physicians are with the side effects of OCS. **Materials and Methods.** A cross-sectional observational study was conducted among physicians that are members of the Slovenian Family Medicine Society. **Results.** The study included 122 family physicians from all 12 Slovenian regions. The great majority (86.9%) reported they had previously prescribed OCS to asthma patients. The largest share of these (45.1%) tended to prescribe a limited number of tablets, although many (42.6%) also prescribed the entire pack. Regarding the adverse effects associated with OCS, the physicians listed a range of potential problems, highlighting hyperglycemia and exacerbated diabetes, the impact on bone density, a suppressed immune system and increased risk of infection as the most common. **Conclusion.** In the future, it is vital to improve family physicians' awareness of when OCS may be prescribed to treat severe asthma, and to define the clinical pathway for severe asthma, which should also involve interdisciplinary collaboration.

Key Words: Family Physician ▪ Oral Corticosteroids ▪ Referrals ▪ Severe Asthma ▪ Treatment.

Introduction

Asthma is a chronic inflammatory disease of the airways and one of the most common chronic lung diseases. Ten percent of the population in the developed world has been diagnosed with asthma, and physicians at all levels of healthcare deal with the disease. In Slovenia, the prevalence of asthma in adults aged 18 to 65 years is quite high, at 16% (1). Asthma patients may not experience any problems; they may only experience individual symptoms, such as shortness of breath, coughing, and wheezing; or they may suffer from severe asthma, which often worsens over time. Most asthma patients are managed by primary care physicians, and 22% are regularly treated by a specialist (2, 3).

Roughly 17% of asthma patients are prescribed a high-dose inhaled therapy, but their asthma is still not under control. This is referred to as difficult-to-control asthma. Its causes may vary from an incorrect inhalation technique and poor adherence, to treatment of comorbidities that can exacerbate asthma (4). Severe asthma is a subtype of difficult-to-control asthma and comprises cases in which the asthma remains uncontrolled even though all the causes of difficult-to-control asthma have been suitably addressed. It is estimated that around 2.4% to 4% of asthma patients have severe asthma. These patients are also eligible for biological therapy (5). Uncontrolled asthma is characterized by poor symptom control (frequent use of a rescue inhaler, activities limited by asthma, or nocturnal awakening caused by asthma) or frequent exacerbations that require two or more courses of oral corticosteroids (OCS) in a 12-month period, or one or more asthma-related hospitalizations in a 12-month period (3, 6).

The goal of asthma management is to control symptoms and reduce the risk of asthma exacerbation, permanently reduced lung function, and severe exacerbations that may also be fatal. Recommendations by the Global Initiative for Asthma (GINA) (3) focus on the latest high-quality evidence available, and scientific consistency. Its reports are updated and posted online annually. They are the most frequently cited evidence-based recommendations for the optimal management of asthma in adults and children. The GINA recommendations also form the basis for the Slovenian guidelines (1).

Inhaled corticosteroids (controllers) are used for the initial anti-inflammatory treatment of asthma, and they are considered the primary treatment. Relievers are used as needed in the event of problems or disease exacerbations. In addition to short-acting beta antagonists, an ICS-formoterol combination inhaler (i.e., a specific long-acting and rapid-onset bronchodilator) may also be used as a reliever.

In the event of acute asthma exacerbation, the physician should prescribe OCS in the recommended dose of 32 mg of methylprednisolone for 3 to 5 days (1). An extensive study conducted among the general population showed that even a single OCS treatment episode was associated with an increased risk of major adverse events. OCS are among the most common causes of adverse drug events (7, 8). Due to various adverse effects, such as hypothalamic–pituitary–adrenal (HPA) axis suppression, osteoporosis, arterial hypertension, diabetes, and increased risk of infection, OCS may only be used for acute asthma exacerbations and by severe asthma patients that do not respond well to other therapies. OCS use is usually short-term, and the goal is to minimize it once stable asthma control is achieved. Sadatsafavi et al. documented the trends in OCS use, establishing that maintenance OCS use declined from 9.12% between 2000 and 2002, to 6.35% between 2011 and 2013. In turn, episodic OCS use increased, averaging from 0.82 episodes per patient-year between 2000 and 2002, to 0.93 episodes per patient-year between 2011 and 2013 (9).

Asthma is one of the most common chronic lung diseases. The heterogeneity of its phenotypes and the varying burden of the disease are the main challenges to achieving optimal asthma control. The goal of asthma management is to achieve good control of symptoms and minimize the risk of exacerbations, persistent airflow limitation, and asthma-related death. The primary medications used to treat asthma are inhaled corticosteroids and bronchodilators. If asthma worsens or the patient suffers from severe asthma, OCS treatment is required. Due to the well-documented side effects of OCS, it is recommended that patients that use OCS frequently be identified and referred to a pulmonologist. To achieve the best possible clinical results in asthma patients, several guidelines provide recommendations for patients that require a specialist referral. The Slovenian recommendations for treating asthma also recommend that the diagnosis of asthma be confirmed or excluded by a pulmonologist. If suitable asthma control cannot be achieved at the primary care level, the patient needs to be referred to a specialist (1). Such referrals can help clear up any uncertainty in the initial diagnosis, offer tailored treatment options to patients with persistent symptoms, and provide patients access to healthcare providers with expertise in asthma management. Hence, specialist referrals have a significant impact on disease prognosis and the patient's health status (10).

The aims of this study were as follows: to identify in which cases family physicians decide to prescribe OCS to treat asthma, to determine the factors affecting their decision, and to study Slovenian family physicians' familiarity with OCS side effects.

Methods

A cross-sectional, non-interventional (observational) study was conducted among members of the Slovenian Family Medicine Society, which is part of the Slovenian Medical Association. The empirical part was based on a quantitative non-experimental explorative method, using a questionnaire. The questionnaire for examining the

awareness of the burden of OCS was developed in collaboration with the International Primary Care Respiratory Group (IPCRG) and Slovenian pulmonologists. A cross-sectional study was conducted among family physicians across Slovenia, who were invited to participate in the study by email. Their email addresses were obtained from the Slovenian Family Medicine Society member database. The members that agreed to participate in the study were sent a link to the online questionnaire (https://www.1ka.si/a/aa266bc7).

Respondents

The study was carried out from October 1st to November 27th, 2023, and it included 122 family physicians (out of 143 invited) from all twelve Slovenian statistical regions, the majority of whom came from the Central Slovenia region (Table 1).

Among the 122 respondents that completed the questionnaire, there were 33 men (27%) and 89 women (73%). The oldest respondent was 72 years old and the youngest was 28. The average respondent age was 45.8 years, and over three-quarters were included in the on-call roster. Most were employed at health centers (94 respondents or 77%), and 28 (23%) were concession holders.

Ethics Statement

The study was approved by the Slovenian Medical Ethics Committee (decision no. 0120-172/2023/4).

Statistical Analyses

We processed the collected data statistically. Descriptive statistics were used, such as proportions and/or absolute numbers. In some cases we also calculated averages or arithmetic means. When correlating the variables, we used cross tabulation as a technique to investigate the relationship between two variables. The Chi-square test

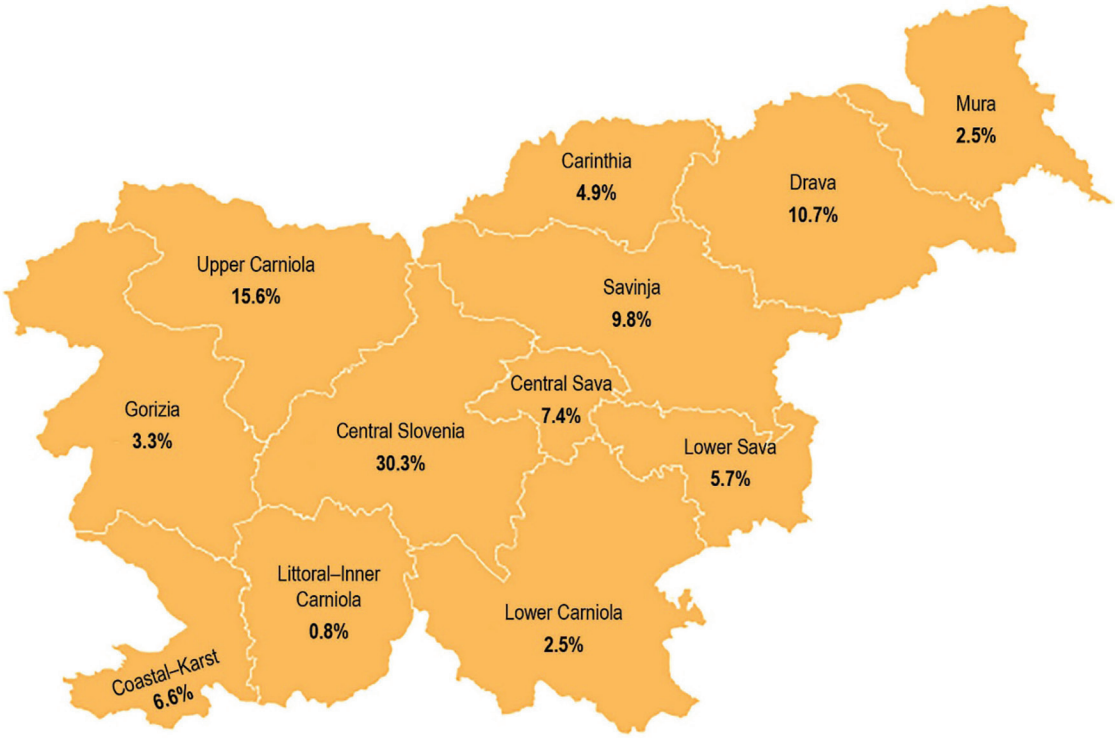


Figure 1. Respondents by statistical region.

was used. All calculations were performed using the SPSS software package, version 12.0. Since the survey used a sample and not all doctors in Slovenia, the results obtained do not automatically lead to population-level conclusions. Therefore, we used a measurement known as the p-value to determine statistical significance. The results were considered statistically significant if there was a confidence level of 95%, which means the P-value is 0.05 or less.

Results

Most respondents (86.9%, or 106 out of 122) reported they had already had experience prescribing OCS to asthma patients. The largest share of these (45.1%) tended to prescribe a limited number of tablets, which means that they dispensed the tablets to patients themselves, but many (42.6%) also prescribed the entire pack.

When asked whether they check how many times a patient had already received OCS (e.g., at the ER or when hospitalized), the respondents provided the following answers: "yes, always" (43.4%), "sometimes" (54.9%), and "no, never" (0.8%). They check this in various ways: they check e-prescriptions (87.0%), they ask the patient (82.1%), or the patients tell them about this themselves or they present their medical results (69.1%). The next question asked the respondents what they felt constituted excessive frequency of OCS use among asthma patients. Their answers were as follows: when they require it once a year (45.1%), two to three times a year (45.9%), or more than four times a year (5.7%). Under "Other," the respondents also provided the following answers: "if they require it twice a day"; "any time they require it"; and "in principle, they should never receive OCS because that is a sign of uncontrolled asthma." There were only statistically significant differences between responding doctors in terms of gender, whereas the differences between the age variables were not significant (Table 1).

Family physicians consider a referral to a pulmonologist a useful mechanism, which they use in various cases, mainly when OCS are prescribed for the first time or if the patient needs OCS to control asthma, especially more than twice a year. The p-value was 0.7, which means we could not draw conclusions about the entire population (Table 2).

In terms of the adverse effects associated with OCS, the respondents listed a range of potential problems. They were asked to what extent they associate certain side effects with taking OCS (1-not at all, 10-significant influence). In their opinion, OCS have the highest influence on diabetes control and osteoporosis. The respondents assigned the lowest average score to adverse effects related to risk of stroke/heart attack (Figure 2).

Table 1. Doctors' Opinion about the Excessive Frequency of Oral Corticosteroid Use in Asthma Patients

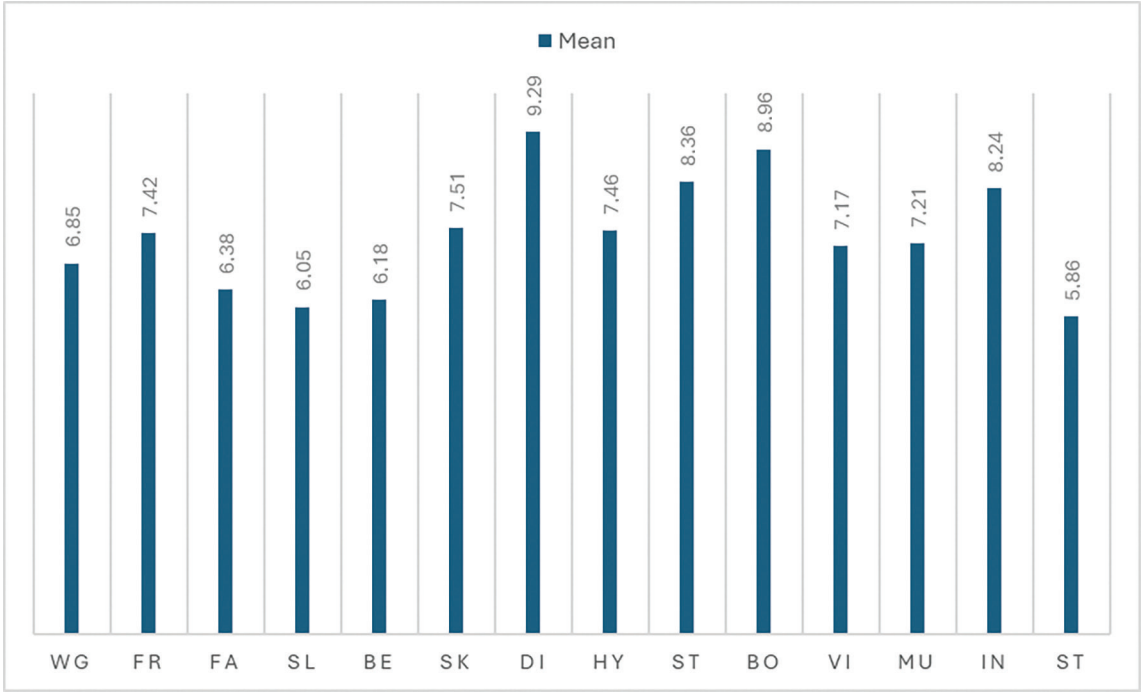
Characteristics of responding doctors	1 a year (N; %)	2 to 3 times a year (N; %)	4 times a year (N; %)	Other (N; %)	Total (N; %)
Gender					
Male	21 (63.6)	10 (30.3)	2 (6.1)	0 (0.0)	33 (100.0)
Female	34 (38.2)*	46 (51.7)	5 (5.6)	4 (4.5)	89 (100.0)
Total	55 (45.1)	56 (45.9)	7 (5.7)	4 (3.3)	122 (100.0)
Age (years)					
18–30	1 (14.3)	6 (85.7)	0 (0.0)	0 (0.0)	7 (100.0)
31–50	41 (54.7)	28 (37.3)	3 (4.0)	3 (4.0)	75 (100.0)
> 51	13 (32.5)	22 (55.0)	4 (10.0)	1 (2.5)	40 (100.0)
Total	55 (45.1)	56 (45.9)	7 (5.7)	4 (3.3)	122 (100.0)

*P=0.039. Chi-square test.

Table 2. When Patients taking OCS* are Referred to a Pulmonologist

Characteristics of responding doctors	When OCS are first prescribed	If patients require OCS twice in previous year	If asthma cannot be controlled without OCS	If patients are already managed by a pulmonologist	Total
Total					
N; (%)	49 (40.2)	36 (29.5)	32 (26.2)	5 (4.1)	122 (100.0)
18–30 yrs					
N; (%)	3 (42.9)	1 (14.3)	3 (42.9)	0 (0.0)	7 (100.0)
31–50 yrs					
N; (%)	32 (42.7	23 (30.7)	18 (24.0)	2 (2.7)	75 (100.0)
> 51 yrs					
N; (%)	14 (35.0)	12 (30.0)	11 (27.5)	3 (7.5)	40 (100.0)

*OCS=Oral glucocorticoid



WG=Weight gain; FR=Fluid retention, swelling, bloating; FA=Fatigue; SL=Sleep disorders; BE=Behavioral changes, excessive irritability, agitation; SK=Thinning skin, skin problems; DI=Impact on diabetes control; HY=Hypertension; ST=Stomach problems, indigestion, pain, ulcers, gastritis; BO=Weak bones, osteoporosis; VI=Visual problems, cataract; MU=Muscle weakness; IM=Suppressed immune system, increased risk of infection; SR=Increased risk of stroke, heart attack.

Figure 2. Family physicians' association of specific adverse effects with Oral Corticosteroids.

Discussion

According to the Medical Chamber of Slovenia, 1,295 family physicians are integrated into the public healthcare system in Slovenia, 983 of whom work at health centers. Our study included 9.4% of all family physicians. The response rate was good: 85%. Only a small share of physicians reported having had no experience prescribing OCS. On the basis of the recommendations, the use of OCS is limited to 3 to 5 days in the event of asthma exacerbation, and the following patients should be referred to a pulmonologist: patients with asthma

that cannot be controlled by inhaled therapy; patients that have visited the ER, been hospitalized, or been prescribed OCS at least once over the previous year due to exacerbations; and patients that have been prescribed more than three packs of a reliever over the previous year (1, 3). In Slovenia, methylprednisolone is only available in packs of 20-50 tablets, and as a result most physicians prescribe a limited number of tablets to avoid uncontrolled use. The study showed a good awareness of the OCS burden in treating asthma. Practically all physicians reported that during appointments they check whether the patient has required OCS in the past, either by reviewing the patient's medical history or checking e-prescriptions. Most physicians can identify when asthma is not well controlled, and they refer the patient to a pulmonologist when OCS therapy is required for the second time; nearly half of these already make a referral when OCS is required for the first time. However, it is alarming that 5.7% of physicians only make the referral after the patient has already required OCS for the fourth time, or if the patient has been taking OCS twice a day. There is still room here to raise physicians' awareness of the OCS burden. Physicians that make a specialist referral if the asthma could not be controlled without OCS were in third place in terms of frequency.

The study did not inquire about comorbidities and potential referrals made because of them. However, it is acknowledged that these may have a significant impact on both patient management and referrals. The presence of comorbidities can complicate the diagnosis of asthma or the assessment of symptoms because they can cause respiratory symptoms. Gastroesophageal reflux disease, sinusitis, allergic rhinitis, and nasal polyposis may exacerbate asthma symptoms and contribute to some diagnostic uncertainty. The NAEPP guidelines recommend that patients with sinusitis, nasal polyps, aspergillosis, severe rhinitis, vocal cord dysfunction, gastroesophageal reflux disease, or chronic obstructive pulmonary disease be referred to a specialist (11-13).

The short-term and long-term risks associated with OCS use include: musculoskeletal, digestive, cardiovascular, endocrine, psychiatric, ocular, dermatological, and immunological side effects, and there is undisputable evidence linking long-term OCS use with infections, osteoporosis and bone fractures, cataracts, adrenal insufficiency, diabetes, and hypertension.

In addition, even episodic use of systemic corticosteroids has been proven to be associated with neurological symptoms, such as insomnia, mania, depression, anxiety, or aggressive behavior. Dyspepsia, hypertension, dyslipidemia, increased risk of infection, muscle atrophy, and increased appetite are also possible. There have also been reports of increased use of healthcare services, which may be associated with both the burden of the primary illness and the side effects of OCS. Steroid-dependent asthma patients have a shorter life expectancy and higher mortality due to cardiovascular and lung complications. In addition, they have been reported to have more ER visits and hospitalizations than non-steroid-dependent patients (14-17).

Among the risks associated with using OCS, family physicians ranked hyperglycemia and exacerbated diabetes, impact on bone density, and a suppressed immune system and increased risk of infection in the top three places. The risk of cardiovascular disease (stroke or ischemic heart disease), sleep disorders, and behavioral changes (excessive irritability or agitation) were identified as lower risks.

Here, too, there is still room for increasing family physicians' awareness of the impact of OCS use, including short-term ones. Sleep disorders and behavioral changes, which can be caused by OCS, should not be overlooked. Problems such as insomnia, mania, depression, anxiety, or aggressive behavior can have a significant impact on patients' quality of life, and so special attention should be paid to these in patient management. Moreover, OCS treatment, including short-term therapies, can cause other adverse effects, such as dyspepsia, hypertension, and increased appetite, which can lead to weight gain and metabolic disorders. Therefore, it is key for physicians and patients to monitor and carefully assess any adverse

effects of OCS together. Regular check-ups, laboratory tests, and appropriate guidance based on the patients' individual needs are vital for reducing the risks and ensuring that these medications are safe and effective.

Conclusion

On the basis of the study conducted, it may be concluded that Slovenian family physicians are well informed about the burden of OCS in treating asthma. Nearly half prescribe a limited number of OCS tablets, preventing patients from making arbitrary decisions about their use. This approach is important because it allows physicians to control the risk of any adverse effects caused by OCS, and to encourage patients to take their medications prudently and responsibly.

Physicians actively seek out patients that require OCS and refer them to a pulmonologist, most often after they require OCS for the second time. This shows that they are aware of the importance of specialist treatment, and that they strive for suitable and holistic management of asthma patients. However, a small share of physicians still believe that patients that use OCS frequently do not require a consultation with a pulmonologist. These viewpoints offer an opportunity for educating and informing physicians further about the necessity of specialist control of asthma patients, especially those with a severe phenotype. The study also showed differences in physicians' familiarity with the side effects of OCS. Most can identify the basic adverse effects, such as osteoporosis, diabetes, and increased risk of infections, but only a small share are also acquainted with more specific side effects that may affect an individual. This shows a need for regular training and updating of physicians' knowledge about safety and risk management in using OCS to treat asthma. This would improve the quality of managing asthma patients and reduce any complications associated with long-term OCS therapy.

What Is Already Known on This Topic:
Oral corticosteroids (OCS) are crucial and effective as a short course treatment for asthma exacerbations, and are sometimes used as maintenance therapy in most severe cases. However, OCS treatment episodes have been associated with an increased risk of serious adverse events. OCS are among the most common causes of adverse drug reactions, such as suppression of the hypothalamic–pituitary–adrenal (HPA) axis, osteoporosis, arterial hypertension, diabetes and increased risk of infection. Therefore, OCS should only be used with caution in acute asthma exacerbations and in patients with severe asthma who do not respond well to other therapies.

What This Study Adds:
This is the first study to investigate the use of OCS for asthma, prescribed by family physicians in Slovenia. Slovenian family physicians are well informed about the risks of OCS. They prescribe a limited number of OCS tablets and prevent patients from making their own decisions about their use. However, there is still room for increasing family physicians' awareness of the effects of OCS use and the need for regular training on safety and risk management when using OCS for asthma treatment.

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Conflict of Interest: The authors declare that they have no conflict of interest.

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Appendix 1. Questionaire

Oral Glucocorticoid (OCS) Burden Awareness Questionnaire
Association of Family Medicine Doctors

Gender: M F
Age:

Region of Residence*

Statistical region	
Central Slovenia	Drava
Littoral–Inner Carniola	Mura
Coastal–Karst	Central Sava
Gorizia	Carinthia
Upper Carniola	Lower Sava
Savinja	Lower Carniola

*Mark.

Duration of Employment

1 – 5 years
5 – 10 years
10 – 15 years
> 15 years

Type of Employment Organization

Health Center
Concessionaire

Participation in on-call service: Y N
Participation in emergency medical care: Y N
Teaching at the university: Y N

1. **Have you already prescribed OCS to a patient with asthma or do you have patients with asthma in your practice who need or who ever had to introduce OCS?**
   a. Y
   b. N
2. **If yes, did you prescribe them a whole box or were they only given a limited amount of OCS tablets "to take home"?**
   a. Whole box
   b. Limited amount of tablets
3. **Do you have insight into how many times the patient received OCS (if he received the medicine in the emergency room or during hospitalization)?**
   a. Yes, always
   b. Sometimes, depends on _____
   c. No, never

4. **How do you check this?**
   a. E-prescriptions
   b. Ask patient
   c. The patient tells/brings the report himself
   d. I don't check

5. **When do you think your patient with asthma needs OCS too often?**
   a) If once per year
   b) If 2-3 times per year
   c) If > 3 times per year

6. **When do you refer such a patient to a pulmonologist?**
   a. At the first intervention with OCS
   b. If he needed OCS at least 2 times in the last year
   c. If his asthma remains unregulated without OCS

7. **To what extent do you associate certain side effects with taking OCS**
   1-not at all; 10-significant influence

Possible side effects of OCS	A single epsode of taking OCS	Occasional intake (>90 days difference between OCS interventions)	Frequent intake (<90 days diference btween OCS interventions)
	1-10	1-10	1-10
Weight gain			
Water retention/ swelling/bloating			
Fatigue			
Sleep disorder			
Behaviour change (excessive excitement, restlessness)			
Skin problems (thinning)			
Impact on diabetes control			
Hypertension			
Gastrointestinal problems (Stomach problems (indigestion, pain, ulcers, gastritis...)			
Osteoporosis			
Vision problems (glaucoma, cataract)			
Loss of muscules			
Reduced immune response/risk of infections			
Risk of stroke/heart attack			

8. **What is your level of satisfaction with the use of OCS in patients with asthma?**

Degree of Satisfaction	Don't konw	0	1	2	3	4	5	6	7	8	9	10
Efficiency	○	○	○	○	○	○	○	○	○	○	○	○
Easy to take	○	○	○	○	○	○	○	○	○	○	○	○
Overall satisfaction	○	○	○	○	○	○	○	○	○	○	○	○

0=Unsatisfied; 10=Very satisfied;OCS=Oral glucocorticoid.