Corticoid-associated complications in elderly

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Abstract

Background: Corticosteroids are widely prescribed products in the elderly particularly in systemic diseases and have been indispensable in controlling a variety of disease states. The various complications associated with this drug class warrant caution and monitoring with each formulation, especially with an older patient population.

Aim: The aim of our study was to evaluate the frequency and type of side effects and complications of long-term corticosteroid therapy in the elderly.

Methods: We conducted a retrospective study of 23 patients aged 65 and older hospitalized in the Internal Medicine Department of the Habib Thameur hospital from January 2000 to December 2004. Corticoid-related adverse effects were recorded throughout the follow-up period.

Results: There were 20 women and 3 men aged 66 to 87 years with a mean age of 75.7 years. The diagnoses were 8 cases of temporal arteritis, 7 cases of rheumatoid arthritis, 3 cases of multiple myeloma, 2 scleroderma, 1 case of systemic lupus erythematosus, 1 case of retroperitoneal fibrosis and 1 case of psoriatic arthritis. We selected 66 complications. Infectious complications were found in 26 cases (39.3%), 11 cases (16.7%) of iatrogenic diabetes, arterial hypertension in 9 cases (13%), skeletal complications in two cases, psychiatric complications in two cases, ophthalmologic complications in one case.

Conclusion: Despite lifestyle rules and adjunctive therapy, complications seem to be frequent. To minimize the disadvantages of prolonged corticosteroid treatment, regular monitoring and careful screening is imperative to detect and handle them in time.

Introduction

Corticosteroids have been in use for longer than 40 years. Over time, they have become indispensable in controlling a variety of disease states. Currently, glucocorticoids (GC) are available in numerous formulations: oral, topical, ophthalmic solutions and ointments, oral inhalers, nasal formulations, parenteral and rectal preparations. GC, especially when they are used throughout the course in geriatrics is not devoid of side effects and complications due, in part, to physiological changes of agin. The aim of our study was to evaluate the frequency and type of side effects and complications of long-term corticosteroid therapy in the elderly.

Materials and methods

A retrospective study was performed in 23 patients aged 65 years older and collected in internal medicine department of the Habib Thameur hospital from January 2000 to December 2004. The adverse effects of corticosteroids were recorded throughout the monitoring period. We selected the following as inclusion criteria:

an age greater than or equal to 65 years, at least one hospitalization during the included period, and the indication of a general glucocorticoid treatment on long-term excluding inhaled and topical corticosteroids. We noted the following for each patient: age, sex, medical history, reasons for hospitalization, clinical features, paraclinical explorations conducted, diagnosis retained. We systematically analyzed the prescription of treatment and the treatment protocol described by specifying: the type of drugs used, the type of use (oral or IV bolus), the period of the different phases (in particular the treatment time of attack), levels of degression and maintenance therapy, the dose used during each phase in mg / kg / day, the terms of degression, the occurrence of relapses and the evolutionary times and recurrence. We evaluated our patients, for side effects and complications that occurred during the evolution recalling the therapeutic adjuvant used. Data were entered using Excel software and analyzed using SPSS version 11.5.

Results

The complete retrospective study of the 23 patients can be seen in Table 1.

There were 20 women and 3 men aged 66 to 87 years with a mean age of 75.7 years. The diagnoses were 8 cases of temporal arteritis, 7 cases of rheumatoid arthritis, 3 cases of multiple myeloma, 2 scleroderma, 1 case of systemic lupus erythematosus, 1 case of retroperitoneal fibrosis and 1 case of psoriatic arthritis. We selected 66 complications (Table 2). Infectious complications were found in 26 cases (39.3%): 2 viral infections, 7 fungal infections and 17 bacterial infections including 4 urinary infections, 3 bronchopulmonary infections, 3 skin infections, 2 Otorhinolaryngologic infections, 2 stomatological infections, 1 osteoarticular infection, 1 gastrointestinal infection and 1 case of reactivation of latent tuberculosis (Table 3).

Among the metabolic complications we identified 11 cases (16.7%) of iatrogenic diabetes that was aggravated by corticosteroids in 6 cases or discovered during treatment in 5 cases. High blood pressure (hypertension) aggravated or induced by corticosteroid treatment has been notified in 9 patients (13%). Osteoporosis is reported in 2 cases (3%), depression in 2 cases (3%), cataracts in 1 case.

Discussion

As in the literature, infectious complications were most common in our study followed by metabolic complications. Infectious complications were particularly found with systemic diseases such as vasculitis or giant cell arteritis, or connective tissue disorders such as rheumatoid arthritis or lupus erythematosus, infection being the leading cause of death in the latter disorder[1]. Thus, in a study on complications due to steroid therapy in 164 patients aged 75 and older and suffering from temporal arteritis, a total of 111 complications were reported, including infectious complications in 31 cases and 20 cases of pulmonary infection[2]. In contrast, a second study reviewing the complications of corticosteroid therapy in giant cell arteritis and polymyalgia rheumatica, including a total of 500 patients from 5 different studies, found a low number of infectious complications: in total, 9 patients including 7 cases of herpes zoster[3]. In rheumatoid arthritis, many infections are reported, even with steroids at a dose below 10 mg / day[4]. In the current literature, there are many observations describing severe infections that have been found (e.g. shingles, fungus ...)[5]. In a series[5] about the adverse effects of corticosteroid therapy in rheumatoid arthritis, there were three more severe infections in the group treated with long-term corticosteroids compared with the group not receiving cortisone. In total in this series[5], 8 patients with herpes zoster were identified, 5 of pneumonia, 4 of septic arthritis and 2 cases of urinary tract infections among a total of 22 severe infections. On the other hand, we must insist on the morbidity associated to long-term corticosteroids during systemic lupus erythematosus[6,7]. Although our sample is small, our results are comparable to those of Chevalet[2], as we found that infections accounted for 39.3% of total complications of long-term corticosteroid treatment in our investigations.

Among the metabolic complications, we identified 11 cases (16.7%) of iatrogenic diabetes, and this was aggravated by corticosteroids in 6 cases or discovered during treatment in 5 cases. According to Agard[8], diabetes affects 10% of patients with giant cell arteritis. Treatment based on a diabetic diet and insulin therapy should be preferred to oral antidiabetic drugs[8]). Corticosteroids, (even at low doses), can reveal diabetes, justifying minimum carbohydrate restriction, or can exacerbate pre-existing diabetes, temporarily insulin use[9]. High blood pressure (hypertension) aggravated or induced by corticosteroid treatment has been noted in 9 patients, at a rate of 13%. For 5 of the patients, hypertension was aggravated to a degree significant enough to warrant remission to previous antihypertensive treatment. For the other 4 patients, hypertension appeared, but was managed with the initiation of a low-sodium diet or mild antihypertensive therapy. Hypertension is more frequent during steroid treatment, but its relationship with dose and duration of treatment is unclear. Pre-existing hypertension appears to be a risk factor which is why thiazide diuretics are recommended in the first place[10]. Hypertension is the most important parameter to monitor. According to Agard[8], it is often pre-existing in giant cell arteritis and is aggravated in 15 to 30% of cases which requires increasing the antihypertensive treatment. Among our 23 patients, we observed a case of femoral neck fracture in the 7th month of corticosteroid therapy in a woman of 72 years treated for temporal arteritis at a dose of 10 mg / day, and treated by nail plate with secondary loosening. This incident suggests an iatrogenic cause. A second patient had clinical features suggestive of vertebral fracture associated with radiographic images confirming the diagnosis. This complication is associated with taking long-term steroids, as in the patient's history; there was no case of previous vertebral collapse. According to some authors, the side-effects of corticosteroid therapy in giant cell arteritis are more common in patients aged 75 years or over receiving at least 40 mg / day prednisone treatment[5]. Furthermore, in a meta-analysis combining 11 studies collecting data from more than 1,000

Table 1 **The retrospective study of the 23 patients including the adverse effects of corticosteroids.**

Case	Age	Sex	Antecedents	Hospitalized for	Diagnosis	Glucocorticoid	Complications
1	85	F	Cataract operated Diabetes	Temporal headache Paresthesia of scalp fever	Temporal arteritis	0.7 mg/Kg/d during 4 weeks then digression until 5 mg/j during 18 months	Herpes zoster Iatrogenic diabetes
2	79	F	Hypertension Diabetes	Temporo-frontal headache Paresthesia of scalp Arthralgia Biological inflammatory syndrome	Temporal arteritis	0.7 mg/Kg/d during 4 weeks then digression until 5 mg/j during 18 months	Infectious Pulmonary disease Iatrogenic diabetes Arterial hypertension
3	72	F	–	Temporal headache Prolonged fever Weight loss Biological inflammatory syndrome	Temporal arteritis	0.7 mg/Kg/d during 4 weeks then digression until 5 mg/j during 18 months	Urinary infection Iatrogenic diabetes
4	75	F	Hypertension Cardiac failure cataract	Temporal headache Intermittent claudication of jaw Weight loss Biological inflammatory syndrome	Temporal arteritis	0.7 mg/Kg/d during 4 weeks then digression until 5 mg/j during 18 months	Intestinal infection Arterial hypertension
5	82	F	Diabetes	Weight loss Biological inflammatory syndrome	Temporal arteritis	0.7 mg/Kg/d during 4 weeks then digression until 5 mg/j during 18 months	Dental abscess Iatrogenic diabetes Cataract
6	72	H	Smoking	Atrocious headache Paresthesia of scalp Intermittent claudication of jaw	Temporal arteritis	0.7 mg/Kg/d during 4 weeks then digression until 5 mg/j during 18 months	Urinary Infection Iatrogenic diabetes
7	72	H	Smoking	Temporo-frontal headache Intermittent claudication of jaw Weight loss Biological inflammatory syndrome	Temporal arteritis	0.7 mg/Kg/d during 4 weeks then digression until 5 mg/j during 18 months	Onyxis Dental abscess Arterial hypertension
8	87	F	Hypertension Diabetes Cataract	Temporal headache Paresthesia of scalp Intermittent claudication of jaw Weight loss	Temporal arteritis	0.7 mg/Kg/d during 4 weeks then digression until 5 mg/j during 18 months	Infectious Pulmonary disease Iatrogenic diabetes
9	71	F	Hysterectomy	Polyarthritis Weight loss Biological inflammatory syndrome	Rheumatoid arthritis	10 mg/j for life	Urinary infection Iatrogenic diabetes
10	66	F	Hypertension Diabetes Obesity	Polyarthritis	Rheumatoid arthritis	10 mg/j for life	Eczema marginatum Iatrogenic diabetes

Case	Age	Sex	Antecedents	Hospitalized for	Diagnosis	Glucocorticoid	Complications
11	**66**	**F**	Pulmonary tuberculosis Cataract	Polyarthritis Weight loss Biological inflammatory syndrome	Rheumatoid arthritis	10 mg/j for life	Reactivation of tuberculosis Arterial hypertension
12	**66**	**F**	–	Polyarthritis Biological inflammatory syndrome	Rheumatoid arthritis	10 mg/j for life	Erysipelas Iatrogenic diabetes
13	**78**	**F**	Cataract	Anemia	Rheumatoid arthritis	10 mg/j for life	Intertrigo Arterial hypertension
14	**69**	**F**	Hypertension Smoking	Arthritis of knee	Rheumatoid arthritis	10 mg/j for life	Otitis
15	**68**	**F**	Obesity Smoking	Diabetes	Rheumatoid arthritis	10 mg/j for life	Onyxis Iatrogenic diabetes
16	**77**	**F**	–	lower back pain Weight loss Monoclonal gammaglobulinemia	Multiple myeloma	Dexamethasone treatment monthly as part of an established protocol	Urinary infection Arterial hypertension
17	**71**	**F**	Hypertension fracture of neck of femur	Bone pain Weight loss Biological inflammatory syndrome Renal failure	Multiple myeloma	Dexamethasone treatment monthly as part of an established protocol	Erysipelas Arterial hypertension
18	**70**	**F**	–	Weight loss	Multiple myeloma	Dexamethasone treatment monthly as part of an established protocol	Sinusitis Arterial hypertension
19	**68**	**F**	Hypertension	Sclerodactyly Cutaneous sclerosis Arthritis Weight loss	Scleroderma	10 mg/d	Intertrigo Osteoporosis Depression
20	**72**	**F**	Hypertension	Arthralgia Myalgia Biological inflammatory syndrome	Scleroderma	0.5 mg/Kg/d	Sinusitis Intertrigo Arterial hypertension
21	**71**	**F**	Hypertension Diabetes Vertebral compaction	Photo sensitive rash Edema of lower limbs Proteinuria Haematuria	Systemic lupus erythematosus	1 mg/Kg/d during 6 weeks then digression until 10 mg/j	Herpes zoster Iatrogenic diabetes Osteoporosis
22	**67**	**H**	Hypertension Thrombosis of left lower limb	Renal failure	Retroperitoneal fibrosis	0.5 mg/Kg/d during 3 months then digression until 5 mg/Kg/d	Septic osteoarthritis Depression
23	**73**	**F**	Hypertension Psoriasis of elbows and knees Hysterectomy	Weight loss Fever Cough	Psoriatic arthritis	30 mg/d during 4 weeks then digression until 10 mg/Kg/d	Erysipelas

Table 2 Complications of long-term corticosteroid treatment identified in the 23 patients of the study.

Complications	Number	%
Infections	26	39.3
Iatrogenic diabetes	11	16.7
Arterial hypertension	9	13
Osteoporosis	2	3
Depression	2	3
Cataracts	1	1.5

patients treated for giant cell arteritis, should help target surveillance of subjects at risk[12]. We found one case of steroid-induced cataracts diagnosed in the 42nd month of corticosteroid therapy in a patient treated for rheumatoid arthritis. Eye problems, mainly represented by a posterior subcapsular cataract, and did not tend to regress to the withdrawal of corticosteroid therapy, even at low doses[5]. Cataract is deemed to be a complication of high-dose corticosteroids or related to the total dose and duration of treatment. This complication has also been reported with low dose corticosteroids, but it is uncommon. Its relative risk is 1.8 to 2.5 times higher with patients, steroids was noted to cause side effects in 29% of patients, and cause a complication in 10% of rheumatology cases[8]. Glucocorticoid-induced osteoporosis is the most common complication of temporal arteritis for at least 10% of patients and 15% at 1 year of treatment of those aged over 75 years. Rheumatological complications related to corticosteroids are the most prevalent complication in those over 75 years. Within a group of 229 people treated with prolonged corticosteroid therapy, a prevalence of 46% of vertebral fractures was observed in the age group 70–79 years vs. 32% in that age group not using steroids, and respectively 60% versus 40% after 80 years. The subjects of 70–79 years have a vertebral slice fracture risk 5 times higher than those less than 60 years[11]. In two of our patients (8.6%), we observed the appearance of a depression with mood, character and behavior. According to some authors, psychiatric disorders do not appear to be increased with low doses of cortisone[2]. In a series involving subjects aged 75 years, psychiatric complications were reported in 13 cases including 7 cases of depressive disorders and, 6 cases of agitation with confusion or mania[2]. In 126 subjects with giant cell arteritis, 20 patients (16%) had psychiatric complications with corticosteroids. The onset of these disorders occur most often in the first month of treatment, taking on various forms such as: mood with irritability, sleep disorder, depression, manic states syndrome and anxiety disorders in vascular dementia[12]. The systematic implementation of a Mini Mental State or Geriatric Depression Scale in all patients receiving prolonged oral corticosteroids especially before the onset of rapid cognitive decline or psychiatric symptoms especially in prolonged steroid treatment[13]. A mucocutaneous disorder was reported in one case, and these are linked to metabolic disturbances and obesity through fat overload or facial-nerve block. These treatment-related disorders are more difficult to prevent since they are often also linked to the condition being treated long-term[14].

Table 3 Type of infection complications in the 23 patients of the study.

Etiology	Localization	Type	Number (26)
Viral	–	Herpes zoster	2
Bacterial	Pulmonary	Disease of the lungs	3
		Reactivation of tuberculosis	1
	Urinary	Urinary infection	4
	Cutaneous	Erysipelas	3
	Osteoarticular	Septic osteoarthritis	1
	Otorhinolaryngologic	Sinusitis	2
	Gastroenterologic	Intestinal infection	1
	Stomatologic	Dental abscess	2
Mycotic	–	Eczema marginatum	1
		Intertrigo	3
		Onyxis	2
		Otitis	1

Conclusion

Glucocorticoids are among the most commonly prescribed agents in clinical practice. Their varied physiological effects make them ideal agents for treating several disease states. Infectious and metabolic complications were the most common in our study. Physician education on risk factors might improve prescribing glucocorticoids in elderly patients. The knowledge of drug-use patterns is extremely important, particularly when treating a member of the aged-population who is a high-risk subject.

Author Contributions

All authors participated in the completion of this work. They contributed in the practice study, interpretation of results and discussion.

Competing Interests

No competing interests were disclosed.

Grant Information

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Version 1

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The significance of this retrospective study is pretty limited as the hypothesis (which is not novel) is applied to a target population that is highly heterogeneous in terms of the underlying conditions requiring the use of steroid therapy.

The included patients suffer from auto-immune diseases (rheumatoid arthritis, SLE), cancers (multiple myeloma), temporal arteritis all of which could be affecting the risk of side-effects. In addition, treatment duration is also another factor susceptible of affecting the course of side effects that were seen. Some patients require lifelong therapy (10 mg/day) while others have been treated for only 18 months (and 4 weeks). Dosage and the type of corticosteroids (prednisone and dexamethasone) are not consistent among the different groups. To summarize these points, duration, dosage and the underlying causes should be carefully taken into account before setting up the inclusion/exclusion criteria since they all represent factors susceptible of greatly impacting on the patients' response to therapy and susceptibility to side-effects. For example, patients with multiple myeloma are at high risk of developing bacterial infections irrespective of corticosteroid therapy. The other unknown parameter that has not been mentioned is the patients' adherence to treatment. How was steroid adherence monitored, especially in patients with steroid-related neuropsychiatric adverse effects?

Other concerns:
The study question of the relative risk of adverse effects in elderly patients treated with long-term corticosteroids is interesting but not novel. Others concerns include the relatively small group size and the fact that there is no relative risk as a form of risk ratio (RR) and odd ratio (OR) attached to the study which, again would require the inclusion of a control group. Adding an equal number of hospitalized patients of the same age group but different diagnoses excluding the use steroid therapy would have been possibly a better control group.

I have read this submission. I believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Competing Interests: No competing interests were disclosed.

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The work carried out in this research article is in no way novel, and it provides very little in terms of being an important and relevant study.

The study design uses a very small sample size (23 patients) and the inclusion criteria of the subjects is poor. Because of this weak study design, the work itself has little to no applicability.

Other reasons why the work is of poor scientific value is that the work is;

1. It is a retrospective analysis, therefore the collection of the data is not standardized.
2. There are is a mix of different diseases (all treated with prednisone) which themselves carry their own cause of complications.
3. The doses of the glucocorticoids were different in each case as was the length of the therapy.
4. There was no control group for the study.

We have read this submission. We believe that we have an appropriate level of expertise to state that we do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Competing Interests: No competing interests were disclosed.

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Omar González-Santiago, Universidad Autónoma de Nuevo León, Mexico

This article should have been presented as a case serie instead of a research article. The authors could have described, according clinical record, the most relevant patient. Dosing, drug interactions, other comorbidities etc

Competing Interests: None