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THE PRESCRIPTION OF CORTICOSTEROID THERAPY BY GENERAL PRACTITIONERS IN THE CITY OF MARRAKECH

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I- INTRODUCTION

Glucocorticoids, indispensable drugs due to their anti-inflammatory and immunosuppressive action, have revolutionized the prognosis of numerous diseases since their discovery in 1935. Despite their effectiveness, their use is associated with clinical and biological side effects, such as osteoporosis, infections, diabetes, hypertension, and others, which can compromise patients' prognosis. Approximately 1% of the population in the United Kingdom is treated with corticosteroids at any given time. Complications often lead to poor patient compliance. While the prevention of osteoporosis, particularly through vitamin and calcium supplementation and bisphosphonates,[1] is subject to clear recommendations, other adjuvant measures are not consensual.

Due to the widespread prescription of corticosteroids by both specialists and general practitioners, and the need for regular monitoring, the central role of the general practitioner in managing this treatment is crucial. A survey conducted among general practitioners in Marrakech aims to assess their practices in relation to recommendations, with the ultimate goal of improving the quality of care delivered to patients.

II- Objective of the Study

The study aims to evaluate the role of corticosteroid therapy in the practice of general practitioners in Marrakech, focusing on prescription, treatment management, monitoring, and associated side effects.

III- Methodology

Study Type: This is a descriptive cross-sectional study evaluating practice, conducted declaratively and anonymously among general practitioners in Marrakech.

Study Duration: The total study period is one and a half months, from February 12 to March 26, 2018.

Participants: General practitioners from both public and private sectors in Marrakech were included, with a list obtained by internet search.

Sampling: Accidental sampling by internet search for email and postal addresses of general practitioners on www.pj.ma.

Data Collection: A questionnaire consisting of 25 questions, some closed and others semi-open, was distributed to doctors, covering nine items such as general data, indications and contraindications for corticosteroid therapy, prescription frequency, pre-therapeutic assessment, adjuvant measures, monitoring methods, side effects, and tapering and withdrawal measures.

IV- RESULTS

1. General Data

The study involved 130 doctors from both public and private sectors. Out of this total, 95 doctors responded positively, while 35 declined to participate. Regarding the questionnaire retrieval time, it was collected over an average period of 5 days. Some were collected in just 2 days, while others required up to a week, with a maximum of three weeks. Notably, 23 questionnaires were completed on-site. As for the response rate, out of the 130 doctors approached, 95 actively participated in the study, representing an overall response rate of 73% (Figure 1).

2. Socioprofessional Distribution of Participating Doctors

Regarding age, the average age of general practitioners was 47, with an age range from 29 to 67. The most represented category was doctors aged between 41 and 50, constituting 31% of the sample (Figure 2). Regarding gender distribution, a relative parity was observed with 51% women and 49% men among participants, resulting in a M/F ratio of 0.98 (Figure 3). Concerning years of

practice, there was notable diversity, ranging from 2 to 36 years, with an average of 18 years. It was observed that 40% of doctors had experience between 10 and 20 years, while 40% had over 20 years of experience in general medicine (Figure 4). As for the distribution by practice sector, a clear distinction emerged: 57% of participating doctors practiced in the private sector, while 43% worked in the public sector (Figure 5).

3. Analysis of Questionnaire Responses

Analyzing the questionnaire responses revealed several aspects. Regarding short-term corticosteroid therapy, the average prescription duration ranged from 3 to 7 days, with 67% of doctors prescribing it for an average of 5 days (Figure 6). Indications varied by medical specialties, with asthma crises dominating in pulmonology (94%), acute laryngitis in otolaryngology (83%), and urticaria in dermatology (90%) (Figures 7, 8, 9). For prolonged corticosteroid therapy, the most frequent indications were rheumatoid arthritis (85%) and asthma (73%) (Figure 10). Doctors generally prescribed an initial dose of 1mg/kg/day (60%) and avoided this therapy in cases of uncontrolled diabetes (92%) or uncontrolled hypertension (80%) (Table 1).

Regarding pre-therapeutic assessment, there was evident diversity in practices. The most requested biological assessments were fasting blood glucose in 57% of cases, blood electrolyte levels in 43% of cases, a complete blood count in 38% of cases followed by postprandial blood glucose in 34% of cases (Figure 11).

Adjuvant measures to corticosteroid therapy often included a low-sodium diet (82%) (Table 2). For monitoring, clinical examination primarily relied on weight measurement (89%) and blood pressure measurement (88%), with capillary blood glucose measured by 64% of general practitioners. Side effects were estimated by 16% of doctors, with 38% not answering this question. The main side effects included increased susceptibility to infections (59%), abrupt patient discontinuation (55%), and hypertension (48%). However, 14% of doctors had encountered no side effects (Figure 12).

Corticosteroid withdrawal was generally performed by doctors themselves (64%), with 33% referring the patient to an endocrinologist. Tapering indications included partial regression of clinical symptoms (73%) and the occurrence of severe adverse effects (52%). The majority of doctors followed a rapid tapering protocol to half-dose, then gradual.

At cessation, some incidents were anticipated, including rebound effect (13% estimated a frequency of 3 out of 10 patients), corticosteroid dependence (16% estimated a frequency of 2 out of 10 patients), and adrenal insufficiency (21% estimated a frequency of 1 out of 10 patients). The main clinical signs mentioned to suspect adrenal insufficiency were fatigue (79%) and hypotension (75%).

V- DISCUSSION

1. Emergency Corticosteroid Prescription

Corticosteroids are prescribed in various situations and for different durations depending on the treated pathology. In emergencies, corticosteroids are administered parenterally for their rapid anti-inflammatory action, essential in situations endangering vital organ function, such as cerebral edema, Quincke's edema, acute adrenal insufficiencies, acute respiratory distress syndrome, and status asthmaticus. They are also used as a complement during anaphylactic shock.[2]

2. Short-term Corticosteroid Prescription

Regarding short-term courses, they are prescribed for a duration long enough to treat the pathology while avoiding corticosteroid side effects. The average duration of prescription varies from 3 to 7 days, with a trend towards reduction over the years, often limited to a maximum of 7 days. General indications for short courses include asthma attacks, acute bronchiolitis, broncho-obstructive manifestations, ENT infections, acute laryngitis, upper respiratory infections (sore throat, rhinopharyngitis, sinusitis, acute otitis media), acute urticaria, eczema, and psoriasis.

In pulmonology, asthma attacks are the main indication, followed by acute bronchiolitis. Prescriptions often align with British recommendations,[3] advocating for prednisolone for at least 5 days for asthma attacks. For acute bronchiolitis, corticosteroid therapy is less recommended, except in cases of likely infantile asthma.

In ENT, acute laryngitis is the main indication, showing clinical improvement after systemic corticosteroid administration. However, the use of corticosteroids in upper respiratory infections is not supported by expert recommendations.

In dermatology, corticosteroids are prescribed to treat acute urticaria, eczema, and psoriasis, although second-generation antihistamines are recommended as the first line of treatment for urticarial.[4]

Despite their effectiveness, the use of corticosteroids must be cautious due to potential side effects, and the prescription duration must be carefully evaluated based on the specific pathology.

3. Prolonged Corticosteroid Therapy

a. Frequency of Prolonged Corticosteroid Prescription

According to a study by Perdoncini-Roux et al among general practitioners in the Sentinelles Network, less than 5% initiated prolonged corticosteroid therapy. In contrast, a study by Belaksir et al in Casablanca showed that over half of general practitioners initiated at least one prolonged systemic corticosteroid therapy each

month.[5] Our study reveals that only 22% of doctors initiated prolonged corticosteroid therapy monthly, and 14% did not prescribe it at all.

b. Indications

According to Belaksir et al, rheumatoid arthritis was the main indication for prolonged corticosteroid prescription (over 50%). A British study by Fardet et al indicates that rheumatoid arthritis, Horton's disease, and polymyalgia rheumatic,[5] represent two-thirds of prescription reasons. Our results show that the main indications were rheumatic diseases (85%) and asthma (73%), followed by cervical-brachial neuralgia (44%) and chronic back pain (25%).

c. Prescription Modalities

c.1. Choice of Molecule

Prednisone is the reference corticosteroid due to its good balance between anti-inflammatory and side effects. It is also manageable, available in different tablet doses.

c.2. Routes and Modes of Administration

Oral administration is preferred for long-term treatment. Other routes include parenteral, percutaneous, rectal, nasal, ocular, auricular, intra-articular, and respiratory.[6] Boluses, administered by infusion, are used for certain systemic diseases.

c.3. Dosage

Dosage varies from high to low, depending on needs. For prolonged corticosteroid therapy, the initial dose is gradually reduced to the effective minimum dose, ideally between 0.1 and 0.3 mg/kg/day.[7] Morning administration is recommended for better synchronization with the circadian rhythm of physiological cortisol synthesis.

d. Contraindications

Some situations, such as certain forms of psoriasis, cirrhosis, and vaccination with live attenuated vaccines, are absolute contraindications. Relative contraindications, accompanied by dietary or therapeutic measures,[8] include uncontrolled diabetes, gout, evolving psychotic states, osteoporosis, evolving ulcers, uncontrolled hypertension, infections not controlled by specific treatment, viral hepatitis, and glaucoma not controlled by hypotensive treatment.[9] Over 75% of general practitioners in our study were aware of these contraindications.

e. Special case of use

e.1. Pregnancy

Initially, corticosteroids were associated with the risks of Cushing's syndrome in the fetus and adrenal insufficiency in the newborn, but this idea proved to be incorrect. The placenta metabolizes corticosteroids into inactive derivatives, rendering corticosteroids, regardless of duration or dosage, devoid of teratogenic or fetal toxic effects. The recommended molecules for oral use during pregnancy are prednisolone, prednisone, or methylprednisolone. Administration through other routes requires informing the healthcare providers during delivery to check the newborn's adrenals. Precautions are similar to those generally taken for corticosteroid use.[10]

e.2. Breastfeeding

The use of corticosteroids is permitted during the postpartum period. The psychological, nutritional, and anti-infective benefits of breastfeeding are not contraindications to corticosteroid therapy. The recommended oral corticosteroids are the same as during pregnancy. The intake of corticosteroids and breastfeeding should be spaced by approximately 4 hours to reduce the passage of the drug into breast milk. Local forms require avoiding prolonged contact of the child with the treated area and cleaning the skin before each feeding.[11]

e.3. Child

Short-term corticosteroid therapy does not affect the child's growth. In the case of prolonged corticosteroid therapy, alternative administration or a single morning dose may reduce the risk of growth retardation. Monitoring for side effects is similar to that in adults.[12]

e.4. Elderly

In addition to the issues related to corticosteroid therapy in adults, the elderly are prone to osteoporosis and ocular issues. Enhanced monitoring of bones and eyes is recommended.

f. pre-therapeutic assessments

A prior medical assessment is essential before corticosteroid treatment to identify contraindications and limit adverse effects. The interview, clinical examination, and various paraclinical assessments, such as blood glucose measurement, blood ionogram, and lipid profile, are necessary. Bone densitometry may be performed in case of osteoporosis risk factors, and an ophthalmic assessment is recommended.[13] In our study, blood pressure measurement, searching for infectious foci, and weight measurement were the most frequently considered elements.

g. Treatment modalities

Corticosteroid treatment requires morning intake to maintain the circadian rhythm of cortisol secretion. High doses in the initial treatment should be reduced to a minimum effective dosage for maintenance treatment. The choice of corticosteroid, route of administration, and the use of adjunct measures are also crucial. The duration of treatment depends on the disease's evolution and the patient's tolerance.

h. Adverse effects and preventive measures

The risk of adverse effects depends on the dose, duration, and route of administration of corticosteroids. Prolonged intake, even locally, can lead to side effects, with variability in their occurrence. Knowledge, monitoring, prevention, and treatment of side effects are crucial for

optimal patient management. Studies have shown that the majority of patients on prolonged corticosteroid therapy experience at least one side effect, often dose-dependent.[14]

1. Infectious risk: Corticosteroid therapy increases susceptibility to infections, with an increased risk of serious or opportunistic infections. A 1989 meta-analysis shows a relative risk of infection under corticosteroids of 1.6.[15]
2. Corticoid-induced diabetes: Glucocorticoids promote hyperglycemia. Corticoid-induced diabetes is correlated with the total dose of glucocorticoids received and the duration of treatment. Biological monitoring and a controlled carbohydrate diet are recommended.
3. Effects on lipid metabolism: Glucocorticoid effects on lipid metabolism can lead to hyperlipidemia, affecting treatment adherence. Statin-type lipid-lowering treatment is often necessary.
4. Hydro-electrolytic metabolism actions: Glucocorticoids influence hydro-electrolytic metabolism, causing increased sodium reabsorption and facilitating potassium elimination.[16] Monitoring of potassium levels is recommended.
5. Musculoskeletal effects

a. Osteoporosis: Corticosteroid therapy can cause corticosteroid-induced osteoporosis, with fractures in 30 to 50% of patients. Preventive measures, such as densitometric examinations, are recommended.
b. Corticosteroid myopathy: Myopathy is a common complication (15% under corticosteroid therapy). Regular physical activity is recommended.
c. Aseptic osteonecrosis: Corticosteroid therapy is a risk factor for this rare complication, requiring early diagnosis.
d. Growth delay and tendon rupture: These adverse effects, especially in children, are associated with prolonged corticosteroid therapy.

6. Gastroduodenal effects: Under corticosteroid therapy, there are risks of nausea, vomiting, and gastralgia. A 1994 meta-analysis shows no significant association with gastroduodenal ulcers (UD), but the risk of UD increases with the co-prescription of nonsteroidal anti-inflammatory drugs (NSAIDs).[17] Proton pump inhibitors (PPIs) are recommended in case of co-prescription of NSAIDs, a history of UD, or somatic complaints.
7. Cutaneous effects: Corticosteroids lead to various skin effects, such as a decrease in collagen synthesis, causing stretch marks, acne, erythema, and delayed healing. Hair loss, hirsutism, petechiae, and ecchymosis are also observed.[18] Skin disorders are mentioned by 38% of physicians in the study.
8. Ophthalmological effects: Long-term corticosteroids can cause ocular complications, including corticosteroid cataracts and glaucoma. The risk is estimated between 11% and 15% for cataracts and 12.8% for glaucoma.[19] In the study, 14% of physicians encountered ophthalmological complications. Regular monitoring is recommended, but the frequency is not specified.
9. Neuropsychiatric effects: In the study, only 8% of general practitioners (GPs) observed neuropsychiatric disorders in patients under long-term corticosteroid therapy (LTCS). This underestimation by practitioners is similar to that observed in other studies, where patients report neuropsychiatric manifestations more frequently than doctors recognize them.[20] The prevalence of these disorders varies, but some studies show up to 78% of cases, mainly minor, with symptoms such as fatigue, insomnia, irritability, and cognitive disorders. Although 32% of GPs monitor the mental state of their patients under LTCS, 56% avoid prescribing corticosteroid therapy during evolving psychotic states.
10. Hypertension: General practitioners unanimously recognize the need to monitor the blood pressure of patients under long-term corticosteroid therapy (CTLC), with 88% of them conducting regular measurements. Forty-eight percent of general practitioners have encountered cases of hypertension in patients under CTLC. Although glucocorticoids are associated with hypertension, the precise mechanism remains poorly understood. Recommendations regarding a low-sodium diet vary, but studies question its effectiveness. An ongoing study (CORTISEL) could provide clarification.[21]
11. Cushing's Syndrome: Cushing's syndrome, resulting from prolonged exposure to glucocorticoids, presents various symptoms, including weight gain, skin fragility, muscle wasting, hormonal and neuropsychiatric disorders. In the survey, 31% of GPs describe this complication.
12. Abrupt cessation by the patient: The sudden discontinuation of corticosteroid therapy exposes the risk of acute adrenal failure. In the study, 55% of GPs describe this adverse effect. Previous studies have shown that up to 20% of cases of acute adrenal insufficiency were related to the abrupt cessation of corticosteroid therapy.[22]

i. Monitoring of corticosteroid therapy

In the context of prolonged corticosteroid therapy, close monitoring is essential to assess its effectiveness on the pathology, detect possible complications, and mitigate their progression through complementary measures. This monitoring relies on biological analyses and clinical observations, adapted to the severity of the symptoms of the initial disease and the patient's tolerance to corticosteroids.

1. Monitoring of the treated disease: Vigilance focuses on clinical symptoms, paraclinical, biological, radiological examinations, etc. This dual approach allows understanding the evolution of the treated pathology.
2. Corticosteroid therapy monitoring: Specific monitoring of corticosteroid therapy includes treatment adherence (dosage, schedule), adherence

to the dietary regimen and adjunct measures, as well as treatment tolerance. General practitioners rely on parameters such as weight, blood pressure, capillary blood glucose, edema search, skin examination, evaluation of mental state, and temperature measurement.[23]

The results of our study indicate that the majority of general practitioners prioritize clinical monitoring, emphasizing weight and blood pressure. However, variations are observed in the frequency of prescribed paraclinical examinations.

j. Modalities of tapering and withdrawal

1. Generalities about withdrawal: The withdrawal of corticosteroid therapy, a delicate stage of treatment, requires a gradual reduction of doses to avoid serious adverse effects. Among the risks incurred, adrenal insufficiency is the most frequent complication of prolonged corticosteroid therapy.
2. Risks and clinical signs of adrenal insufficiency: Clinical signs of adrenal insufficiency are often nonspecific, such as fatigue and digestive disorders. Our study reveals that 21% of general practitioners believe that one in ten patients could develop adrenal insufficiency.
3. Treatment modalities for adrenal insufficiency: In case of adrenal insufficiency, the administration of a natural glucocorticoid, hydrocortisone, is recommended. The withdrawal must be done with caution to avoid withdrawal syndrome.
4. Obstacles to corticosteroid tapering: The "3R" rule (rebound, relapse, resistance) can hinder tapering. Resistance to corticosteroid therapy is rare, rebound occurs with abrupt cessation, and relapse can occur after discontinuation or during the tapering phase.
5. Tapering modalities: Several tapering regimens are recommended, with divergent opinions on how to proceed. Some suggest a gradual reduction to a physiological replacement dose. Our results show that 73% of general practitioners reduce corticosteroid therapy as soon as there is partial regression of clinical symptoms.[24]
6. Treatment cessation modalities: Expert opinions vary on treatment cessation modalities, but most agree on a gradual dose reduction. In our study, 73% of general practitioners state that they themselves carry out the tapering protocol.

k. Corticotrope axis stimulation tests

1. Importance of stimulation tests: Corticotrope axis stimulation tests are crucial to assess adrenal function post-corticosteroid therapy. However, our results indicate that no physician has performed the synacthen test, highlighting underutilization of these tests in routine practice.
2. Interest and limitations of tests: Although stimulation tests are relevant, they cannot always reliably predict the clinical event. The substitution with hydrocortisone after insufficient results on the synacthen test remains a topic of debate due to its impact on prolonging corticosteroid therapy and its side effects.[25]

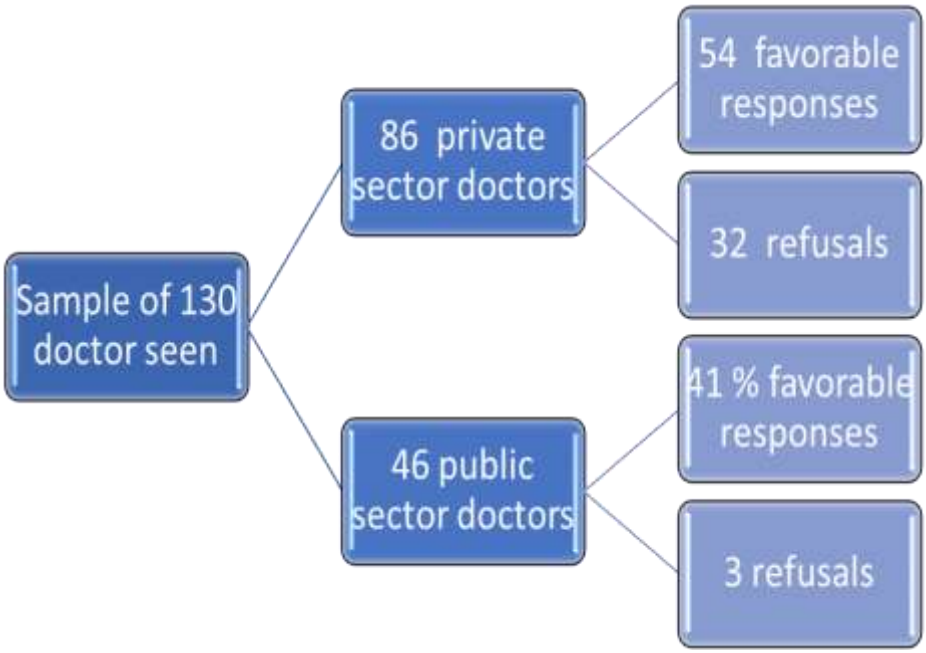

Figure 1: Number of participating doctors.

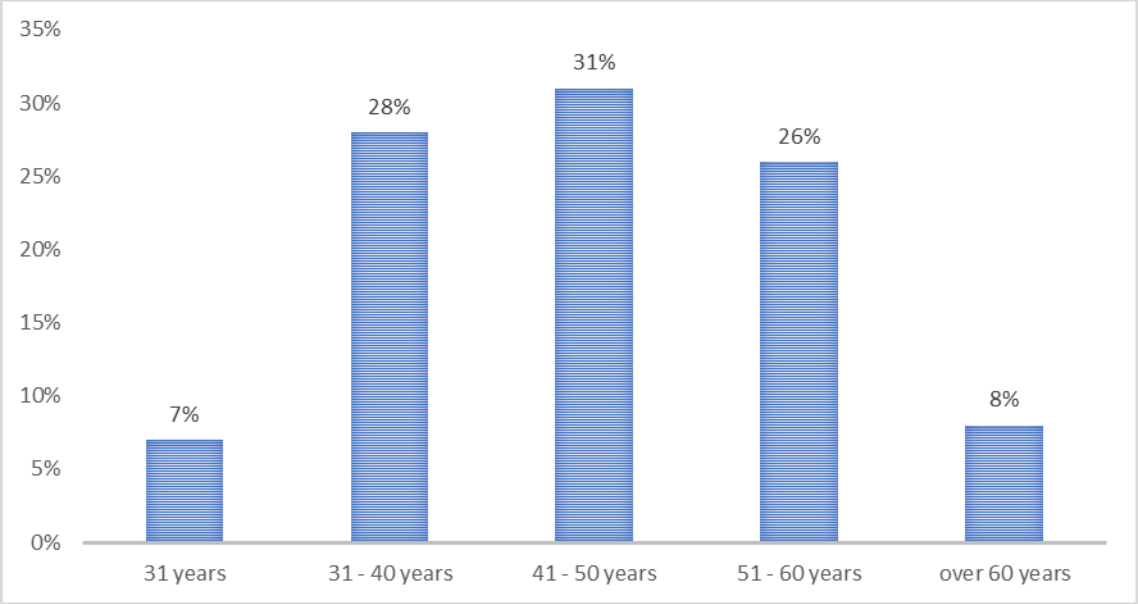

Figure 2: Distribution of doctors by age.

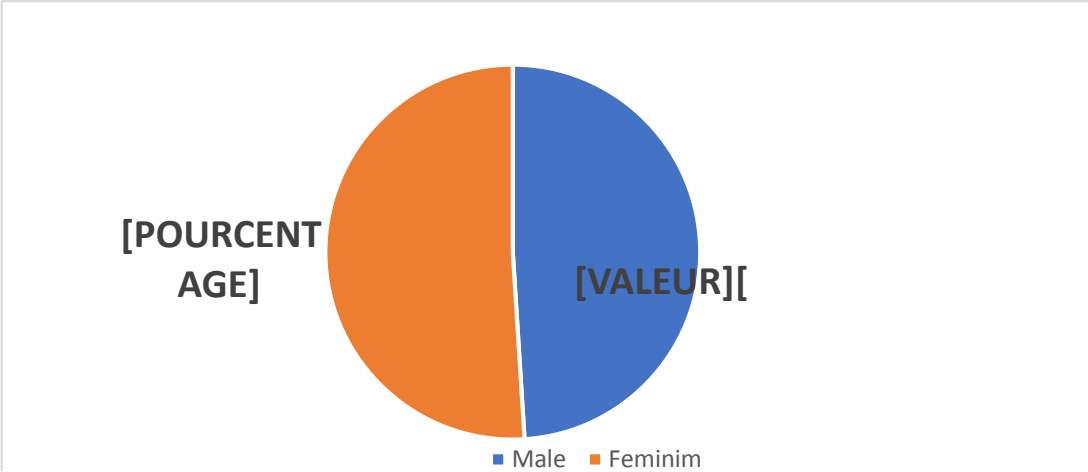

Figure 3: Distribution of doctors by gender.

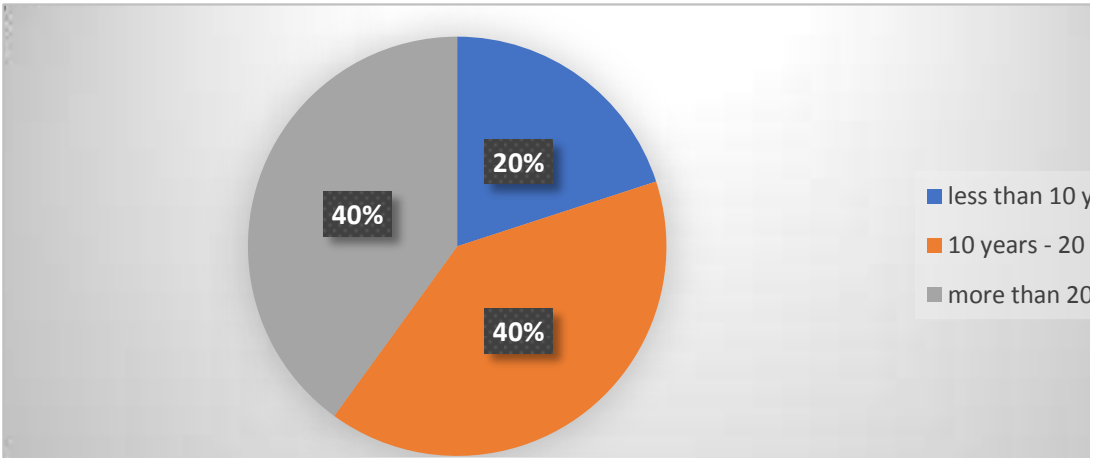

Figure 4: Distribution of physicians based on seniority in practice.

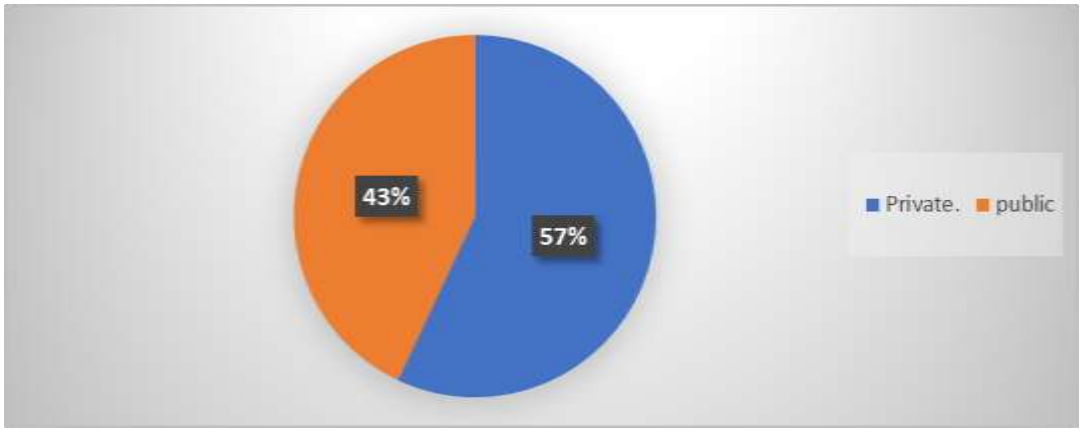

Figure 5: Distribution of physicians according to the practice sector.

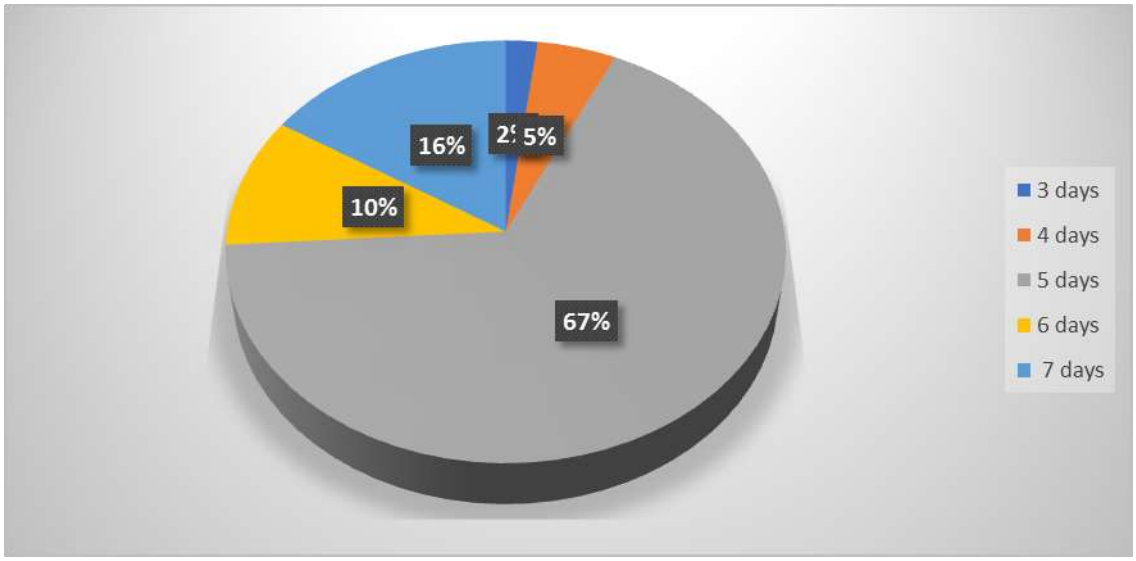

Figure 6: Duration of short-term corticosteroid prescription.

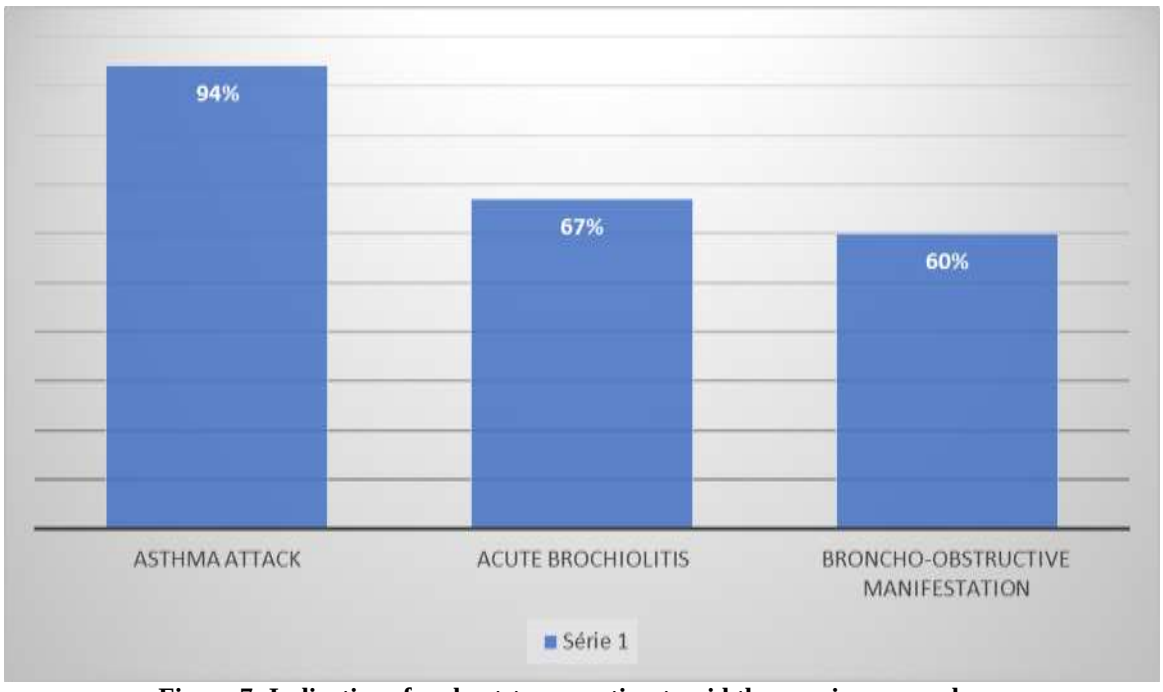

Figure 7: Indications for short-term corticosteroid therapy in pneumology.

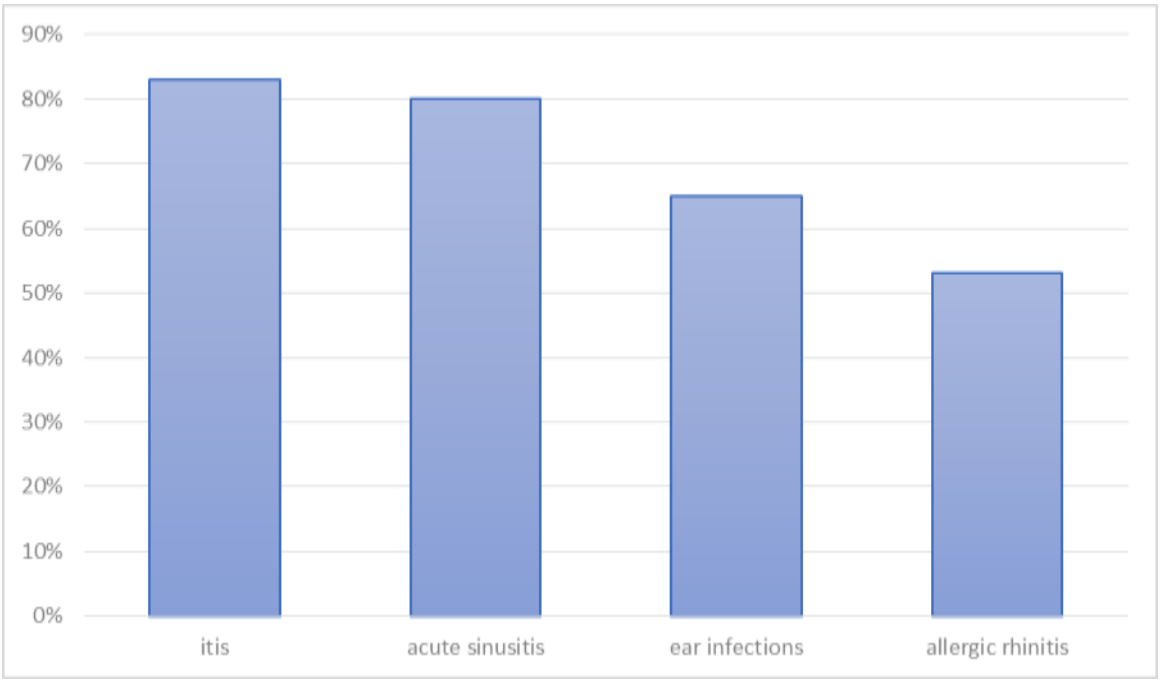

Figure 8: Short-term Corticosteroid Therapy Indications in Otolaryngology (ENT).

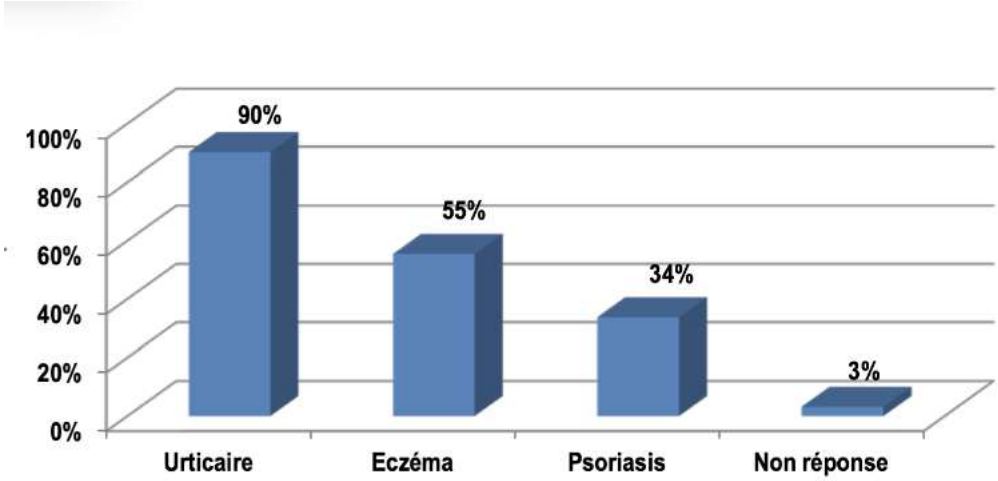

Figure 9: Indications for short-term corticosteroid therapy in dermatology.

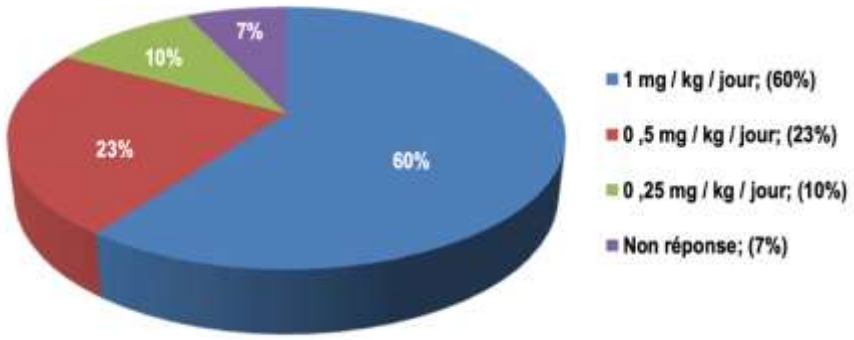

Figure 10: Dosage for prescribing prolonged corticosteroid therapy.

Table I: Contraindications of corticosteroid therapy.

Contra indication	Number of cases	Percentage
Uncontrolled diabetes	87	92%
Uncontrolled high blood pressure	76	80%
Infections	73	77%
Peptic ulcer	73	77%
Osteoporosis	58	61%
Glaucoma	55	58%
Psychotic states	53	56%
Cirrhosis	52	55%
Non reponses	1	1%

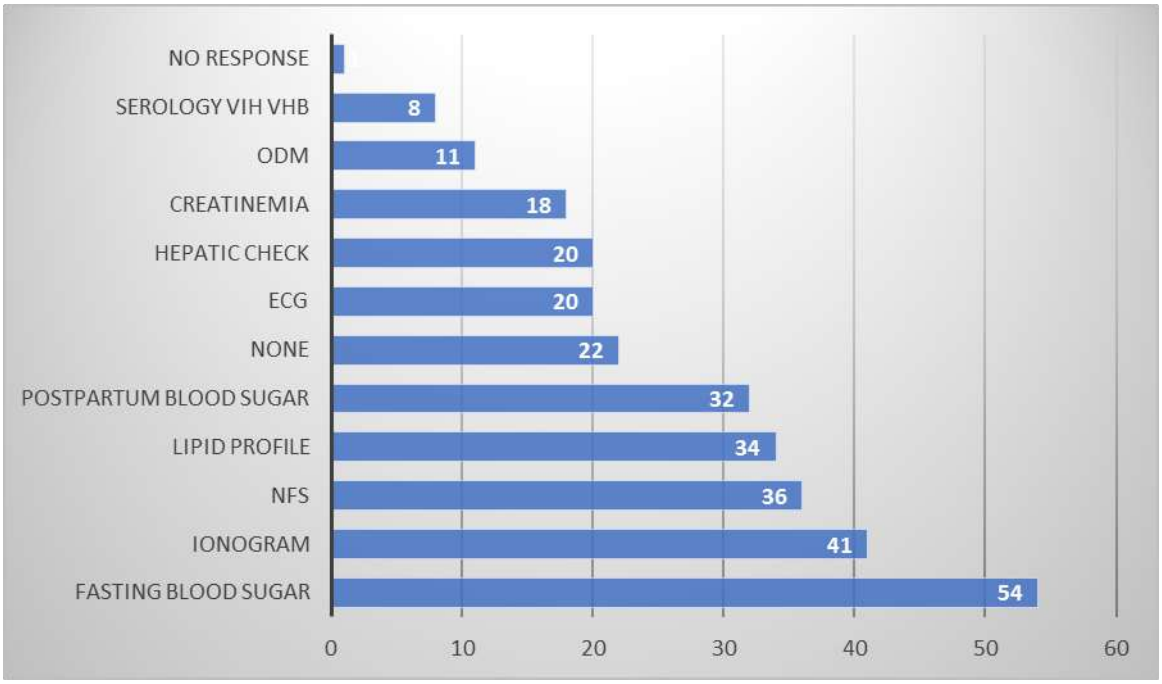

Figure 11: Frequency of Prescription of Pre-therapeutic Paraclinical Assessments

Table II: Frequency of prescription of different adjunct measures to corticosteroid therapy.

	Always	*Sometimes*	*Never*	*No answer*
Vitamin-calcium treatment	33%	47%	13%	7%
Low sodium diet	82%	14%	0%	4%
Low carbohydrate diet	28%	26%	34%	12%
Proton pump inhibitors	35%	26%	19%	10%
Biphosphonate	0%	13%	76%	11%
Potassium Intake	27%	23%	41%	9%
Regular physical activity	32%	48%	13%	7%

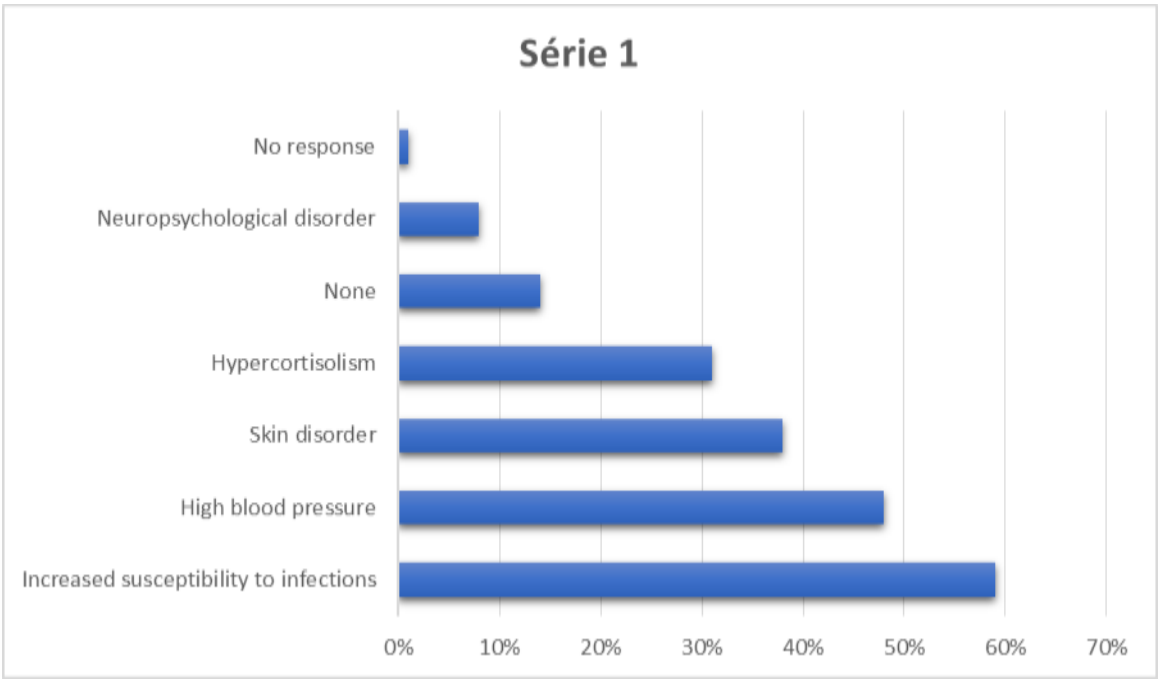

Figure 12: Frequency of side effects with prolonged corticosteroid therapy.

VI- Recommendation

The study proposes measures to improve the management of prolonged corticosteroid therapy by general practitioners, based on survey results and participant expectations. These measures include strengthening coordination between general practitioners and specialists through a shared monitoring booklet, training young general practitioners through simulation courses, updating knowledge through continuous medical education, developing prescription assistance software, enriching the study with the patient's perspective, the need for national or international recommendations, and developing a good practice guide for general practitioners.

VII- CONCLUSION

The study explores the diversity of practices among general practitioners in Marrakech regarding corticosteroid prescription, highlighting challenges related to the lack of consensus and controlled studies. The aim is to improve the quality of care by comparing these practices with recommendations. The analysis of 95 questionnaires reveals significant divergences. Pending reinforced coordination between general practitioners and specialists, as well as protocols and recommendations, the study suggests a good practice guide for general practitioners.

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