

Internal Medicine

EVALUATION OF TOLERANCE TO LONG-TERM CORTICOSTEROID THERAPY IN PATIENTS WITH SYSTEMIC DISEASES:

A Monocentric Observational Study

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ABSTRACT

Introduction: Although glucocorticoids play an undisputed role in systemic, inflammatory and autoimmune pathology, their prolonged administration is often associated with dose- and time-dependent adverse effects. The purpose of this study was to assess tolerance to long-term glucocorticoid therapy, describe risk factors and protective measures in the context of clinical practice in the Internal Medicine Department of the CHU of Mostaganem.

Materials and Methods: A prospective longitudinal cohort study was conducted among 30 patients followed for more than three months (on average 23.11) receiving a glucocorticoid treatment (average dose: 7.5 mg/day of prednisone). Data were collected using structured questionnaires and analyzed using SPSS software with appropriate parametric and non-parametric tests.

Results: In this cohort, the female population prevailed over the male one. The most common adverse events reported were Cushing's signs (75%), insomnia (70%), fungal (53.3%), and bacterial (43.3%) infections, osteoporosis (16.7%). Of particular interest was the occurrence of glucocorticoid-induced diabetes, which was positively associated ($p = 0.006$) with sarcoidosis. Participants reported weight gain as the most bothersome side effect (40%), while females experienced more sex-related side effects compared to males ($p = 0.008$).

Discussion: The present findings are consistent with the existing literature on this topic, which highlights the impact of prolonged glucocorticoid use on various organs. Furthermore, the association between glucocorticoid-induced diabetes and sarcoidosis identified in our study provides new evidence for the need for targeted metabolic monitoring in this category of patients. Additionally, a prospective design allowed us to document the difficulties of glucocorticoid dose tapering, as well as the significant psychological burden resulting from morphological changes due to glucocorticoid use. These findings emphasize the fact that the issue of prolonged glucocorticoid administration cannot be resolved within the framework of pharmacological intervention only.

Conclusion: Prolonged corticosteroid therapy is associated with significant iatrogenic morbidity, which may not be adequately monitored and controlled in real-world clinical practice. In order to optimize the benefit-risk ratio, it is necessary to implement a strategy that goes beyond the framework of pharmacological treatment and includes rational preventive measures and therapeutic patient education (TPE) in order to combat corticophobia and harmonize professional practices.

Keywords: Glucocorticoids; Systemic diseases; Iatrogenic morbidity; Long-term therapy; Therapeutic patient education; Risk factors.

INTRODUCTION

Since their clinical introduction by Philip Hench and his colleagues at the Mayo Clinic in 1948, glucocorticoids have dramatically transformed the prognosis of numerous previously intractable diseases [1]. Their remarkable anti-inflammatory, immunosuppressive, and anti-tumor properties have made them an invaluable foundation in the management of a wide variety of immune-mediated and inflammatory conditions across both in a medical and a surgical setting [2-6].

The optimal use of these drugs is, However, often challenged by a plethora of dose- and time-dependent adverse effects [7,8]. To address these challenges, a prospective longitudinal cohort study was conducted within the Internal Medicine Department of the CHU of Mostaganem. The study aimed to evaluate the tolerance of these drugs amongst patients receiving a long-term glucocorticoid therapy, identify associated risk factors, and analyze implemented protective measures. Ultimately, this research provides the medical field with the necessary data to improve patient safety and everyday quality of life.

OBJECTIVES

Primary Objective

Assess the prevalence and clinical, biological and behavioral risk factors for adverse effects related to prolonged corticosteroid therapy in an internal medicine ward.

Secondary Objectives

Evaluate the impact of adherence to the treatment, the compliance to a lifestyle and diet adjustment and the understanding of the treatment by the patient on the occurrence of side effects.

Analyze the correlation between the duration of the treatment and the occurrence of adverse effects.

Assess the relevance of the additional measures prescribed and elaborate a specific educational program for patient's monitoring related to treatment with long term glucocorticoids.

Raise awareness among professionals about the importance of psychological support and monitoring of these patients.

MATERIALS AND METHODS

The purpose of this study is to determine the effects of long-term systemic glucocorticoid treatment in patients with autoimmunity or inflammatory diseases. The prospective longitudinal cohort study was conducted in the Internal Medicine Department of the CHU of Mostaganem in an 11-month period between August 4, 2024, and July 4, 2025, including patients under prolonged glucocorticoid treatment for more than 3 months with a daily dose of prednisone higher than or equal to 7.5 mg/day. Non-inclusion criteria comprised short-term glucocorticoid treatment (less than 3 months) and non-systemic diseases, whereas exclusion criteria involved patients who declined to participate, were lost to follow-up, or developed severe intervening comorbidities. The data were collected using a structured questionnaire and analyzed using SPSS (v29.0.1.1), with qualitative variables described as frequencies and percentages and quantitative variables as means

and standard deviations. Group comparisons were performed using the Chi-square test, Fisher's exact test, Mann-Whitney, and Kruskal-Wallis tests, whereas bivariate associations were evaluated using Pearson or Spearman correlation coefficients based on the Shapiro-Wilk test results (). The study strictly followed ethical guidelines, utilizing informed consent while ensuring the anonymity and confidentiality of all participants' data."

RESULTS

A total of 30 patients (mean corticosteroid treatment duration: 23.11 months) were recruited in this study conducted at the University Hospital Center (UHC) of Mostaganem over an 11-month period. The sex ratio was significantly higher among females (0.30). The most frequent therapeutic indications were systemic lupus erythematosus and sarcoidosis, which accounted for nearly a half of all cases. Fifty percent of the patients received prednisone as a first-line treatment, whereas 86.6% of them were prescribed a corticosteroid-sparing strategy associated with systematic adjuvant therapy. On the other hand, patients' lifestyles were rarely adapted to chronic glucocorticoid therapy: only 10% of them engaged in regular physical activity. After a comprehensive clinical examination, multiple adverse effects were identified. In particular, Cushing's syndrome was manifested by upper trunk weight gain (75% of patients) and typical signs such as insomnia (70%), irritability (66.7%), and anxiety (56.7%) (Figure 1) [27]



Fig1. photos of patients who developed cervico-facial lipodystrophy [27]

Besides, glucocorticoid-induced diabetes developed in 23.3% of cases, which was found to be positively correlated with sarcoidosis (Fisher's test, $p = 0.006$). Hypertension was another frequent metabolic complication that was noted in 16.7% of patients. Moreover, the analysis revealed a number of visceral and endocrine adverse effects, including menstrual irregularities (30.4%), hirsutism (60.8%) (Figure 2) [27]

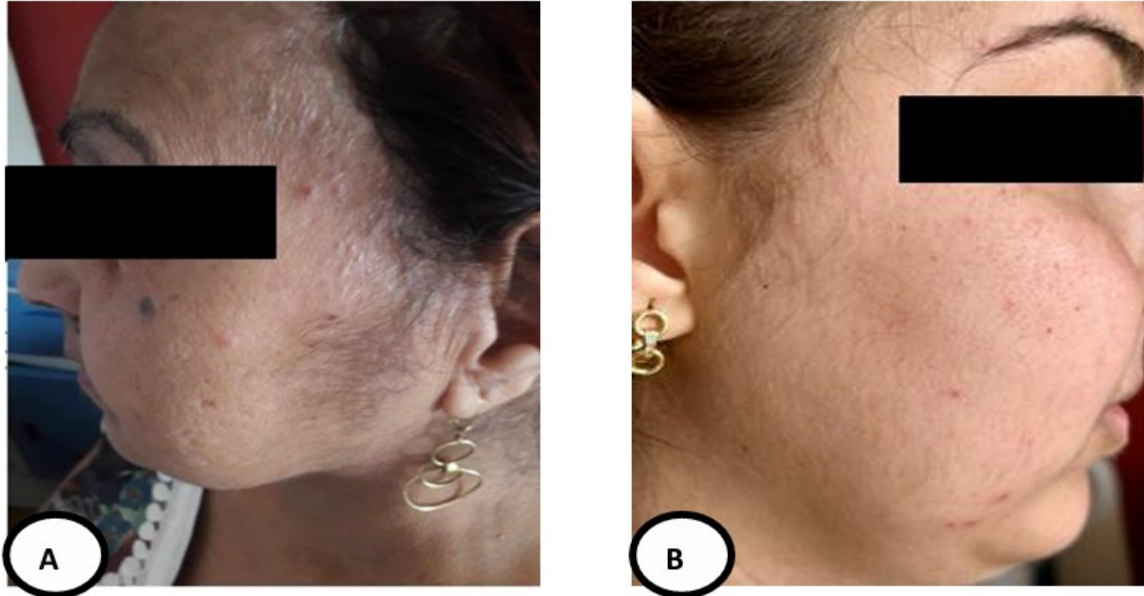


Fig 2. hirsutism secondary to prolonged corticosteroid therapy in female patients, A and B multiple localization, of the department) [27]

and acne (36.7%) (Figure 3) [27] .

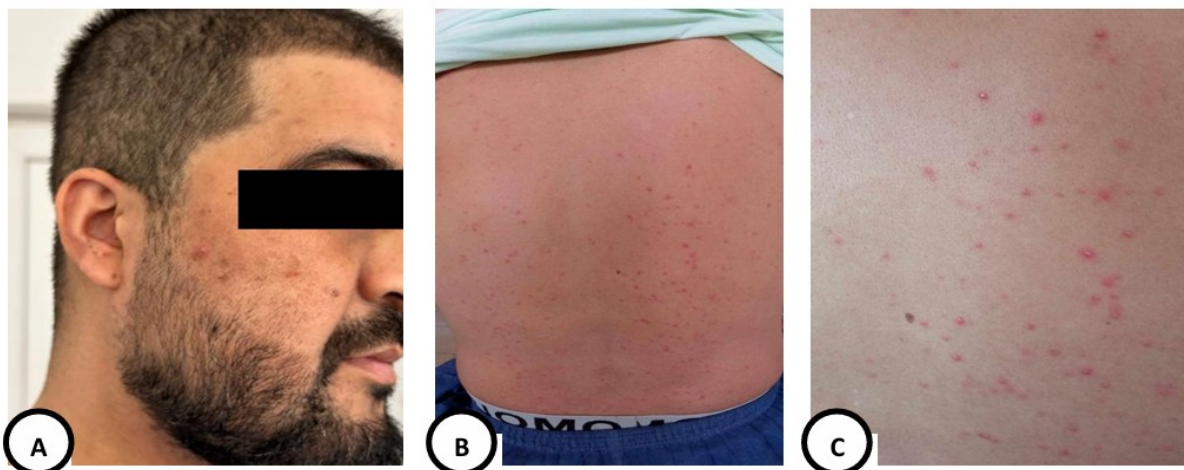


Fig 3. photos of patients known to the department who presented with steroid acne A. Face acne, B. and C. Back acne [27]

Osteoporosis was a typical complication of long-term prednisone treatment, which was documented in 16.7% of female patients, whereas aseptic necrosis of the femoral head was detected in one individual. The survey also reported a high incidence of infections, including fungal (53.3%) (Figure 4) [27],



Fig 4. photo of a female patient from the department who presented with oral thrush [27]
bacterial (43.3%) (Figure 5) [27] ,



Fig5. photo of a female patient from the department who presented with corticosteroid-induced furunculosis. A. Mammary and inframammary region, B. Pelvic region. [27]

and viral (23.3%) ones. In addition, eye conditions such as cataracts (6.7%) and glaucoma (10%) were common adverse effects of glucocorticoid treatment. Finally, the study found that weight gain was the most debilitating adverse effect in 40% of patients (Figure 6) [27].

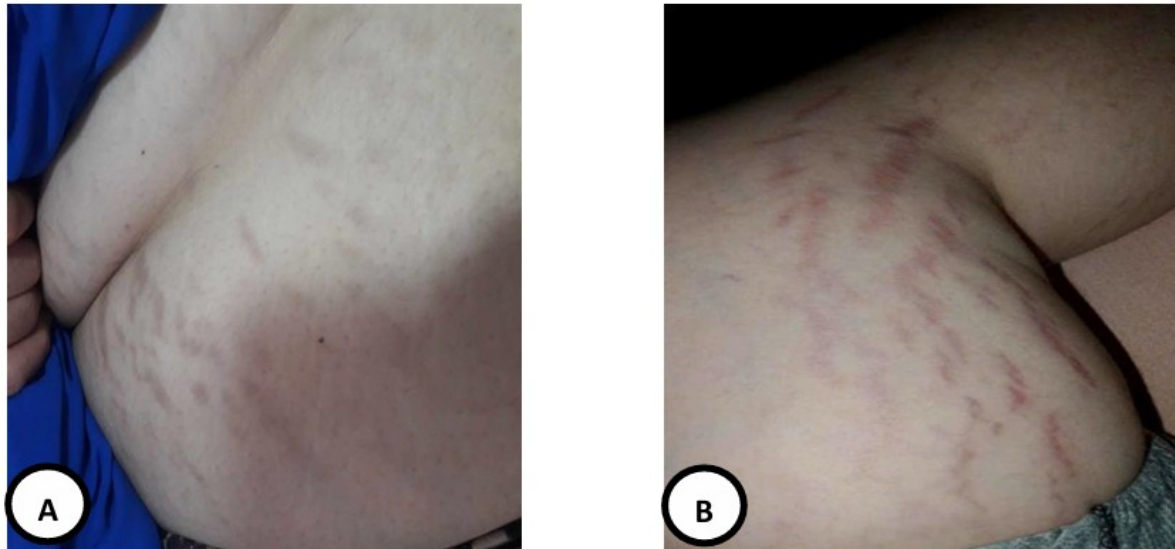


Fig 6. Photo of female patients from the department who presented with purplish striae A. Abdominal region, B. thigh region [27]

According to the Pearson chi-square test, female patients were significantly more likely to report sex-related adverse effects compared to males ($\chi^2 = 20.726$; $p = 0.008$).

DISCUSSION

The current monocentric observational study performed in the Internal Medicine Department of the CHU of Mostaganem on 30 patients aims to assess the tolerance of corticosteroids in long-term therapy in systemic diseases, bearing in mind that although glucocorticoids are the essential cornerstone in the management of these conditions due to their powerful anti-inflammatory and immunosuppressive properties [2], managing their long-term handling is characterized by major iatrogenic morbidity largely documented in the international literature. The analysis of our cohort underlines a clear female predominance and an age profile similar to that of the literature on systemic diseases, such as systemic lupus erythematosus or rheumatoid arthritis, affecting a vulnerable population to metabolic and trophic complications [8-10]. In our series, the initiation of corticosteroid therapy was dictated by the severity of visceral involvements threatening the functional or vital prognosis, with the preferential use of prednisone and prednisolone being in perfect accordance with international pharmacological standards of prescription of synthetic corticosteroids [9,11] whose intermediate half-life (between 12 and 36 hours) allows a single morning administration aiming to respect the nycthemeral rhythm of cortisol secretion and minimize, as far as possible, adrenal suppression, although the chronicity of treatments makes this suppression almost inevitable in the long term [12,13]. One of the major teachings of our work is the difficulty of weaning or reducing corticosteroid doses, with the literature confirming that dose reduction poses the risk of immunological relapse, where too rapid a decrease exposes patients to an inflammatory resurgence of the causal disease often requiring a re-escalation of doses [14,15], as well as iatrogenic chronic adrenal insufficiency resulting from the prolonged inhibition of the hypothalamic-pituitary-adrenal axis, which mandates a strict tapering regimen often supported by rigorous therapeutic education advocated in the reference manuals [13,16,17]. The richness of the

iatrogenic profile observed in our cohort matches point-for-point with the classical bibliographic data, whether considering metabolic and endocrine complications (cushingoid syndrome, weight gain, and corticosteroid-induced diabetes linked to the action of glucocorticoids on hepatic gluconeogenesis and peripheral insulin resistance) [7-9], osteoarticular complications (corticosteroid-induced osteoporosis and the risk of aseptic necrosis of the femoral head, justifying international prevention consensus by calcium and vitamin D supplementation, and bisphosphonates) [18-20], infectious vulnerability through alteration of cellular and humoral immunity [21,22], or trophic and ophthalmological complications (skin fragility, purpura, atrophy, and posterior subcapsular cataracts) requiring close multidisciplinary follow-up [8,23,24]. Finally, the statistical analysis of our series demonstrates a positive correlation between the cumulative duration of corticosteroid exposure and the overall iatrogenic load, validating observations on cumulative dose-dependent and duration-dependent toxicity [8,10], whereas bodily and morphological modifications, felt by patients as the most debilitating daily side effect, weigh heavily on therapeutic compliance and underline the vital importance of associating psychological support and active therapeutic patient education (TPE) with medical prescription [25, 26], demonstrating in conclusion of this confrontation with international references that the management of glucocorticoids requires the rigorous application of steroid-sparing strategies, the use of the minimum effective dose and the systematic prevention of their iatrogenicity [8,11].

CONCLUSION

In conclusion, despite the undeniable interest in treating various systemic, inflammatory and autoimmune diseases with glucocorticoids, the beneficial effects of corticosteroid therapy are inseparable from significant iatrogenic morbidity during prolonged or high-dose prescriptions. Although a wide range of corticosteroid-induced complications is well described, including various metabolic, bone, infectious, cardiovascular and psychiatric events, our work underlines a critical observation that their prevention and screening in the real world are in a large extent unsystematic, ranging from heterogeneous practices to sheer reliance on a single physician's judgment, limited efficiency of evidence and the lack of specific randomized trials. Hence, a modern corticosteroid-treated patient with prolonged prescriptions needs more than a drug prescription: an integrated and multidisciplinary strategy is mandatory to optimize the benefit-to-risk ratio. In this context, therapeutic patient education (TPE) and combating «corticophobia» is of particular importance to improve the adherence to therapy, to understand the disease and better cope with all its psychosocial consequences of drug treatment. The optimization of this strategy may include the distribution of validated educational tools (dietary advice sheets, specific patient information booklets), strict individual tapering calendars and development of multidisciplinary educational programs as well as continuing education for professionals, which are the only guarantees for harmonizing practices and providing benefits to the patient.

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