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Survey of Patient Knowledge and Awareness of "Sick Day Rules" in Rheumatology Patients on Long Term Glucocorticoid Therapy

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Abstract

Aims

Rheumatic disease (RMD) patients treated with long-term glucocorticoids (GC) are at risk of developing tertiary adrenal insufficiency. With this survey we aimed to assess the knowledge of RMD patients taking long-term glucocorticoid therapy regarding risk of adrenal insufficiency and understanding of the "steroid sick day rules".

Methods

RMD patients taking ≥2.5 mg prednisolone daily for ≥3 months were recruited from the Rheumatology outpatient department in Beaumont Hospital, Dublin. Patient knowledge and previous counselling of steroid sick day rules was determined using an 8-point questionnaire carried out face-to-face or via phone call.

Results

51 RMD patients on GC therapy were recruited. 3/51 (5.9%) of patients reported that they had been counselled on the Sick Day Rules. 2/51 (3.9%) carried a steroid emergency card or MedicAlert bracelet. Few patients would increase their steroid dose appropriately in response to infection, vomiting or peri-procedure [14/51 (27.5%); 9/51 (17.7%) and 5/51 (7.2%), respectively].

Conclusion

We demonstrate a significant deficit of patient knowledge around the precautions for long-term GC use in rheumatic diseases. We suspect that our results may be generalisable to many other RMD units. We are currently reviewing our procedures around healthcare professional and patient education, issuing of information leaflets, emergency cards or MedicAlert bracelets etc. to at risk patients.

Keywords **-** Tertiary Adrenal Insufficiency; Adrenal Crisis; Cortisol Deficiency; Glucocorticoid Education.

Introduction

Glucocorticoids (GC) are endogenous hormones crucial for organism homeostasis, the physiological secretion for which is regulated by the hypothalamic-pituitary-adrenal (HPA) axis [1,2]. Owing to their anti-inflammatory effects, synthetic GCs are used as immunosuppressive treatment for a wide variety of inflammatory and autoimmune diseases[2]. They are commonly prescribed in rheumatology practice via oral and intra-articular routes.

Adrenal insufficiency (AI) is caused by failure of the adrenal cortex to produce cortisol[3]. AI can be caused by pathology of the adrenal gland (primary AI), hypothalamic-pituitary dysfunction (secondary AI) or exogenous glucocorticoid therapy (tertiary AI) [1,2]. Excess exogenous or endogenous glucocorticoids exert a negative feedback on both the hypothalamus and pituitary gland, suppressing the release of corticotrophin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) respectively. Chronic administration of exogenous GCs also induces atrophy of pituitary corticotrophs cells and adrenocortical tissue [1,2]. TAI is associated with all forms of exogenous glucocorticoids and carries a risk of adrenal crisis when stress dose steroid dosing is not employed [1].

Previous reviews of adrenal crisis have identified failure to follow sick day rules as a risk factor for the development of adrenal crisis[4]. The UK Society for Endocrinology and British Society for Rheumatology recommend that patients taking prednisolone 5 mg/day or equivalent for 4 weeks or longer across all routes of administration (oral, topical, inhaled, or intranasal) should be issued with a Steroid Emergency Card[5]. The card includes patient details, diagnosis, and the emergency management of adrenal crisis with the aim to improve outcomes in this population.

The COVID-19 pandemic has presented many challenges to healthcare providers and systems. Relevant to this study, patients with rheumatic disease (RMD) on prednisolone >10mg/day were shown to have increased risk of hospitalisation with COVID-19[6], however it is unclear if this was attributed to a crisis or missed crisis event or secondary to an immunosuppressive effect. Regardless, there is still a need for standardisation of care and improved guidelines on the management of patients on immunosuppressive glucocorticoids.

The aim of this study was to assess the knowledge of the “Steroid Sick Day Rules” in rheumatology patients on GC therapy. We wanted to determine if patients possessed a steroid emergency card or MedicAlert bracelet for their GCs. We also wanted to assess if patients recalled counselling on the precautions around GC use by a healthcare professional previously. We hope to highlight a potential educational opportunity in this cohort and therefore decrease the risk of adrenal crisis and improve patient safety.

Methods

Our evaluation was conducted in Beaumont Hospital, a large tertiary referral centre in Dublin, Ireland between March 2020 – July 2021. The audit was approved by the hospital audit department. Our audit tool was based on the Royal College of Physicians (RCP) 2020 guidance for the prevention and emergency management of AI [5].

Suitable participants were recruited by reviewing the charts of patients attending the rheumatology outpatients department at Beaumont Hospital and by filtering the Beaumont DAWN database, a software programme where rheumatology patient information is stored and categorised by disease process and treatment regimen. Patients were included if they had an established diagnosis of a rheumatology disease requiring treatment with ≥2.5 mg prednisolone daily or equivalent for >3 months. We included doses as low as 2.5mg/day as there is evidence to suggest these patients are still at risk of tertiary adrenal insufficiency [7].

Eligible patients were invited to participate voluntarily by completing a questionnaire either in person or via telephone conducted by medical and nursing staff. Verbal consent for same was obtained. The questionnaire recorded patient characteristics including age, sex, clinical diagnosis necessitating GC therapy, and prednisolone equivalent dose of GC. We also asked if patients carried a steroid emergency card or a MedicAlert bracelet; whether or not a health care professional had previously discussed the "Steroid Sick Day Rules" with them and whether they would inform every healthcare professional that they were on glucocorticoid therapy.

The questionnaire also included a series of clinical scenarios to determine if patients would alter their steroid dosing in situations including active infection; vomiting or diarrhoea; and prior to dental, endoscopic or surgical procedures (table 2). Patients who were not aware of sick day rules were given verbal education at the time of interview on dose specific steroid dosing to commence if they are unwell and to seek medical advice regarding further dose adjustment.

Results

Fifty-one patients were identified as eligible, and all completed the questionnaire. Demographic data is outlined in table 1. The majority of patients were female (n= 41) and 47% (n=24) were aged between 30-50 years. The median prednisolone equivalent dose taken was 5mg (IQR=5mg) and the majority of patients had been taking GC therapy for greater than five years (n=24). Indications for GC therapy included Rheumatoid Arthritis (n = 1), Polymyalgia Rheumatica (n = 7), Vasculitis (n = 11), Systemic Lupus Erythematosus (n = 31), and Polymyositis (n=1).

Table 1. Demographic characteristics, dose in prednisolone equivalent, and indication for long-term steroid.

	n	% Or (Range)
Age	18-30 years (1)	2%
	30-50 years (24)	47%
	50-70 years (15)	29.4%
	>70 years (11)	21.6%
Gender – females	41	80.4%
Prednisolone equivalent dose (median)	5mg	(2mg – 25mg)
Duration of corticosteroid therapy	3-12 months (5)	9.8%
	1-5 years (22)	43.1%
	>5 years (24)	47.1%
Indication for long term steroid	Rheumatoid Arthritis (1)	1.9%
	Polymyalgia Rheumatica (7)	13.8%
	Vasculitis (11)	21.6%
	SLE (31)	60.8%
	Polymyositis (1)	1.9%

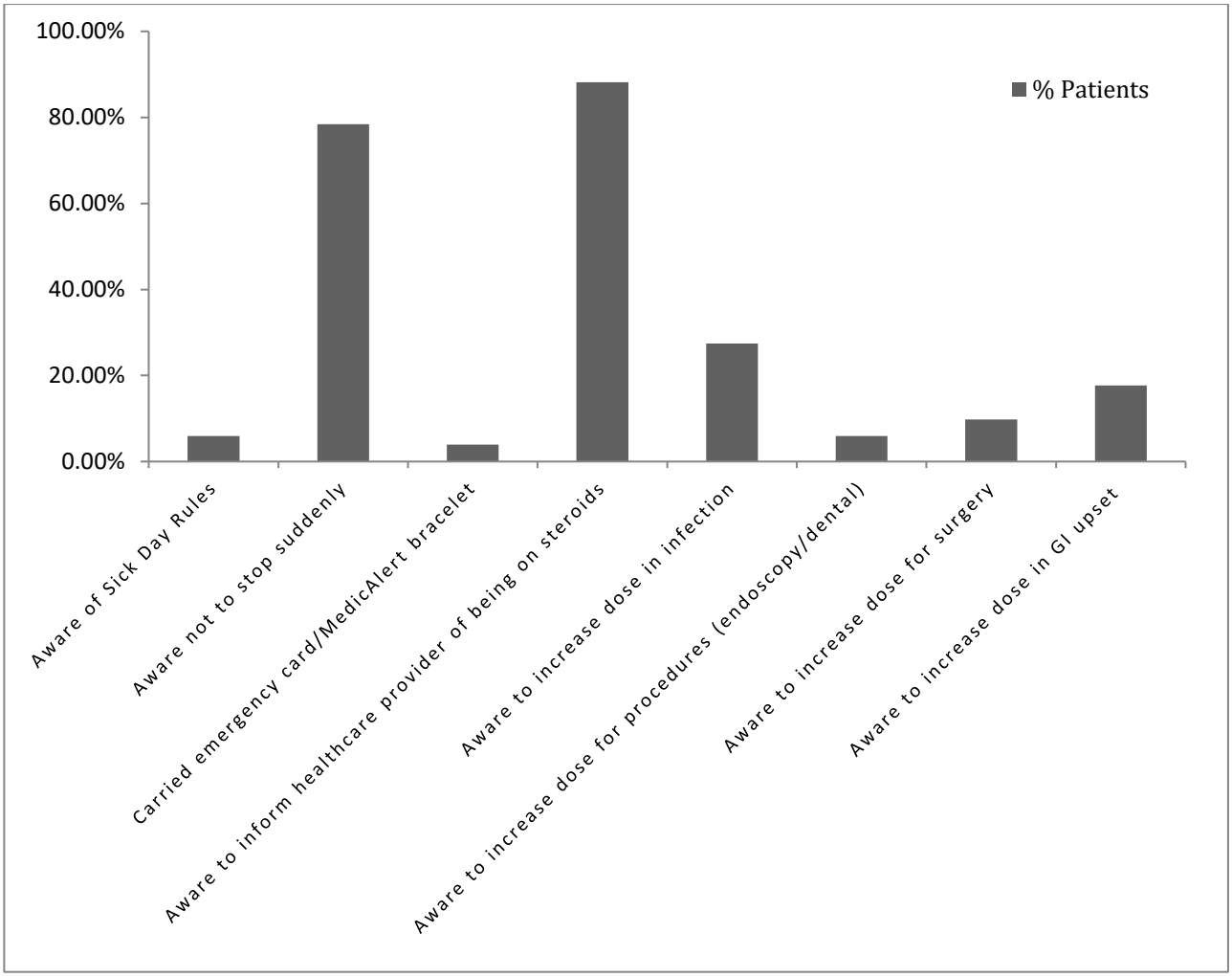
Only three patients 3/51 (5.9%) responded that they were aware of the 'Steroid Sick Day Rules'. In total 2/51 (3.9%) carried a steroid Alert Card or ID bracelet. Of patients who were on taking greater than or equal to 5mg equivalent Prednisolone dose (82%, n=41) only 2.4% (n=1) patients carried a steroid alert card or bracelet.

The majority of patients were aware that GC should not be withdrawn suddenly (n = 40) and to inform healthcare professions that they are on GC therapy (n = 45). However there was poor awareness demonstrated in other aspects of sick day management including increasing steroid dose during infection (n = 14), increasing steroid dose during vomiting/diarrhoeal illness (n = 9), awareness of need for increased steroids peri-procedurally (e.g. endoscopy, dental procedure, n= 3) or peri-operatively (n = 5). Figure 1 outlines questionnaire results in percentages.

Table 2. Steroid questionnaire to review awareness of precautions.

Aware of sick day rules?	Yes/No
Aware steroid should not be stopped suddenly	Yes/No
Aware needs steroid emergency card or MedicAlert bracelet?	Yes/No
Aware needs to inform healthcare profession of being on steroid?	Yes/No
Aware to increase dose during infection?	Yes/No
Aware to increase dose for procedure (endoscopy/dental)	Yes/No
Aware to increase dose for surgery?	Yes/No
Aware to increase dose in gastrointestinal upset?	Yes/No

Figure 1. Results in percentages of patient questionnaire responses.



Discussion

Our study emphasises a significant deficit in patient awareness of precautions around long-term glucocorticoid use for rheumatic disease. Glucocorticoids are used for the treatment of a wide variety of diseases including Polymyalgia Rheumatica, Giant Cell Arteritis, Rheumatoid Arthritis, Systemic Lupus Erythematosus and Vasculitis[8]. This is of concern because adrenal insufficiency secondary to long-term glucocorticoid use is relatively common[9]. A recent cross sectional study in 42 patients with rheumatoid arthritis on prednisolone 5mg/day for >6 months demonstrated a high prevalence of prednisolone induced AI as defined by an insufficient response to a Synacthen (corticotrophin) stimulation test. 48% of participants (20/42) had an insufficient adrenal response to the Synacthen test. Including only patients who had not received concomitant treatment with any glucocorticoids (intra-articular, intra-muscular, topical preparations) within the previous 3 months, 13/33 (39%) had an insufficient response[10].

The threshold of glucocorticoid exposure for the development of TIA is unclear however it is generally accepted that patients taking >5mg prednisolone per day for >4 weeks are at risk of tertiary AI. It has been shown that the risk of tertiary AI increases with greater cumulative glucocorticoid exposure[8].

However, a systemic review of glucocorticoid therapy and adrenal insufficiency carried out in 2020 demonstrated adrenal insufficiency in some patients at doses <5mg prednisolone equivalent dose/day, <4 weeks of exposure and following tapered withdrawal[7]. Such glucocorticoid regimens are commonly prescribed in rheumatology practice and for this reason, we included patients on <5mg prednisolone equivalent daily doses, despite RCP guidelines identifying patients on higher doses as at risk for adrenal insufficiency[5].

It follows that a significant proportion of rheumatology patients on long-term glucocorticoids may be at risk of adrenal crisis. There is no universally accepted definition for adrenal crisis, however Rushwood et. al described adrenal crisis in an adult as an acute deterioration in health status associated with absolute hypotension (systolic blood pressure <100 mmHg) or relative hypotension (systolic blood pressure >20 mmHg lower than usual), with features that resolve within 1 to 2 hours after parenteral glucocorticoid administration[11]. The data around the incidence of crisis in tertiary adrenal insufficiency is scant, however based on evidence from primary and secondary adrenal insufficiency studies the incidence of adrenal crisis is estimated to be between 5.2 – 8.3 crisis per 100 patient years [4, 12, 13]. Adrenal crisis is important as it contributes to mortality in adrenal insufficiency[11]. A recent prospective study following 423 patients with adrenal insufficiency (primary and secondary), demonstrated 0.5 adrenal crisis related deaths per 100 patient-years[12].

Patient education is effective in improving self-management and correct dose adjustment of stress related glucocorticoids in patients with adrenal insufficiency[14]. In an Irish study carried out in 2017, patients taking glucocorticoids for immunosuppression demonstrated a significant lack of awareness of precautions for steroid use when compared to endocrine patients on replacement therapy and fewer patients recalled having received written information around these precautions[15]. Our data further supports this data with only 5.7% of patients (n=3) reporting that they were aware of the Sick Day Rules. Also, though the majority of our patients were aware not to abruptly cease GCs, many patients reported concerns about a rebound of disease activity rather than concerns regarding AI. These responses however were not formally recorded and could be explored in future research.

Recently published guidance on the prevention and emergency management of adults with adrenal insufficiency recommends that patients at risk of adrenal insufficiency taking >5mg prednisolone per day for >4 weeks be issued with a Steroid Emergency Card[5]. These should prompt healthcare providers to consider adrenal crisis and initiate appropriate management in patients carrying the card as well as signposting to the latest guidance on the management of adrenal crisis.

Both the NHS and the European Society of Endocrinology have developed Steroid Emergency Cards, which are readily available and should be issued by healthcare providers. Despite this, Steroid Emergency cards are unavailable at present in Ireland and compliance with carrying alerts of any form is poor[15, 16, 17]. Salehmohamed et al demonstrated that only 7% of patients on immunosuppressive glucocorticoids carried steroid therapy identification[15]. In our cohort only two patients (3.9%) carried a MedicAlert bracelet.

Education of healthcare providers is also an important component in the management of patients with adrenal insufficiency. In a UK survey of 100 healthcare providers (doctors and specialists nurses), only 50% always or usually counselled patients about steroid sick day rules, and 28% did this rarely or never [18]. Education of healthcare professionals is particularly critical in the time of COVID-19. Gianfrancesco et al found that prednisolone exposure of ≥10mg/day was associated with higher odds of hospitalisation with acute COVID-19 in rheumatology patients[6]. Also many of the adverse effects of long-term glucocorticoid use including elevated BMI, obesity, and hypertension were shown to be poor prognostic factors for patients affected by COVID-19[19,20,21].

In conclusion, patients on long-term glucocorticoids for the management of rheumatology diseases are at risk of adrenal insufficiency and adrenal crisis. Our data indicates poor patient awareness of precautions and safety measures around intercurrent illness or peri-procedural requirements. Furthermore, our data shows that these patients do not carry MedicAlert bracelets or steroid emergency cards, which is not in keeping with current recommendations. This calls for standardisation of guidelines for rheumatology patients at risk of adrenal suppression and promotion of educational material for healthcare providers and patients.

Declaration of Conflicts of Interest:
The authors declare no conflicts of interest to declare.

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