Variability in counselling for adrenal insufficiency in Rheumatology practice: implications for COVID-19 and beyond

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The COVID-19 pandemic has presented challenges and uncertainty for patients and physicians. Corticosteroids are the most commonly prescribed pharmacotherapy in rheumatology. Long-term corticosteroids are prescribed for many rheumatic diseases including rheumatoid arthritis and giant cell arteritis/polymyalgia rheumatica[1]. Diabetes, hypertension and weight-gain (all poor prognostic for COVID-19) are widely recognised adverse events, however the high prevalence of glucocorticoid-induced adrenal suppression (e.g. in 20/42 patients (48%) patients with rheumatoid arthritis receiving prednisolone ≥5mg/day for at least six months[2]) is less well-known.

Patients with adrenal insufficiency should be informed regarding corticosteroid 'sick-day rules', including the risk of life-threatening adrenal crisis if corticosteroids are discontinued suddenly or if there is insufficient stress dosing[3]. Prompt supplementary corticosteroids are required with significant intercurrent infection, including COVID-19, major trauma or surgery; intravenous corticosteroids are needed if vomiting[3]. Despite the importance for patient safety, there are no clear guidelines regarding corticosteroid-sick day rules for rheumatology patients. Consequently, there is variation in practice. Most clinicians 'double the corticosteroid dose', but this crude rule-of-thumb can lead to under- or over- treatment. Clear information for patients is particularly important during the current COVID-19 pandemic due to restricted or modified access to usual levels of healthcare, e.g. delayed or virtual conversion of clinic appointments and difficulty accessing helplines. Recently the World Health Organisation recommended corticosteroids to reduce mortality in critically ill COVID-19 patients[4], but there was a suggestion of worse outcomes with dexamethasone in COVID-19 patients not requiring supplemental oxygen (not usually on corticosteroids). Significantly poorer outcomes were reported in patients receiving ≥10 mg/day prednisolone (n=64)[5] for rheumatic disease, but to the best of our knowledge, there has been no evidence of adverse outcomes attributed to supplemental stress doses of corticosteroids in COVID-19. Here we report results of a survey evaluating corticosteroid sick-day rule counselling and highlight an educational need to prevent adrenal crisis.

In March 2020 the British Society for Rheumatology (BSR) issued "shielding" guidance for patients receiving long-term (>4 weeks) corticosteroids, either at high-dose monotherapy (>20mg/day) or low-dose (≥5mg/day) prednisolone combined with another

immunosuppressant (online supplement). Shielding identified categories of patients as clinically vulnerable, who were advised to take extra precautions during the first peak of the pandemic in England. Some clinicians and patients elected to delay starting or increasing corticosteroids for inflammatory flares, due to perceived safety concerns and to avoid needing to shield. Anecdotally we became aware of safety incidents (adrenal crises) after discontinuation of long-term corticosteroids or inadequate dose increments with concomitant COVID-19 (personal communication with the authors). In April 2020, the BSR updated their advice to reflect Endocrinology consensus guidelines on prevention of adrenal crisis for COVID-19[6]: hospitalised patients on long-term corticosteroids with COVID-19 should receive intravenous corticosteroids and in the community; patients taking 5-20mg prednisolone daily should take 10mg prednisolone twice daily and patients taking >20mg should continue their usual dose, but in divided doses[6]. The twice-daily prednisolone dose (to mimic the stress response[6]), is an unfamiliar frequency of administration in rheumatology practice. We conducted an online survey between 16th May and 16th July 2020, to assess corticosteroid sick-day rule counselling and to improve visibility of the COVID-19-specific corticosteroid guidelines, disseminated via the BSR (electronic newsletter and social media).

Of 100 respondents (93 physicians, 7 specialist nurses), only 50% ‘always’ or ‘usually’ counselled patients about corticosteroid sick-day rules and 28% performed this ‘rarely’ or ‘never’. The timing and content of education was variable (supplementary Figure1). The majority counselled patients when starting (45%) and tapering (42%) corticosteroids and advised not to discontinue corticosteroids suddenly (85%) and to increase doses with intercurrent infection (72%). Although 74% prescribed a variable regimen, 15% advised patients to self-titrate, without contacting a medical professional. Despite recognising that infection may warrant increased corticosteroid doses, 69% clinicians changed their usual management with COVID-19 (the majority (52%) would reduce the corticosteroid dose, 10% would not increase and 7% would advise a lower than usual increment), 10% would give the same advice (as per any other infection) and only 13% followed the recent endocrinology guidance. The majority (74%) would refer someone with suspected adrenal insufficiency for endocrinology consultation without performing any investigations themselves; the remaining demonstrated variability in timing and testing for adrenal insufficiency. After being directed to the endocrinology COVID-19-specific guidelines[6], 71% changed their management and 16% stated that they had not read the guidance.

We aimed for a sample size of 100 respondents, which was selected as a reasonable compromise between generalisability of the results and feasibility. Although the survey was conducted during the peak of the first wave of the COVID-19 pandemic, there was rapid engagement, with the target of 100 responses achieved within a short time interval. Respondent characteristics reflected the BSR professional body, as the majority of respondents were consultants.

To our knowledge, this is the first evaluation of corticosteroid sick-day rules in rheumatology, which are highly relevant, given that many patients with rheumatic disease receive long-term prednisolone. Patients receiving long-term prednisolone are more vulnerable to infection and may have poorer outcomes with COVID-19[5], however approximately half may have adrenal insufficiency and are at risk of adrenal crisis with significant intercurrent infection,, as highlighted by the National Patient Safety Alert[7]. Patients with primary adrenal insufficiency on replacement corticosteroids exhibit greater knowledge of sick-day rules than patients receiving corticosteroids for non-endocrine immunosuppressive indications, who therefore may be at higher risk of adrenal crisis[8].

Our results demonstrate variation in practice. Despite knowledge that intercurrent infection may necessitate corticosteroid dose increment, most clinicians would reduce the dose with COVID-19. This highlights a significant unmet educational need amongst rheumatologists. This is an immediate and critical patient safety issue, given a global second wave of COVID-19 and the advent of seasonal influenza. We also call for specific guidance and clinician training for patients on long-term corticosteroids, to standardise sick-day rule counselling across specialties, including considerations of the type or severity of stressors (e.g. infection, surgery and trauma) and issuing the steroid emergency card[7]) and the evaluation of adrenal insufficiency. Recent guidelines recommend peri-operative stress-dosing[9], despite the limited evidence-base[10]. Supplemental steroid-dosing during times of physiological stress is considered the safest approach.

Figure 1 Survey Results

Survey results from 100 respondents in the U.K. Data are presented as percentages. Where indicated respondents may have selected more than one option. In Figure B and C, the option 'other' was a free text response from one Rheumatology consultant or equivalent 'increasing prednisolone for long-haul aeroplane flights' (not a standard indication for increasing corticosteroid dose). N/A Not applicable; IV intravenous

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