Maintenance oral steroids are not required in severe asthma

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To the Editor:

Historically, adult asthma guidelines have included the use of maintenance oral corticosteroids (mOCS) at the higher end of disease severity when other conventional treatments have failed to achieve disease control [1, 2]. Registry data suggests that 52% of patients with severe asthma in the UK are on mOCS at a median daily dose of 10 mg prednisolone [3] while the International Severe Asthma Registry indicates 20–63% of patients worldwide are on mOCS [4].

Severe asthma is a multimorbid disease state including numerous comorbidities that can cause breathlessness and lead to inappropriate prescription of mOCS [5]. Corticosteroid use increases the risk of numerous comorbidities including type 2 diabetes mellitus, osteoporosis, dyspeptic disorders, cardiovascular disease including myocardial infarction, psychological effects, weight gain and adrenal insufficiency (AI) [6, 7]. The risks of these adverse effects are dose dependent, developing after cumulative lifetime exposures of 0.5 g prednisone equivalent [8].

The steroid sparing benefits of asthma biologics are well known [9] but some patients do not fit eligibility criteria for biologics, while biologics may not be necessary for others. In addition, mOCS treatment can reduce blood eosinophil counts (BECs) and may limit patient eligibility for biologic therapy [10].

Minimising unnecessary and inappropriate exposure to mOCS in patients with severe asthma can reduce morbidity from known adverse effects. Severe asthma centres manage patients across a large catchment area and regular face-to-face reviews may not always be feasible in a majority working-aged patient cohort. Here, we present the outcomes from a virtual oral corticosteroids (OCS)-weaning clinic for adult patients, not on biologics, with severe asthma (diagnosed as per American Thoracic Society/European Respiratory Society criteria [11] by the severe asthma centre multidisciplinary team). Pre-weaning mOCS adherence was confirmed using a prednisolone assay.

Patients had a telephone review by an asthma clinical nurse specialist (CNS) every 2–4 weeks and their steroid dose was weaned based on a protocol co-developed with an endocrinologist. The rate of OCS down-titration was based on baseline mOCS dose. Briefly, prednisolone was reduced by 5 mg every week until patients were on 20 mg·day^{-1}, 5 mg every fortnight until they reached 10 mg·day^{-1}, 1 mg every week until reaching 5 mg·day^{-1}, and then 1 mg every 2–4 weeks until reaching 3 mg·day^{-1}. Depending on patients' symptoms, AI was screened for with an early morning cortisol measurement when patients were between 3–5 mg prednisolone and defined as unlikely if cortisol>300 nmol·L^{-1} (wean continued by 1 mg every 2 weeks until off mOCS), possible if cortisol between 150–300 nmol·L^{-1} (weaning paused at 3 mg and test repeated in 8 weeks) and likely if cortisol <150 nmol·L^{-1} (weaning paused and test repeated in 3–6 months).

During each consultation the CNS reviewed asthma symptoms, clinical status using the asthma control questionnaire (ACQ), self-management plan and any symptoms of AI. Patients and their family received education on symptoms and signs of AI, were reminded of the importance of adherence to inhaled therapies and steps to take if they developed symptoms of an exacerbation. If patients experienced increased breathlessness or any new concerning symptoms, they attended for face-to-face review and biomarker assessment (BEC and fraction of exhaled nitric oxide (F_{ENO})). When indicated, patients were referred to other members of the asthma multi-disciplinary team: clinical psychologist or respiratory physiotherapist.

Shareable abstract (@ERSpublications)
Protocol–guided multidisciplinary team supported steroid weaning is effective in reducing maintenance OCS use in most biologic-naïve patients with severe asthma, supporting the concept that maintenance OCS are inappropriate treatments for severe asthma https://bit.ly/4cgrJEL

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Retrospective data were reviewed for all patients referred to the clinic between April 2021 and June 2023. Results are presented as median (interquartile range). Proportions were compared using Fisher's exact or chi-square test and quantitative variables were compared using ANOVA (with Dunn's multiple comparison test) or Mann–Whitney U-test.

Of the 42 patients reviewed in the clinic, 69% were female, with age 57 (48–68) years. A high prevalence of multimorbidity was seen with at least one comorbidity in 41 out of 42 (98%). These included: breathing pattern disorder in 23 out of 42 (55%), obesity in 23 out of 42 (55%), gastroesophageal reflux disease in 21 out of 42 (50%), chronic rhinitis in 21 out of 42 (50%), anxiety or depression in 22 out of 42 (52%), diabetes in 16 out of 42 (48%) and osteopenia or osteoporosis in 8 out of 42 (19%). All patients were on high dose inhaled corticosteroids (⩾2000mcg BDP equivalent). At baseline, two patients (5%) declined biologics, nine patients (21%) had failed a biologic previously and the remaining 31 patients (74%) did not meet national prescribing criteria for a biologic (at that point in time).

Baseline mOCS dose was 10 mg (10–20 mg) and patients had been on mOCS for a duration of 60 months (17–117 months) equating to 18 g (6–47 g) of lifetime exposure (excluding exacerbations). Over 10 months (4–12 months) patients were weaned to a daily dose of 5 mg (3–8 mg). 25 out of 42 (60%) were weaned off prednisolone for asthma. However, steroid associated AI was common in these 25 patients with 72% remaining on ⩽5 mg prednisolone due to AI. There was no change in ACQ or F_{ENO} with steroid weaning but there was a trend towards an increase in BEC (p=0.06). Three patients developed BEC ⩾300 cells·L^{-1} but did not require a biologic as they had no exacerbations and were no longer on mOCS for asthma.

During the weaning process, 29 out of 42 (69%) patients briefly increased their steroid dose (up to 40 mg daily for 5–7 days) for increased symptoms; six of these were admitted to hospital. These patients were assessed and either: a) biologics were started (n=9); b) mOCS wean was continued if clinically appropriate (n=13, including two who had a hospital admission of less than 24 h); or c) weaning was paused until more focused comorbidity management could be implemented (n=7). No patients presented with symptoms suggestive of adrenal crisis. Table 1 compares clinical characteristics of patients who weaned off mOCS for asthma, patients who started biologic therapy and patients who were unable to wean mOCS. Of the nine patients (21% of the overall cohort) who started a biologic, mOCS had been weaned from 10 mg (10–14) to 6 mg (5–10) prior to biologic initiation. In this group ACQ significantly increased with steroid weaning (p=0.03), but biomarkers (BEC and F_{ENO}) remained unchanged.

TABLE 1 Clinical characteristics of patients who weaned off maintenance oral steroids for asthma, patients who needed to start biologic therapy and patients who were unable to wean

	Weaned off mOCS for asthma (n=25)	Started on a biologic (n=9)	Unable to wean/poor engagement (n=8)	p-value
Age (years)	56 (51–71)	53 (47–62)	49 (40–63)	0.32
Baseline daily dose (mg)	10 (5–18)	10 (9–17)	25 (15–40)	**0.008**
Duration (months)	60 (12–90) Range: 4–492	36 (14–192) Range: 7–480	66 (27–120) Range: 12–204	0.81
Total OCS (g)	11 (4–40)	18 (5–50)	57 (14–99)	0.13
Dose at the end of data collection (mg)	4 (0–5)[#]	6 (5–10)	10 (10–23)	**<0.0001**
ACQ6 at baseline	2.66 (2.20–3.46)	1.58 (0.87–2.33)	3.40 (1.13–3.83)	0.12
ACQ6 end	2.63 (1.63–3.62)	3.67 (1.16–4.42)	3.17 (2.00–4.66)	0.64
Blood eosinophils baseline (cells per µL)	100 (100–200)	100 (0.0–200)	100 (25–500)	0.65
Blood eosinophils end (cells per µL)	200 (100–250)	200 (75–700)	200 (150–250)	0.80
F_{ENO} baseline (ppb)	25 (9–33)	24 (12–50)	[¶]	0.79
F_{ENO} end (ppb)	18 (13–32)	15 (11–69)	[¶]	0.89
GORD	14 (56%)	5 (56%)	2 (25%)	0.39
Breathing pattern disorder	15 (60%)	4 (44%)	4 (50%)	0.69
Anxiety/depression	11 (44%)	3 (33%)	4 (50%)	0.83
BMI >30 kg·m^{-2}	15 (60%)	3 (33%)	5 (63%)	0.39
Smoking status	4 (16%) current smokers 4 (16%) ex-smokers	2 (22%) ex-smokers	3 (38%) ex-smokers	

Data are presented as median (interquartile range) or n (%), unless otherwise stated. Results in bold are statistically significant. Analysis completed using ANOVA, Mann–Whitney U-test or Fisher's exact test as appropriate. ACQ6: asthma control questionnaire; BMI: body mass index; F_{ENO}: fractional exhaled nitric oxide; GORD: gastro-oesophageal reflux disease; mOCS: maintenance oral corticosteroid; OCS: oral corticosteroid. [#]: OCS dose in these patients is for adrenal insufficiency. [¶]: Only available for two patients.

During the steroid wean, 3 patients (7%) had input from the clinical psychologist and 10 patients (24%) needed additional input from the specialist respiratory physiotherapist. Compared to patients without known breathing pattern disorder (n=19), patients with known breathing pattern disorder (n=23), had no significant difference in reduction in mOCS dose or ability to wean off OCS for asthma.

Patients attended a median of seven (5–11) telephone appointments and most patients (26out of 42, 62%) missed at least one appointment. Missed appointments may be suggestive of lower patient engagement and a smaller proportion of those who missed two or more appointments weaned off mOCS for asthma compared to those who missed none or one appointment (3 out of 9 (33%) *versus* 26 out of 33 (79%); p=0.016). The overall dose reduction in mOCS was similar in both groups.

8 out of 42 (19%) were discharged from the CNS clinic due to poor patient engagement (n=4), systemic symptoms limiting weaning (increased joint pains, n=2) or patient choice (n=2). At baseline, these patients had been on a higher dose of mOCS compared to patients who weaned off mOCS for asthma (25 mg (range 15–40) *versus* 10 mg (range 5–18), p=0.008).

Overall, we have demonstrated that protocol-guided OCS weaning supported by an asthma CNS in a virtual clinic was successful in weaning steroids even in patients with multiple comorbidities and who had been on mOCS for several decades. Most patients (60%) were able to wean off prednisolone for asthma completely and 21% of patients went on to start biologic therapy. Registry and single-centre studies have shown that systematic assessment of patients with severe asthma reduces mOCS burden independent of biologic use [12, 13]. Previously presented data has demonstrated face-to-face, biomarker-directed CNS clinics can successfully – and in some cases, more rapidly – wean mOCS, with 90% of patients weaning off mOCS by 12 weeks [14]. Our clinic reviewed patients once they had undergone systematic assessment and as it was largely virtual, intense biomarker surveillance was not routinely conducted but performed judiciously. While this may seem more pragmatic, it may raise safety concerns. Within our cohort, serious adverse events were rare, largely through very regular virtual contact and patient education. While some patients self-started a course of steroids and six patients had an asthma-related hospital admission this proportion was similar to pre-OCS weaning. We now focus more on patient and carer education on the role of steroids, recognising that not all episodes of breathlessness need steroid treatment. Close monitoring enabled identification of patients who truly needed biologics.

The steroid burden in patients with severe asthma is high and our data demonstrates that with CNS support, structured steroid weaning protocols alongside comorbidity management in a largely virtual setting is effective in reducing mOCS use. Concerted efforts should be made to wean mOCS before reaching for biologics as only 21% of our cohort were initiated on biologics. Our results suggest that for the majority of severe asthma patients, mOCS had been an unnecessary and inappropriate treatment and mOCS should not be initiated in severe asthma.

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