Dexamethasone for Cancer-Related Fatigue

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To the Editor: We applaud Yennurajalingam et al1 for their double-blind, placebo-controlled study investigating the impact of a 14-day course of dexamethasone 4 mg twice daily on cancer-related fatigue (CRF). The authors make a key finding that CRF and quality of life (QOL) are significantly improved by the use of dexamethasone. However, in addition to several methodological issues that the authors correctly acknowledge (high drop-out rate, absence of moderate-severe fatigue in some patients, lower baseline Functional Assessment of Chronic Illness Therapy-Fatigue questionnaire scores in dexamethasone-treated patients), we would add several further points, as there is significant danger that clinicians may extrapolate the data further than the authors intend.

Yennurajalingam et al2 assessed CRF on day 15 after a 14-day course of dexamethasone. A major limitation of the study is that data was not collected at later time points. In clinical practice, dexamethasone is typically prescribed for longer than 14 days in supportive care patients.2,3 Moreover, if a given intervention is successful (ie, reduction in CRF with dexamethasone), it is not unreasonable to believe that either a clinician or patient will continue the treatment. Unfortunately, the study from Yennurajalingam et al does not allow us to be certain of the efficacy or safety of dexamethasone beyond 14 days, thus limiting its applicability to routine clinical practice in the supportive care setting.

The use of high-dose corticosteroids (dexamethasone 8 mg = 50 mg prednisolone = 200 mg hydrocortisone), while appropriate for a short periods of time, carries significant risk of morbidity which may adversely affect QOL.4 Yennurajalingam et al5 conclude that the use of dexamethasone is not associated with increased adverse events (AEs), however there was a trend towards higher rates of grade ≥ 3 AEs in dexamethasone-treated patients (P = .14). This is an important finding since the relatively small number of events could foreseeably have resulted in the analysis being underpowered. We also note the list of AEs evaluated in this study did not include hyperglycemia, a well-recognized complication of corticosteroids that is reported to occur in up to one third of palliative care inpatients.5 Also, it is known that the risk of Pneumocystis (carinii) jiroveci pneumonia increases with longer-term corticosteroid use.6 Thus, the possibility of higher toxicity rates—potentially negating QOL benefits with longer-term usage of dexamethasone—cannot be excluded by this study.

Although this study investigated the impact of a single intervention on CRF, we would contend that the optimal management of CRF requires a holistic approach.7 In particular, addressing psychological well being8 (which was not improved by dexamethasone), pain control and exercise,9 sleep hygiene,10 and nutrition are paramount to improving CRF. Nor should we exclude the potential benefits of palliative systemic agents in reducing tumor burden and consequently partially alleviating CRF. Although the intention of Yennurajalingam et al1 was undoubtedly not to provide a single quick-fix strategy for improving CRF, our concern is that some clinicians may view the use of dexamethasone as such.

Given the dearth of high-quality blinded, randomized, placebo-controlled trials in supportive and palliative care, Yennurajalingam et al are to be congratulated for their study. However, in regards to the impact of their data on clinical practice, it is important to consider the short-term use of dexamethasone in this study, the potential toxicity of corticosteroids, and the need for an integrated, multidisciplinary approach to managing this distressing and difficult symptom.

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