Role of Inhaled Budesonide in the Treatment of Tuberculous Pyrexia

To the Editor:

The article by Pietinalho et al.1 reporting the use of inhaled budesonide in pulmonary sarcoidosis, has prompted us to share our experience in the use of inhaled corticosteroid as adjunctive therapy in tuberculous pyrexia. Similar mechanisms of cytokine production and release through activation of lung T-lymphocytes, in patients with sarcoidosis and in those with tuberculous alveolitis, have been described.2 In the latter setting, cytokines like TNFα, IL-1, and other interleukins might be responsible for the pyrexia that occurs in some patients with tuberculosis (TB).3 Modulation of cytokine release by systemic corticosteroid, along with the administration of antituberculosis drugs, can logically control the unremitting pyrexia.4 The duration of such therapy is usually 4 to 10 weeks.4,4 Inhaled corticosteroid, if demonstrated to be efficacious, may be the preferred alternative because of the following advantages, namely, (1) circumvention of interaction with antituberculosis drugs, especially rifampin,5 and (2) much lower risk of systemic side effects, and suppression of the hypothalamo-pituitary-adrenal axis.6 Thus, the inhaled route might allow safe deployment of steroid treatment in TB patients with relative contraindications to systemic corticosteroid therapy, such as diabetes mellitus, hepatitis B/hepatitis C-related liver diseases, and HIV coinfection.

Previously, we reported somewhat favorable experience with 9 HIV-negative patients with tuberculous pyrexia, who were treated for 2 weeks with inhaled budesonide at a dosage of 800 µg tid, via the dry powder inhaler.7 After this, we studied another 5 HIV-negative patients. When the results of all 14 patients were analyzed together, 9 of the 14 patients (64.3%) achieved defervescence (mean time required, 3.8 days; range, 2–6 days). When the mean maximum oral temperatures, for 7 days before and after starting inhaled corticosteroids, for all 14 patients were compared using the Wilcoxon signed ranks test (SPSS Software; SPSS, Inc; Chicago, IL), the decrease was significant: mean ± SD = 0.9 ± 0.5°C (p = 0.001; z = 3.238). Of these nine patients, two developed transient recrudescence or fever. Both conditions were resolved without recourse to systemic corticosteroid. Acceptance and tolerance by patients of inhaled budesonide was good. Two patients had hypothalamo-pituitary-adrenal axis function assessed and were found to be normal.

Our preliminary experience suggests that inhaled corticosteroid is efficacious in some patients with tuberculous pyrexia. The exact accountable mechanism is not clear. Inhaled budesonide, having high topical potency, may work via local-regional distribution through the ramifying bronchial vascular meshwork in the airways, partially anastomosing with the pulmonary microcirculation of the alveoli. Drugs absorbed gastrointestinally, following swallowing, are largely inactivated by first-pass metabolism and do not contribute much to systemic bioavailability. Systemic bioavailability secondary to lung bioavailability definitely occurs, but the contribution is insignificant.6 It is vitally important to delineate the possible characteristics of both patient and disease that are associated with favorable response. A randomized study comparing the efficacy of systemic and inhaled corticosteroids in patients with tuberculous pyrexia appears warranted. Finally, studies of the blood, or preferably of the bronchoalveolar-lavage fluid cytokine profiles, before and after treatment with inhaled or systemic corticosteroid would further our understanding of the immunopathogenesis of tuberculous pyrexia and of the impact of different modes of steroid treatment.

References

4 Alzeer AH, FitzGerald JM. Corticosteroids and tuberculosis: risks and use as adjunct therapy. Tubercle Lung Dis 1993; 74:6–11
5 Grange JM, Winstanley PA, Davies PDO. Clinically significant drug interactions with antituberculosis agents. Drug Safety 1994; 11:242–251

Blood Transfusion—Always a Minimum of Two Units?

To the Editor:

The issue of blood transfusion was raised in an excellent article by Erik Fransen et al.1 and by the editorial comment of Harold L. Corwin.2 One more point needs to be added to the discussion. It is generally agreed that routine blood transfusion is of no merit. Most physicians and surgeons also agree that hematocrit or