The clock keeps ticking for intravenous methylprednisolone

Florian Then Bergh

Patients with multiple sclerosis may benefit more from night-time rather than daytime infusion

Glass-Marmor and colleagues¹ randomised 17 patients with multiple sclerosis in acute relapse to receive intravenous methylprednisolone (MP) in the morning or at night, together with infusion of placebo at the other time point, in an inpatient setting (see page 886). When admitted for a subsequent relapse, those originally treated in the morning had intravenous MP at night, and vice versa. In this way, daytime and night-time treatments were compared within the same subject. Steroid administration at night was favoured by several measures, such as speed of remission of neurological impairment, frequency of adverse events and patients' subjective preferences.

The study is obviously preliminary: it reports on a small sample, the Expanded Disability Status Scale is a fairly crude disability measure and spasticity (which often responds particularly well to intravenous MP) was not specifically assessed. In addition, the symptoms and severity of the two relapses were most likely

different, and this is hard to fully take into account in the comparison of the two treatment regimens. However, the trial is interesting both biologically and clinically. The rationale of administering glucocorticoids at night is that plasma levels of endogenous cortisol and their impact on immune function are lowest in the evening, and therapeutic effects may be particularly pronounced in this milieu.² Admittedly, the dosage administered therapeutically literally floods any available intracellular hormone receptor molecule, and a discussion about comparatively small physiological changes may appear inappropriate. However, the results reported here may be taken to support this hypothesis. Clinically, safe night-time administration neatly matches recent approaches to home based treatment by trained family members, which has been shown to be equally effective and far cheaper than inpatient or clinic based therapy.³ Patients with frequent relapses, in particular, or the occasional patient selected for regular intravenous

MP^{4 5} would benefit from such modern approaches, resulting in less disruption of their everyday routines.

The study of Glass-Marmor and colleagues¹ should serve as a basis for more thorough research, with a state of the art, double blind, multicentre design, including more quantitative neurological scores and laboratory markers of immunological and endocrine effects. It does show, however, that there is still much room for improvement in one of the most widely accepted multiple sclerosis treatments.⁶

J Neurol Neurosurg Psychiatry 2007;**78**:788.
doi: 10.1136/jnnp.2006.109272

Correspondence to: Dr Florian Then Bergh, Department of Neurology, University of Leipzig, Liebigstrasse 22A, Leipzig, Germany; thenberf@medizin.uni-leipzig.de

Competing interests: None.

REFERENCES

- 1 Glass-Marmor L, Paperna T, Ben-Yosef Y, et al. Chronotherapy using corticosteroids for multiple sclerosis relapses. *J Neurol Neurosurg Psychiatry* 2007;**78**:886–8.
- 2 Petrovsky N, Harrison LC. The chronobiology of human cytokine production. *Int Rev Immunol* 1998;**16**:635–49.
- 3 Chataway J, Porter B, Riaz A, et al. Home versus outpatient administration of intravenous steroids for multiple-sclerosis relapses: a randomised controlled trial. *Lancet Neurol* 2006;**5**:565–71.
- 4 Zivadinov R, Rudick RA, De Masi R, et al. Effects of IV methylprednisolone on brain atrophy in relapsing-remitting MS. *Neurology* 2001;**57**:1239–47.
- 5 Then Bergh F, Kumpfel T, Schumann E, et al. Monthly intravenous methylprednisolone in relapsing-remitting multiple sclerosis—reduction of enhancing lesions, T2 lesion volume and plasma prolactin concentrations. *BMC Neurol* 2006;**6**:19.
- 6 Filippini G, Brusaferrri F, Sibley WA, et al. Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. *Cochrane Database Syst Rev*. Chichester: Wiley Interscience, 2000;CD001331).