Myokymic discharges can be produced locally in normal subjects with transient forearm ischaemia. In patients with inflammatory polyradiculoneuropathy, lowering serum ionised calcium may increase axonal excitability and lead to myokymic burst amplification and increased clinical myokymia. Finally, microneurographic recordings of two patients with myokymia and peripheral neuropathy resembling Charcot-Marie-Tooth disease demonstrated hyperexcitability of motor and sensory fibres.

Similarly, a low excitability threshold of the axonal membrane appears to be necessary for the production of isolated fasciculations, and fasciculating neurons are often the first to be excited by stimuli of weak intensity. Grouped discharges and doublets have been seen occasionally in patients with motor neuron disease. Our case suggests that motor neuron disease may cause sufficient nerve injury and hyperexcitability to produce myokymic discharges and generalised myokymia.

Myokymia and abundant fasciculations cannot be reliably distinguished clinically, and, as in our case, abundant isolated discharges and myokymic discharges may coexist. In any case, to avoid misdiagnosis, both fasciculations and myokymia need to be interpreted in light of other neurologic signs and symptoms, as well as appropriate laboratory investigations.

Methylprednisolone in multiple sclerosis: a comparative dose study

Sir: Pulsed therapy with intravenous methylprednisolone is widely used in patients with multiple sclerosis who have suffered symptomatic relapse. Open studies, comparisons with ACTH and controlled trials have all supported this form of treatment, although a recently completed multicentre comparison of methylprednisolone with ACTH has shown no advantage of the former (Kennard C, personal communication). The mode of action of the drug is not clear. Recent work suggests that there may be no direct effect on immunological events, but other factors involved in cell damage and associated oedema may be influenced.

The optimum amount of steroid required may vary between individuals and between relapses. Upper limits are restricted by the anticipated side effects of very high dosage, but there has been little comparison of dose ranges. To explore one aspect of this question, a series of 32 patients in relapse were randomised to receive a single 1 g intravenous injection of methylprednisolone or five consecutive injections of 1 g daily. Relapse was defined as a clinical progression of the disease during the previous month. The two treatment groups were equally matched according to age, disease duration and disability. Kurtzke functional and disability scores were obtained before and after treatment and the study was conducted in an open fashion.

On comparing the assessments immediately before the injections with those one month after the treatment course, the mean change in the Kurtzke functional score was 2·8 in the 1 g group and 4·8 in the 5 g group. The corresponding mean changes in the Kurtzke disability scores were 0·8 and 1·9.

When analysed by the Mann-Whitney Test for non-parametric data, the differences in the disability scores were significant (p < 0·05): The 15 individuals in the five injection group either improved or in three instances were unchanged. Three of the 17 patients receiving a single injection continued to deteriorate after treatment, yet each improved following a further five injections.

It is unlikely that the open design of this study has caused a bias in the results and it is concluded that in many patients the lower dose of methylprednisolone is not suitable. Our present policy is to tailor the methylprednisolone dose to the patient. A regime comprising a five day course of daily 0·5 g injections, followed by 5 days of reducing oral prednisolone, appears satisfactory in most cases of relapse.

These data were presented at a Symposium on Steroids and CNS disease, and will be published in a book of the same title by John Wiley & Sons Ltd.

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Letters

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Neuroleptic malignant syndrome due to sulpiride

Sir: Neuroleptic malignant syndrome (NMS) is recognised as a lethal complication of neuroleptic drugs, in which hyperthermia and hyperthermia occur. We have seen a case of a woman who developed NMS following a single use of sulpiride, a selective D-2 dopamine (DA) receptor blocker, as either DA agonist or antagonist.

The patient was a 70 year old woman who had no family history of note and had been well until 14 March 1986, when she was found to have hypertension. Trichlormethiazide, trapidil, and benzodiazepine derivatives (tofisopam, 100 mg/day, until December, 1986, followed by chloridiazepoxide, 10 mg/day) were administered for almost a year. In February, 1987, she complained of anorexia, insomnia, headache, and decreased interest in her usual activities. Physical examination revealed normal findings. Because she was depressed a physician started sulpiride, 300 mg three times/day, on 20 February. Soon after this addition, extrapyramidal signs including gait disturbance, dystarthish, dysphagia, and hypersalivation developed. On 26 February she was admitted to hospital because of the anorexia and extrapyramidal signs. The laboratory examination of blood and urine were normal. After the day of admission, the dose of sulpiride was decreased to 150 mg/day. But the extrapyramidal signs did not diminish. On 26 March there was rapid deterioration of the extrapyramidal signs. On March 29, the body temperature began to rise and hyper- salivation and sweating became marked. On 4 April, she was alert, and had a temperature of 37-4°C. Neurological examination revealed marked hypertonus in neck and limbs, akinesia, dysphagia, and dysarthria, which confined her to bed and kept her mute. Pertinent laboratory data included white blood cell count, 8,200/mm³; erythrocyte sedimentation rate (ESR), 12 mm/h; blood urea nitrogen, 19 mg/dl; serum GOT, 65 IU; GPT, 35 IU; C-reactive protein (CRP), 0-7 mg/dl (normal, 0 < 0-5); creatinekinase (CK), elevated markedly up to 2,152 IU (27-118). Urine study, cerebrospinal fluid cytochemical examination, chest radiographs, ECG, and brain CT was normal.

Sulpiride was stopped immediately, but the extrapyramidal signs did not improve and the temperature reached 37-7°C. The patient lapsed into lethargy after several days. The EEG showed diffuse slowing of 6-7 Hz on 9 April. Then, all the medication was stopped and dantrolene sodium 50 mg three times/day was started by nasogastric tube, the dose of which was increased to 100 mg/day by 15 April. Within 5 days after the start, the temperature fell to around 37-0°C and consciousness began to improve. On 14 April, the serum CK level was in the normal range (91 IU), although the hypertonia remained severe. On 19 April, the temperature again rose and reached 38-7°C. This time, the white blood cell count was 7,900/mm³; ESR, 35 mm/hr; CRP, 5-7 mg/dl; and serum CK, 121 IU. The blood culture grew coagulase negative staphylococci. Following treatment with antibiotics, the temperature fell in several days. Following this recovery, the extrapyramidal signs were noted to reduce gradually. By May, the extrapyramidal signs had disappeared completely and routine blood and urine study became normal, although the mild dysorientation and mild delirium remained. In June, dantrolene was stopped and medication with amantidine (150 mg/day), moclofenoxate (600 mg/day), and mianserin (20 mg/day) was started. In August, she was alert and oriented, free from any mental problem, took care of herself, and could walk with a walker. In October, she was discharged without any sign of NMS nor its sequela.

In this patient, the rapid deterioration of motor function characterised by general hyperthermia and akinesia, several autonomic dysfunctions, low grade fever reaching 37-7°C, clouded consciousness, elevated serum CK level, and no trace of infection were noted after 5 weeks' use of sulpiride. Although the fever was not so remarkable, the symptoms of the patient correspond to the description of NMS, which has been noted in association with the use of neuroleptic medication. The use of antidepressant or discontinuance of dopaminergic medication such as levodopa and amantadine have also been known to produce identical symptoms. The marked decrease in functioning of dopaminergic neurons has been postulated as the cause of the development of NMS. Our case is noteworthy because the NMS was produced following a single use of sulpiride as either DA agonist or antagonist. Sulpiride, a substituted benzamide compound, differs from the typical neuroleptics by exhibiting an inability to inhibit DA-stimulated adenylyl cyclase activity and has been proposed as a selective blocker at D-2 receptors. As far as we know, 10 cases of NMS associated with sulpiride have been reported so far. In every case, however, sulpiride was used in combination with the drugs which have been reported in association with NMS or its identical symptoms. In 1984, Hermesh et al reported a case of NMS due to tiapride, another specific D-2 receptor blocker of benzamide group, and suggested the involvement of D-2 receptors in the pathogenesis of NMS. Because sulpiride was used solely as either DA agonist or antagonist, our case offers additional evidence that the selective blockade at D-2 receptors could produce NMS.

Our case is also of interest because sulpiride, as a cause of extrapyramidal signs, is rare compared with typical neuroleptics. But in vitro, sulpiride blocks D-2 receptors with approximately the same potency as chlorpromazine. This discrepancy between the D-2 receptor blocking effect in vivo and in vitro may in part be attributed to its poor ability to cross the blood-brain barrier. In our case, the extrapyramidal signs were induced soon after starting the medication with sulpiride of 300 mg/day, a dose which usually does not have complications. This fact suggests that the effects of sulpiride to block central dopaminergic transmission might have been potentiated. Some organic changes in blood-brain barrier function and/or age related decline in functioning of dopaminergic neurons might play a role on this potentiation.

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