Morphine in tardive and idiopathic dystonia

Short Communication

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Received February 9, 2001; accepted April 27, 2001

Summary. Opioids have been shown to improve L-Dopa induced dyskinesias in patients with Parkinson’s disease. In this pilot trial of five patients with tardive and four patients with idiopathic dystonia we tested the effect of morphinsulfate in a retarded form with a dosage of 20–60mg per day.

A substantial improvement of dystonic movements could be observed in four patients with tardive and one patient with idiopathic dystonia. The effect was only transient in tardive dystonia while pain relief mediated by morphine overlasted the effect on involuntary movements.

Keywords: Morphine, tardive dystonia, idiopathic dystonia, opioid system.

Introduction

Tardive dystonia is a well characterized condition (Burke et al., 1982). The reported prevalence ranges from 0.4–13.4% of patients on long-term neuroleptic medication with a spectrum of clinical presentation as broad as in idiopathic dystonia (Friedmann et al., 1986; Yassa et al., 1986; Raja et al., 1995; Van Harten et al., 1996; Adityanjee et al., 1999). Many treatment strategies have been evaluated to alleviate the often disabling movements including anticholinergic medication, benzodiazepines, baclofen, dopamine antagonists, reserpine, verapamil, clozapine, and botulinum toxin (Burke et al., 1982; Factor et al., 1987; Brashear et al., 1998; Ovsiew et al., 1998; Adityanjee et al., 1999; Gerlach et al., 1999). However, improvement of dystonia is often not satisfactory and many patients complain about persistent pain caused by the involuntary movements and muscle spasms.

We recently reported about an improvement of L-dopa induced dyskinesias in patients with Parkinson’s disease by morphine, who were treated with this opioid agonist to alleviate severe sciatica (Berg et al., 1999).
As both L-dopa induced dyskinesias in Parkinsonian and tardive dystonia are believed to be caused by a hypersensitivity of striatal dopaminergic receptors and/or an alteration in the metabolism of neuropeptides (Ebadi et al., 1988) we set out to test the effect of morphine in patients with tardive and idiopathic dystonia, who were unresponsive to other forms of treatment.

**Patients and methods**

Five consecutive patients suffering from tardive (all female, median age 54 ± 19.1 years, range 34–77 years) and four patients with idiopathic dystonia (all male, median age 57 ± 5.4 years, range 50–61 years) unresponsive to other forms of treatment gave informed consent according to the declaration of Helsinki to participate in the trial (Table 1). None of the patients had a history of perinatal or traumatic brain injury, other neurological disorders or a positive family history for neurological disorders. Neurological examination was normal except for dystonia.

Morphinsulfate in a retarded form (Capros, medac/Rhône-Poulenc Rorer, Hamburg) was administered in all patients with an initial dosage of 2–10 mg daily. Dosage could be stepwise increased up to 60 mg according to individual side effects and general acceptance by the patient. In unresponsive patients medication was stopped after two weeks, in responders the treatment medication was continued until the beneficial response disappeared. No other centrally acting drugs were given during the trial. Centrally acting drugs that were tried beforehand (Table 1) were stopped at least 2 months before the trial.

**Evaluation**

Our pilot observation indicated that the response to morphine started several hours after administration and dyskinetic movements almost completely disappeared after the initial 20 mg. Therefore we recorded dyskinetic movements on videotape before and 1–2 days after the initiation of treatment. Scoring of symptoms before and after treatment was done by an investigator experienced in evaluating tardive and idiopathic dystonia according to the Abnormal Involuntary Movement Scale (AIMS) (Simpson et al., 1979). The investigator was blinded for the exact diagnosis and morphine treatment. The further course of dyskinetic movements was documented by the treating doctor. Additionally patients were asked to judge the effect of treatment daily. Patients graded the subjective impression of treatment effect on dyskinetic movements and pain in percent with 0% = no relief, 100% = maximal improvement, no symptoms left.

**Results**

In four patients with tardive and in one patient with idiopathic dystonia, a substantial relief of involuntary movements was noticed according to the AIMS and self-assessment of the patients (Table 1). Relief of dystonic movements lasted for 1–5 days in patients with tardive dystonia. The best effect could be observed 1 to 2 days after treatment was started. Although dosage was increased in some patients to up to 2 × 30 mg only patients who had responded to the initial medication of 2 × 10 mg showed a relief of symptoms with higher dosages, which, however, was not better than at the initiation of therapy and also disappeared after 1–5 days. In the one patient with idiopathic dystonia who experienced initially an almost complete relief of symptoms, however, dystonic movements were alleviated to about 30% (graded by patient and investigator) for more than 6 months. No relation could be observed between duration or severity of dystonic movements and effect of treatment.