Comparative Efficacy of Cyclandelate versus Flunarizine in the Prophylactic Treatment of Migraine

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Summary

In a double-blind, parallel-group randomised trial of 3 months' duration, the efficacy of cyclandelate 800mg twice daily in migraine prophylaxis was compared with that of flunarizine 5mg daily in 40 patients. In comparison with placebo and baseline values, both drugs significantly relieved symptoms of migraine as assessed by indices of pain total index, headache index, analgesic consumption and number of migraine days. Patients taking flunarizine experienced side effects such as drowsiness, weight gain and asthenia, while the most common complaint reported with cyclandelate was gastric upset.

These results suggest that cyclandelate may be a useful alternative in migraine prophylaxis.

The role of cerebral hypoxia or ischaemia in migraine pathophysiology is still unclear. Similarities and differences between transient ischaemic attacks and migraine with focal neurological disturbances have been discussed, and the migraine-like headaches preceding or accompanying transient ischaemic attacks have been proposed as a model for investigating these problems (Nappi & Bono 1982). A central neurotransmitter (dopamine, serotonin) and neuropeptide (endorphins) derangement in the events precipitating ischaemia has been reported (Hosobuchi et al. 1982; Welch 1982); more recently, other events such as spreading depression of cortical activity have also been considered (Amery 1984; Lauritzen 1983; Leão 1944).

The effectiveness of calcium entry blockers in migraine prophylaxis has been related to the prevention of hypoxic or ischaemic phenomena (Meyer & Hardenberg 1983; Meyer et al. 1985; Peroutka 1983; Peroutka et al. 1984).

Cyclandelate, a drug extensively used in cerebrovascular and peripheral vascular diseases (Hall 1976; Reich 1977; Young et al. 1974), has been demonstrated to inhibit smooth muscle contraction (van Nueten & Wellens 1979). In addition, this drug also potently blocks platelet activating factor induced platelet aggregation (van den Hoven et al. 1984). The pharmacological profile of cyclandelate is that of a calcium entry blocker with vasodilator activity, which suggests that it may be effective in migraine prophylaxis. In order to investigate this possibility, a double-blind study was conducted in patients with common migraine comparing the efficacy of cyclandelate with that of flunarizine, a drug with well-documented antimigraine properties (Diamond & Schenbaum 1983;
nausea and vomiting. The diaries enabled the separation, to a certain extent, of migraine attacks from interval headaches. The severity of headache was graded as follows: grade 1, working capacity not affected; grade 2, inability to work; grade 3, bed rest required. The amount of analgesics taken to relieve the headaches was monitored as well. The following parameters were considered: (a) pain total index - monthly number of headache hours multiplied by severity; (b) headache index - monthly number of attacks multiplied by severity; (c) migraine days; (d) analgesic consumption.

Follow-up visits, which occurred every 4 weeks, included an interview with each patient, checking of the headache diary and questioning about any adverse effect of the drug.

1. Patients and Methods

1.1 Patients

The population consisted of 40 outpatients treated at the Headache Centre of the University of Pavia. Men and women between the ages of 18 and 60 years with common migraine, defined according to the criteria given by the Ad Hoc Committee on the Classification of Headache (1962), were eligible for admission to the study. Other criteria for inclusion were a history of migraine of at least 2 years' duration, at least 3 attacks per month, and no specific prophylactic treatment in the last 2 months.

Patients with classic migraine and other types of headache or pain were excluded. Similarly, patients suffering from severe hepatic or renal insufficiency, cardiopathy, arterial hypertension or depression and women who were pregnant or taking oral contraceptives were not admitted to the study.

1.1.1 Study Design

The study was conducted as a double-blind, placebo-controlled, parallel-group trial in which patients were randomised to treatment with either cyclandelate or flunarizine. A medication-free baseline period of 1 month preceded a placebo period of 30 days. Thus, during the first month all patients received 2 tablets of placebo daily (1 after breakfast and 1 after dinner). In the following 3-month period of active treatment, 20 patients received cyclandelate 800mg twice daily (2 coated tablets of 400mg after breakfast and 2 after dinner) while the remaining 20 patients were given flunarizine 5mg in capsule form once daily before retiring.

1.1.2 Patient Assessment

During the trial each patient kept a headache diary (described by Bono et al. 1984), in which were recorded the number, intensity and duration of migraine attacks, and their possible association with