

Naproxen Sodium in Menstrual Migraine Prophylaxis: A Double-Blind Placebo Controlled Study

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SYNOPSIS

In this study, the efficacy of Naproxen sodium (Nxs) in the prophylaxis of Menstrual Migraine (MM) was tested, versus Placebo (PL). Forty women suffering from MM were admitted to a double-blind treatment protocol with Nxs 550 mg twice each day by mouth or Placebo (PL), for 3 months; in the next 3 months all the women were treated with the active drug in an open study. The headache intensity and duration, as well as the number of days of headache and the analgesic consumption, were significantly reduced with Nxs compared to PL.

The efficacy of Nxs, shown also in improving premenstrual pain, and its good tolerability, support the use of this drug in the prophylactic therapy of MM.

Key words: menstrual migraine, prophylaxis, naproxen, NSAID.

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INTRODUCTION

Naproxen sodium (Nxs) is a non-steroidal drug with anti-inflammatory (NSAID) and analgesic effects. The most important action of Nxs is its inhibition of prostaglandin synthesis by reversible binding to cyclooxygenase,¹ the first enzyme in the arachidonic acid cascade of prostaglandin synthesis. Prostaglandins (PG), particularly PGE₂, may be linked to the pathophysiology of migraine in several important ways,² playing a prominent role in producing sterile inflammation following vasodilatation,³ which by itself is painless. More than 20 years ago Bergstrom and coworkers⁴ showed that an intravenous infusion of PGE₁ could trigger migraine-like attacks in healthy volunteers. PGE₁ causes dilatation of the external carotid arteries, whereas PGF₂ induces intracerebral vasoconstriction. Several studies have also shown that platelets from some migraine patients aggregate more readily than those from normals.⁵ If platelet activation is at all involved in migraine, it may be through an occlusion of the brain microvasculature and a release of prostaglandins or secretory substances in the brain.⁷ A prostaglandin hypothesis for menstrual migraine has

been proposed on the basis of a different sensitivity of platelet aggregation in response to prostacyclin and thromboxane.⁸ In recent years Nxs has been widely used in the treatment of acute migraine attacks^{9,10,11} and for the prophylactic therapy of migraine^{12,13,14,15,16} based upon the antiprostaglandin and platelet antiaggregant properties of NSAID drugs.

Naproxen is a propionic acid derivative (d-rotated isomer of 2-6-methoxy-2'-naphthyl-propionic acid); its sodium salt shows, when compared with similar drugs, some pharmacokinetic differences. On the average, Nxs reaches therapeutically effective serum concentrations after 20 to 30 minutes,¹⁷ and the maximum serum concentration is obtained 2 hours following oral administration.¹⁷ It is quickly dissolved in the gastric juice and is therefore absorbed more rapidly.¹⁷ The mean time for peak plasma levels of Naproxen is less than one hour and its biological half-life is 12-15 hours; the steady state is reached within 2 to 3 days.¹⁷

In the present study we evaluated the effectiveness and safety of Nxs compared with placebo (PL) in 40 women affected by menstrual migraine (MM), which is a form of periodical headache that, as is well known, often fails to improve with usual prophylactic treatments.¹⁸

SUBJECTS AND METHODS

Forty women aged between 19 and 45 (M±SD: 37.7±6.9) years were included in the study. They fulfilled the criteria established for "migraine without aura" by the Headache Classification Committee of the International Headache Society.¹⁹

They had shown a menstrually-related periodicity of migraine for 2 to 30 years, with headaches at every cycle. The MM attacks, lasting from 1 to 4 days, worsened their family relationships and interfered with their working activity. All the women had regular attacks the week before, or during, the menses, sometimes during ovulation, and were headache-free for the rest of the cycle. They had regular cycles between 23 and 31 days. All of them were free from endocrinological, metabolic or other organic abnormalities; none of the women had

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