What is the Best Prophylaxis for Menstrual Migraine?

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Evidence-Based Answer

Oral naratriptan results in slightly fewer headache days than placebo in patients with menstrual migraines. (SOR A, based on consistent randomized controlled trials [RCTs].) Naproxen and magnesium therapy are also more effective than placebo. (SOR B, based on single small RCTs.) Frovatriptan may reduce the severity of pain better than transdermal estrogens and naproxen (SOR C, based on a single open-label comparison study), but has not been studied in comparison with a placebo.

Two large, randomized, double-blind placebo-controlled studies (n=290 and n=365) evaluated naratriptan in menstrual migraine.\(^1\) Patients were randomly assigned to take oral naratriptan 1 mg twice daily or placebo for 4 perimenstrual periods or 6 months, whichever occurred sooner. Patients took medication for 6 days starting 3 days before predicted onset of menstrual-related migraines, and completed a patient satisfaction questionnaire.

Patients taking naratriptan reported fewer days with migraines than patients taking placebo in both studies (median 5.0 vs 6.5 days, respectively, in study 1; \(P=0.005\); and median 5.3 vs 6.0 days, respectively, in study 2; \(P=0.018\)).\(^1\)

A small (n=35), double-blind placebo-controlled study evaluated naproxen sodium 550 mg twice daily versus placebo.\(^2\) Patients were randomized to placebo or naproxen for 3 months, and then all were treated with naproxen for 3 months. Dosing started on the 7th day before expected menses and continued through the 6th day of menstrual flow. The key measure, the Pain Total Index (PTI), is calculated using the number of attacks (N), duration in hours (H), and severity (S) (1=mild, 2=moderate, 3=severe) in the following equation: \(PTI=N+(HS)\).

The average PTI significantly decreased from 61.5 the first 3 months on placebo to 39.2 the second 3 months on naproxen (\(P<.02\)). Analgesic consumption was reduced from 4.21 doses the first 3 months on placebo to 2.62 the second 3 months on naproxen (\(P<.05\)). No significant differences were found in the number of days of headache.\(^2\)

A double-blind RCT compared oral magnesium pyrrolidone carboxylic acid (360 mg/d magnesium) with placebo in 20 patients with a 2- to 9-year history of menstrual-related migraine and 15 control patients with no history of migraine.\(^3\) Patients filled out a daily headache diary and the Menstrual Distress Questionnaire (MDQ) for 4 months. Patients took either placebo or magnesium 3 times a day starting on the 15th day of menstrual cycle until the next menstrual flow.

Compared with placebo, magnesium therapy resulted in significantly lower MDQ scores at 2 months (78 in placebo group vs 57 with magnesium; \(P<.05\)) as well as fewer headache days per month (from 4.7 at baseline to 2.4 with magnesium; \(P<.01\)). The placebo group did not have a statistically significant decrease in number of headache days.\(^3\)

An open-label, nonrandomized, parallel-group observational study evaluated oral frovatriptan 2.5 mg, transdermal estrogen 25 \(\mu g\), or oral naproxen sodium 500 mg once daily for 6 days during 1 perimenstrual cycle in 38 patients. Patients were dosed from 2 days before the anticipated onset of menses to 3 days after onset. Severity was determined on a 10-point Likert pain scale. The mean pain score dropped from 4.6 to 2.5 with frovatriptan, from 4.2 to 3.0 for estrogen, and from 4.3 to 3.9 for naproxen (\(P=0.49\) for comparison of frovatriptan with estrogen or naproxen). However, frovatriptan did not decrease the average number of menstrual migraines in a single cycle.\(^4\)

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