Is venlafaxine an effective prophylactic medication for migraine headaches?

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Evidence-based answer

Maybe. Venlafaxine seems to be an effective prophylactic medication for the reduction of migraine headache frequency (SOR: B, small clinical trials vs placebo or active agents).

Venlafaxine is more effective than a combination of propranolol and nortriptyline (SOR: C, small randomized controlled trial [RCT]) and noninferior to amitriptyline (SOR: C, small RCT) for migraine frequency. However, venlafaxine may not be effective for reducing duration or severity of headaches (SOR: C, small RCT).

A 2018 RCT (N=60) examined the effectiveness of venlafaxine for reduction of migraine frequency and severity compared with combination treatment of nortriptyline and propranolol. Patients were nonpregnant adults without aura, experiencing at least three migraines per month and discontinued previous prophylactic medication two weeks before study admission. The intervention group (n=30) received venlafaxine 37.5 mg, once daily for 10 weeks, whereas the control group (n=30) received nortriptyline 25 mg once at night and propranolol 20 mg every 12 hours for 10 weeks. The primary outcomes measured were frequency and severity of headaches (0 to 10 scale, 10 worst pain), secondary outcomes were frequency of nausea, vomiting, and drowsiness episodes per month during the treatment period. Patients in the intervention group had a significant decrease in headache frequency (3.6 vs 4.0 per month, \( P < .001 \)) and severity (6.2 vs 6.6, \( P < .001 \)). Patients in the intervention group also had fewer episodes of nausea (0.33 vs 0.43, \( P < .001 \)) and vomiting (0.06 vs 0.13, \( P < .001 \)) but more

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frequent episodes of drowsiness (0.57 vs 0.35, \(P<.015\)) per month. Limitations of this study include lack of demographical data, leading to questionable generalization of the results.

A 2005 RCT (\(N=60\)) evaluated the efficacy and safety of high-dose and low-dose venlafaxine compared with placebo for migraine prophylaxis in patients diagnosed with migraine without aura. Patients were nonbreastfeeding adults experiencing 3 to 10 headache attacks per month for at least two years, had partial benefits from previous prophylactic medication, and had headaches severe enough to interfere with daily tasks and activities. Patients with major comorbidities and nonmigraine headache were excluded. Patients received extended release venlafaxine 150 mg (\(n=21\)), extended release venlafaxine 75 mg (\(n=20\)), or placebo (\(n=19\)) for 10 weeks. Outcomes measured included number of days with headache, severity of headaches using a 0 to 10 visual analogue scale (VAS) with higher scores indicating worsening severity, duration of headaches in hours, analgesic consumption, and adverse events recorded every two weeks. High-dose venlafaxine significantly reduced the mean number of days with headaches within 10 weeks compared with both the low-dose and the placebo group (mean difference [MD] –4 days vs –2 days vs –1 day, \(P=.01\)). No significant difference was observed between the three groups in headache severity (MD –4 vs –4 vs –1, \(P=.07\)) or in duration (MD –7 vs –7 vs –2 hours, \(P=.48\)). A significant decrease was noted in analgesic consumption in the low- and high-dose venlafaxine treatment groups compared with placebo (MD –5 and –4 vs 0, \(P=.001\)). No difference in side effects was observed between the groups at 10 weeks.

A 2004 randomized, crossover study (\(N=52\)) examined the prophylactic effect of amitriptyline compared with extended-release venlafaxine in patients with migraine with or without aura. Patients were nonpregnant adults with median age of 32 years old, history of migraine for more than one year, and at minimum two attacks per month in the last three months. Patients with psychiatric disorders and major comorbidities were excluded from the study. In group 1 (\(n=26\)), patients received venlafaxine in the first treatment period (4–16 weeks) and amitriptyline in the second treatment period (20 to 32 weeks) for 36
weeks. In group 2 (n=26), patients received amitriptyline in the first treatment period and venlafaxine in second treatment period. During the first four weeks, patients received no prophylactic treatment and a four-week wash-out period was also noted between the two treatment periods. Venlafaxine was dosed as 37.5 mg/day for three days, 75 mg/day for 3 days, and 150 mg for 78 days. Amitriptyline was dosed as 10 mg/day for three days, 25 mg/day for three days, 50 mg/day for three days, and 75 mg/day for 75 days. Outcomes measured were number of migraine attacks, duration of attacks in hours, and severity of attacks graded on a 1 to 3 scale (1=able to work throughout the attack, 2=unable to work but not staying in bed, and 3= staying in bed) per month. Patients were followed up at four, 16, 20, 32, and 36 weeks. Both treatments improved symptoms significantly compared with baseline. However, patients in group one were similar to group two in headache frequency (3.6 vs 4.0, $P>.05$), severity (0.09 vs 0.01, $P>.05$), and all other major side effects per month. Patients in the amitriptyline groups experienced more side effects like hypersomnia (42 vs 6), difficulty concentrating (28 vs 3), and orthostatic hypotension (16 vs 1).
References

