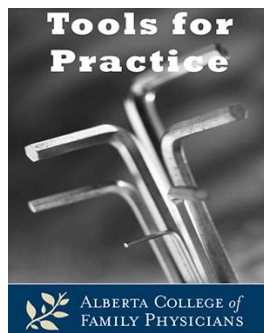


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Riboflavin for Migraine Prophylaxis: Something “2-B” excited about?

Clinical Question: Does daily riboflavin (vitamin B₂) prevent migraines?

Bottom-line: Studies of riboflavin are inconsistent and often have high placebo response rates. Most randomized, controlled trials (RCTs) found no reduction in migraine frequency. One study found for every three adults treated with riboflavin, one patient would have a $\geq 50\%$ reduction in migraine frequency compared to placebo. Adverse effects are poorly reported, but include diarrhea and discoloured urine.

Evidence:

- Adults:
 - Three double-blind randomized controlled trials (RCTs), younger, predominantly female, Western Europe/US. All outcomes reported at three months.
 - 55 patients, ~4 migraines/month, randomized to riboflavin 400 mg daily or placebo (with β -carotene).¹
 - $\geq 50\%$ reduction in frequency: 56% versus 19% (placebo); Number Needed to Treat (NNT)=3.
 - Limitations: Inconsistent statistical applications, origin of funding unclear, limited adverse event reporting.
 - 112 patients, six days of migraine/month, randomized to nutritional product with riboflavin 400 mg, Magnesium/Coenzyme Q₁₀ and other vitamins or indistinguishable placebo divided twice daily.²
 - Both reduced days of migraine/month 1.8 versus 1.3 (placebo). Not statistically significant (NSS).
 - No meaningful differences in other outcomes.
 - More adverse effects with riboflavin (mostly diarrhea or discoloured urine): Number Needed to Harm (NNH)=4.
 - Limitations: Unclear randomization concealment (with more in placebo having co-morbidities).
 - 49 patients: Riboflavin 400 mg with magnesium/feverfew or “placebo” (riboflavin 25 mg).³

- $\geq 50\%$ reduction in frequency 42% versus 44% (placebo); NSS.
- Fewer monthly migraines: 1.8 versus 1.7 (placebo); NSS.
- Limitations: Unclear randomization concealment, possible active comparator, no adverse effects reported.
- Pediatrics:
 - Two placebo-controlled RCTs (Australia/Netherlands) riboflavin 50 mg versus placebo (with carotene) (42 children)⁴ and 200 mg versus identical placebo (48 children):⁵
 - No difference in days with migraine or headache intensity.^{4,5}
 - $\geq 50\%$ reduction in frequency: 44% versus 67% (placebo); NSS.⁵
 - Limitations: Underpowered⁵
 - Third study uninterpretable due to significant differences in baseline characteristics.⁶
- Systematic reviews did not complete meta-analyses (so we focused on RCTs above).⁷⁻¹⁰

Context:

- Prophylaxis is recommended for those with ≥ 3 moderate-severe headaches/month.⁷
 - The best evidence for migraine prophylaxis supports propranolol and amitriptyline, which benefit 1 in 4 and 1 in 8 patients over placebo, respectively.^{11,12}
- Guidelines “strongly recommend” riboflavin (based on low quality evidence)⁷ or suggest riboflavin probably effective⁸ in adults.

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Disclosure:

Authors do not have any conflicts of interest to declare.

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