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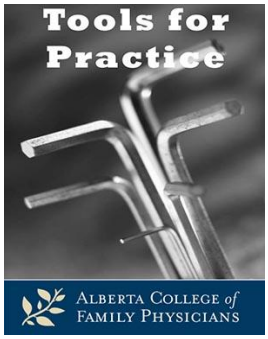

Vitamin D and Low Mood: The easy perky pill.

Clinical Question: Can Vitamin D improve or prevent low mood or depression?

Bottom-line: The present evidence does not support prescribing (or testing) Vitamin D in the treatment or prevention of low mood or depression. Most randomized controlled trials (RCTs) found no effect and the few that found small benefits are at very high risk of bias.

Evidence:

- Vitamin D vs. placebo (or nothing):[1-10]
  - Ten RCTs examined patients with normal mood [example: 4-7 on Beck Depression Inventory (BDI)[1,2,4] and ≤15% depressed].[1-9]
    - RCTs included 44-2263 patients, lasted five days to three years, and gave 400 IU/day to 40,000 IU/week of Vitamin D.
    - Despite multiple outcomes in nine studies, only two showed any impact:
      - Statistically but not clinically significant 1-1.5 point change on a 63-point BDI scale.[1]
      - Statistically significant seven-point change (out of 40) in "positive" mood parameters, no change in "negative" mood parameters.[8]
        - Limitation: Smallest and shortest study, 44 people for five days.
    - Vitamin D had no benefit in prevention of depression.[5,9]
  - Two RCTs examined depressed patients:[6,10]
    - Iranian three month trial of 120 patients given single intramuscular dose of 300,000 IU or 150,000 IU or nothing.[10]
      - Mean improvement in BDI was 9.3, 6.8, and 2.1.
        - 300,000 IU statistically superior to nothing.
    - Subgroup of 57 depressed patients in 489 person RCT.[6]
      - No difference between Vitamin D and placebo for recovery.

Context:

- Observational studies have shown an association between low Vitamin D levels and a higher risk of depression or low mood.[11]
  - This research is at very high risk of bias and cannot show causation.

- Dosing RCT of 600 IU/day vs. 4000 IU/day found no difference in mood.[12]
- Most RCTs included above have multiple flaws and high risk of bias, including poor randomization, lack of blinding, no description of patient characteristics, non-intention to treat analysis, large loss to follow-up, etc.[1-10]
    - In general, RCTs with better design (examples[2,4]) found no effect, while the only RCTs finding benefits were at the highest risk of bias (examples[8,10]).

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