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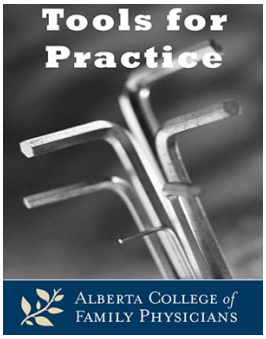
Reviewed: July 2, 2015
Evidence Updated: Case control study (and review in context) added
Bottom Line: Unchanged
First Published: March 5, 2012



Bio-identical hormone micronized progesterone: The same but totally different?

Clinical Question: Is "bioidentical" micronized progesterone (MP) instead of the "synthetic" medroxyprogesterone acetate (MPA) safer and better for menopausal symptom control?

Bottom-line: Theoretical advantages of bioidentical hormones over synthetic hormones are not supported by reliable evidence. Until results from large, randomized controlled trials (RCTs) are available, we risk repeating errors of the past by concluding bioidentical hormones are more or less safe or efficacious than other hormone replacement therapies. Compounding of bioidentical hormones only serves to 'compound' the uncertainty.

Evidence:

- Here is some of the evidence comparing MP with MPA:
  - Menopausal symptoms:
    - RCT with 875 patients: No difference in symptoms[1] or in bleeding episodes[2] (when both used cyclically).
    - Survey study[3] (176 patients): Improvement in quality of life.
      - However, patients included had already switched from MPA to MP, potentially biasing the results.
  - Cardiovascular disease:
    - RCT,[4] 875 patients, three years: MP had slightly greater impact on HDL (increase of <0.1 mmol/L) but clinical outcomes not recorded.
  - Venous thromboembolism:
    - Case control study:[5] Neither MP nor MPA had an effect.
  - Breast Cancer:
    - Cohort study,[6,7] approximately 99,000 postmenopausal women: Authors suggest MP may be preferred to most synthetic progestins.
      - Validity in question due to imbalance in estrogen treatment; multiple subgroup analyses, some apparently post-hoc; and selective grouping of high risk progestins.

        - Case-control study of 1,555 postmenopausal women suggested MP had less risk than MPA.[8]
            - Retrospective nature, small sample size, differences in baseline risk between groups, and lack of clarity on in-situ versus invasive disease all serious limitations.
    - A number of other studies are too small (<25 patients) to provide any meaningful information.[9-11]

Context:

- A thorough review identified three RCTs of bioidentical progesterone cream versus placebo: Only one of three RCTs found improvement in vasomotor symptoms.[12]
- Reliance on observational studies, small RCTs and surrogate endpoints are reminiscent of when synthetic hormones were believed to reduce coronary artery disease by 35-50%.[13,14] Later, a large well-designed RCT showed increased cardiovascular events.[15]
- The Endocrine Society warns claims of improved safety or effectiveness are unproven.[16]
    - Society of Obstetricians and Gynecologists of Canada[17] and others[18,19] strongly recommend against compounding of bioidentical hormones.

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