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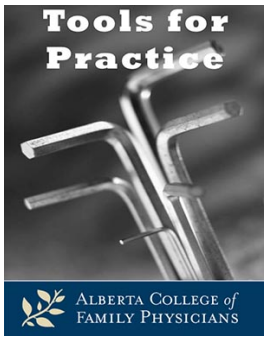

Bringing Up the Best Evidence: Ondansetron in nausea/vomiting of pregnancy

Clinical Question: What are the benefits and risks of ondansetron for nausea and vomiting of pregnancy?

Bottom Line: Ondansetron may reduce nausea or vomiting of pregnancy by 25% for one in two users, compared to doxylamine/pyridoxine. There is real uncertainty if ondansetron in pregnancy is associated with any risk to the fetus. Some observational studies suggesting congenital or cardiac defects may be increased by as much as 1% but these are inconsistent and not supported by better evidence.

Evidence:

- Benefits:
  - One randomized controlled trial (RCT), 36 patients, comparing ondansetron to doxylamine/pyridoxine for five days, results statistically significant:[1]
    - Reduction on 100-point scale:
      - Nausea: 51 ondansetron versus 20.
      - Vomiting: 41 versus 17.
    - Achieved 25% symptom reduction:
      - Nausea: 92% ondansetron versus 41%.
      - Vomiting: 77% versus 35%.
      - Number Needed to Treat: 2-3.
    - Limitations: Used low-dose, immediate release form of doxylamine/pyridoxine.
  - Two RCTs from Malaysia and Iran, 160 and 83 patients respectively, found ondansetron (intravenous[2] or oral[3]) at least as good as metoclopramide in hyperemesis gravidarum.[2,3]
- Harms: Observational studies with inconsistent results of malformation.
  - Major malformation overall:
    - Five cohort studies found no increased risk,[4-8] including the highest quality study[1] and two under-powered studies.[7,8]
    - One cohort found increased risk with ondansetron 4.7% versus 3.5% no ondansetron [Odds Ratio (OR) 1.3, 1.0-1.7].[9]

        - From published abstract only, apparently from same database as the highest quality study (above).
    - Cardiac:
        - The highest quality study found no increased risk.[4]
        - Two found increased risk:[5,9]
            - OR 2.0 (1.3-3.1)[9] again published as abstract only.
            - OR 1.62 (1.04-2.14),[5] including septal defects Relative Risk 2.05 (1.19-3.28).
    - Cleft palate:
        - Two cohorts[4,5] and case-control[10] found increased no risk.
        - One case-control study found increased risk OR=2.37 (1.18-4.76).[11]
        - One case-control study found decreased risk OR=0.4 (0.2-0.8).[10]

Context:

- Limitations of harm studies: Cannot prove causation, possible detection and indication bias, not all birth defects investigated,[11] recall bias,[11] multiple comparisons (about 70),[11] and clinical significance and severity of malformations unknown.[5,9-11] Additional risk factors for birth defects unknown.
- Baseline risk of major malformations ~4%.[12]
- Women frequently overestimate risks of malformations from medications.[13]

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