GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of May 31 - June 4, 2021

SPOTLIGHT: Alternative Treatment Modalities for Chronic Pain

- Elective induction at 39 weeks or watch and wait
- Reducing the incidence of bacterial vaginosis

Alternative Treatment Modalities for Chronic Pain

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Mind-Body Therapies for Opioid-Treated Pain: a systematic review and meta-analysis

Garland EL, Brintz CE, Hanley AW, et al. Mind-Body Therapies for Opioid-Treated Pain: A Systematic Review and Meta-analysis [published online ahead of print, 2019 Nov 4]. *JAMA Intern Med*. 2019; 180(1):91–105.

KEY TAKEAWAY: Mind body therapies (MBT) such as meditation, relaxation, and cognitive behavioral therapy (CBT) are associated with pain reduction and reduction in opioid use in adults.

STUDY DESIGN: Systematic review and meta-analysis of 60 RCTs; N=6,404

LEVEL OF EVIDENCE: STEP 2, downgraded due to heterogeneity

BRIEF BACKGROUND INFORMATION: In response to the current opioid crisis, multiple studies evaluating the use of mind-body therapies as treatment for acute and chronic pain have been conducted. MBTs are emerging as possible tools for decreasing opioid use in pain management.

PATIENTS: Adults ≥18 years prescribed opioids for acute, chronic, procedural, and cancer pain

INTERVENTION: Mind body therapies

CONTROL: Opioids

OUTCOMES: Pain severity/intensity

Secondary Outcomes: Opioid use measured by self-report, urine toxicology, opioid misuse, and disability or functional impairment

METHODS (BRIEF DESCRIPTION):

- A literature review of randomized controlled trials (RCTs) comparing the use of MBTs with opioids for pain control and the decreased use of opioids in adults age ≥18 years of age.
- RCTs were excluded if it did not include pain related outcomes

INTERVENTION (# IN THE GROUP): Varied across the 37 studies

COMPARISON (# IN THE GROUP): Varied across the 37 studies

FOLLOW UP PERIOD: 3 months

RESULTS:

- In patients prescribed opioids for pain, the additional use of MBTs (meditation, hypnosis, relaxation, suggestion studies, and CBT) demonstrated significant improvement, when compared to usual care, in:
  - Pain reduction (29 trials, N=2,916; effect size –0.51; 95% CI, –0.76 to –0.27)
  - Opioid use (8 trials, N=435; effect size –0.26; 95% CI, –0.44 to –0.11)
- Individually significant pain reduction was seen with (when compared to usual care):
  - Meditation (3 trials, N=403; effect size –0.70; 95% CI, –1.1 to –0.31)
  - Hypnosis (11 trials, N=932; effect size –0.54; 95% CI, –0.87 to –0.2)
  - Suggestion studies (3 trials, N=319; effect size –0.68; 95% CI, –1.2 to –0.18)
  - CBT (4 trials, N=293; effect size –0.43; 95% CI, –0.71 to –0.15)
- Significant pain reduction was NOT seen with:
  - Relaxation (9 trials, N=1,818; effect size –0.45; 95% CI, –1.1 to 0.22)
- Meta-analysis could not be performed regarding impact of individual MBTs on opioid dosing due to variation in opioid dosing.
- Pain was measured on a scale of 0–10 and opioid dose was measured in morphine equivalents.

LIMITATIONS:

- Included studies had high levels of heterogeneity.
- Pain duration varied in the included studies from acute to chronic.
- The studies had small sample sizes.
- Some biases present in some trials included lack of blinding and lack of intention to treat.
- There was a wide variation of specific opioids used and their dosing.

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Elective induction at 39 weeks or watch and wait

Elective induction of labor at 39 weeks compared with expectant management: a meta-analysis of cohort studies

Grobman WA, Caughey AB. Elective induction of labor at 39 weeks compared with expectant management: a meta-analysis of cohort studies. *Am J Obstet Gynecol*. 2019; 221(4):304-310. doi:10.1016/j.ajog.2019.02.046

KEY TAKEAWAY: Elective induction at 39 weeks is associated with lower risk of cesarean delivery and other adverse perinatal outcomes for mother and infant compared with expectant management.

STUDY DESIGN: Meta-analysis of observational cohort studies

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: A previous RCT demonstrated elective induction at 39 weeks reduced the frequency of adverse maternal and fetal outcomes. Although this trial changed practice for some obstetrical professionals, it is unknown if the results are generalizable to a wider population outside of a clinical trial. A meta-analysis of observational studies was performed to evaluate the association between elective induction and decreased adverse maternal and neonatal outcomes.

PATIENTS: Women undergoing induction of labor at 39 weeks gestation and women undergoing expectant management

INTERVENTION: Elective induction of labor at 39 weeks gestation

CONTROL: Expectant management

OUTCOMES: Risk of cesarean section

Secondary: peripartum infection, neonatal respiratory morbidity, meconium aspiration syndrome, NICU admission, perinatal mortality

METHODS (BRIEF DESCRIPTION):

- Exclusion Criteria:
  - Randomized trials, or observational studies without data on nulliparous women
  - Medical disease requiring induction at 39 weeks
  - Gestational age >39 weeks
- Data extracted by one author and reviewed by the other.
- New Castle Ottawa scale used to assess the risk of bias.
- Heterogeneity assessed using the I^2 statistic.

INTERVENTION (# IN THE GROUP): 66,019

COMPARISON (# IN THE GROUP): 584,390

FOLLOW UP PERIOD: N/A (outcomes ended with delivery/immediate postpartum period)

RESULTS:

Primary Outcomes:

- Elective induction at 39 weeks associated with lower frequency of cesarean compared with expectant management (5 trials, N=492,446; 26% vs. 29%; RR 0.83; 95% CI, 0.74–0.93; number needed to prevent one cesarean 37).

Secondary Outcomes:

- Elective induction at 39 weeks associated with reduced risk of peripartum infection (4 trials, N=413,662; 2.8% vs. 5.2%; RR 0.87; 95% CI, 0.39–0.72).
- Risk of postpartum hemorrhage and 3rd or 4th degree lacerations similar between elective induction and expectant management groups:
  - Postpartum hemorrhage: 3 trials, N=60,448; 5.2% vs. 4.0%; RR 0.87; 95% CI, 0.54–1.4
  - 3rd or 4th degree laceration: 4 trials, N=144,994; 6.7% vs. 6.4%; RR 0.91; 95% CI, 0.78–1.1)
- Elective induction at 39 weeks associated with lower frequency of:
  - Respiratory morbidity: 5 trials, N=290,780; 0.7% vs. 1.5%; RR 0.71; 95% CI, 0.59–0.85
  - Meconium aspiration syndrome: 3 trials, n=322,606; 0.7% vs. 3.0%; RR 0.49; 95% CI, 0.26–0.92
  - Neonatal ICU admissions: 3 trials, N=188,418; 3.5% vs. 5.5%; RR 0.80; 95% CI, 0.72–0.88
  - Perinatal mortality: 3 trials, N=147,888; 0.04% vs. 0.2%; RR 0.27; 95% CI, 0.09–0.76

LIMITATIONS:

- Data from observational studies may be affected by confounding, selection, and ascertainment bias.
- Significant heterogeneity among studies for some outcomes.

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Reducing the incidence of bacterial vaginosis

Randomized Trial of Lactin-V to prevent Recurrence of Bacterial Vaginosis

Cohen CR, Wierzbicki MR, French AL, Morris S, Newmann S, et al. Randomized Trial of Lactin-V to Prevent Recurrence of Bacterial Vaginosis. *N Engl J Med*. 2020; 382(20):1906-1915. doi:10.1056/NEJMoa1915254

KEY TAKEAWAY: *Lactobacillus crispatus* CTV-05 (Lactin-V) reduces bacterial vaginosis recurrence after metronidazole treatment by 34% at 12 weeks compared to placebo.

STUDY DESIGN: Randomized, double-blind, placebo-controlled, phase 2b trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Up to 50% of women will experience bacterial vaginosis during their reproductive years which may make them more susceptible to other sexually transmitted infections. Despite adequate treatment, up to 70% of women may have a recurrence of bacterial vaginosis. The efficacy of Lactin-V on BV recurrence is unknown.

PATIENTS: Females between the ages of 18 to 45 who had been diagnosed with bacterial vaginosis and completed a course of vaginal metronidazole gel.

INTERVENTION: *L. crispatus* CTV-05 Lactin-V at 2×109 CFU per dose

CONTROL: Matching placebo

OUTCOMES: Percentage with recurrent BV at any follow-up visit including a week 12 visit

Secondary Outcomes: Percentage with recurrent BV at any visit including the week 24 visit; percentage of the Lactin-V group with detectable *L. crispatus* at 12 and 24 weeks; acceptability of Lactin-V

METHODS (BRIEF DESCRIPTION):

- Participants randomly assigned 2:1 via permuted blocks to receive Lactin-V or placebo.
- Lactin-V or placebo vaginally self-administered four consecutive daily doses during week 1 followed by twice-weekly doses for 10 weeks.
- Participants logged administration of Lactin-V/placebo, menstruation, sexual activity, symptoms, and adverse events.
- Follow-up visits at 4, 8, 12, and 24 weeks after. Vaginal swabs obtained at each visit for the assessment of Amsel criteria, determination of Nuget score, and detection of *L. crispatus* by PCR assays.
- Analysis via intention-to-treat.
- Power analysis and allocation/concealment described.

INTERVENTION (# IN THE GROUP): 152

COMPARISON (# IN THE GROUP): 76

FOLLOW UP PERIOD: Outcomes at 12 and 24 weeks

RESULTS:

Primary Outcome:

- Recurrence of BV at week 12 significantly lower in Lactin-V group vs placebo (30% vs. 45%; RR 0.66; 95% CI, 0.44–0.87; NNT=7)

Secondary Outcomes:

- Recurrence of BV at week 24 significantly lower in the Lactin-V group vs placebo (12% vs. 17%; RR 0.73; 95% CI, 0.54–0.92)
- No significant difference in adverse events between groups.

LIMITATIONS:

- Small sample size
- Excluded pregnant women and <18 years of age

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