GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of August 2 - 6, 2021

SPOTLIGHT: Trichomoniasis - The Case When a Longer Duration of Antibiotics is Warranted

Trichomoniasis: The Case When a Longer Duration of Antibiotics is Warranted

Single-Dose Versus 7-Day-Dose Metronidazole for the Treatment of Trichomoniasis in Women: An Open-Label, Randomised Controlled Trial

Kissinger P, Muzny CA, Mena LA, et al. Single-dose versus 7-day-dose metronidazole for the treatment of trichomoniasis in women: an open-label, randomised controlled trial. *Lancet Infect Dis.* 2018; 18(11):1251-1259. doi:10.1016/S1473-3099(18)30423-7

KEY TAKEAWAY: A seven-day dose of metronidazole should be the preferred treatment for trichomoniasis among women.

STUDY DESIGN: Randomized, parallel, multi-site, open-label, laboratory blinded trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Trichomoniasis is the most common non-viral STI among women worldwide, affecting 5% of women and causing significant reproductive morbidity. The treatment of choice has been a single dose of oral metronidazole as it decreases the issue of adherence. There is mounting evidence that there are high rates of persistent infection with single-dose therapy compared to the seven-day course.

PATIENTS: Females 18–64 years old with trichomoniasis

INTERVENTION: Oral metronidazole 500 mg twice daily for 7 days

CONTROL: Oral metronidazole 2 g single dose

OUTCOME: Presence of *T. vaginalis* at test of cure or culture 4 weeks post completion of treatment with metronidazole

METHODS (BRIEF DESCRIPTION):

- Symptomatic participants who tested positive for *T. vaginalis* in one of three cities (Birmingham, AL; Jackson, MS; New Orleans, LA)
- Participants: 623 females, 95% African American, positive for *T. vaginalis* by NAAT or culture, HIV negative, non-pregnant & non-breastfeeding
- Randomized to treatment group (receiving 500 mg of oral metronidazole twice daily for 7 days) or control group (receiving single 2 g dose of oral metronidazole).
- A test of cure by NAAT or culture was completed 4 weeks after treatment for each arm (self-collected vaginal swab).
- Computer-assisted surveys were done at baseline and TOC to assess trichomoniasis symptoms, sexual behavior, and other factors.
- Intent-to-treat analyses, stratified by BV status

INTERVENTION (# IN THE GROUP): 312

COMPARISON (# IN THE GROUP): 311

FOLLOW UP PERIOD: 4 weeks

RESULTS:

- Women in the 7-day dose arm had significantly lower positive rates at TOC than those in the single-dose arm (11% vs 19%; RR 0.55; 95% CI, 0.34–0.70).
- The adherence rate was lower in the 7-day dose arm compared to the single-dose arm but remained over 95% (96% vs 99%; *P*<.01).

LIMITATIONS:

- Lower recruitment than planned could have led to reduced power for the primary outcome .
- Cannot generalize to pregnant, breastfeeding, or HIV-positive women or to men.
- For the positive test of cure results, cannot tell the difference between re-infection versus treatment failure including resistance to metronidazole treatment.
- Unclear how long remnant *T. vaginalis* DNA stays in vaginal fluids that could lead to false-positive TOC.

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Get that Fit Feeling: Compression to Prevent Cellulitis

Compression Therapy to Prevent Recurrent Cellulitis of the Leg

Webb E, Neeman T, Bowden FJ, Gaida J, Mumford V, Bissett B. Compression Therapy to Prevent Recurrent Cellulitis of the Leg. *N Engl J Med*. 2020 Aug 13; 383(7):630–639.

KEY TAKEAWAY: Participants receiving compression plus education had fewer episodes of cellulitis than those receiving education alone.
STUDY DESIGN: Randomized non-blinded trial single site
LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Chronic edema is a risk factor for cellulitis and has high rates of recurrence. Antibiotic prophylaxis can decrease cellulitis recurrence, but no trials have studied managing edema to decrease cellulitis recurrence. Compression is widely used to treat edema, but there are no studies on the effect of compression on recurrent cellulitis.

PATIENTS: Adults with recurrent cellulitis and chronic edema
INTERVENTION: Compression and education
CONTROL: Education alone
OUTCOME: Recurrent Cellulitis
Secondary Outcomes: Cellulitis-related hospitalization, quality-of-life, and leg volume

METHODS (BRIEF DESCRIPTION):

- Participants were selected from a public hospital in Australia or referred by local physicians.
  - Inclusion criteria: >18 years old, history of ≥2 episodes of cellulitis in the same leg in past 2 years, leg edema lasting >3 months
  - Exclusion criteria: Wearing effective compression >5 days per week, clinically unstable
- Participants randomly assigned in 1:1 ratio to compression group + education or education alone.
  - Intervention group: Wore compression garments every day, removing at night. The type of compression garment was individualized based on patient need.
  - Cellulitis prevention education: At initial start of trial and every 6 months
    - Comprised of skin care, prevention of fungal skin infections, healthy body weight, and exercise.
  - Patients in the control group who had an episode of cellulitis was subsequently moved to the compression group.
- Participants evaluated by lymphedema, physical therapist, and general medical practitioners to assess leg volume and quality of life prior to start of trial.
- Patients self-reported cellulitis through interviews every six months to assess:
  - Previously unreported recurrence of cellulitis
  - Quality-of-life measured via measure for limb lymphedema quality of life score (LYMQOL; 0–10 with higher scores indicating better quality of life)
  - Hospitalizations
  - Leg volume

INTERVENTION (# IN THE GROUP): 41
COMPARISON (# IN THE GROUP): 43

FOLLOW UP PERIOD: June 2017 – March 2019

RESULTS:
Primary Outcome:

- Compression with education compared to education alone resulted in fewer episodes of cellulitis (Hazard ratio [HR] 0.23; CI 0.09–0.59).

Secondary Outcomes:

- Compression with education compared to education alone had a significant decrease in leg volume (–181 mL vs 60 mL respectively; between-group difference in change –241 mL; 95% CI, –365 to –117).
- There was no significant difference in hospitalizations between compression and education versus control (7% [3/14] vs 15% [6/43]; HR 0.38; 95% CI, 0.09–1.6).
- There was no significant difference in quality of life score LYMQOL (between-group difference in change 0.8 points; 95% CI –0.7 to 1.7).

LIMITATIONS:

- Further co-variate analyses did not support benefit within subgroups (high BMI, multiple episodes of cellulitis, tinea infection, and wounds), but were not discussed in this paper.
- Cost-analysis not part of study.
- No longer term data to determine if effects last beyond 12 months.

- No review of inclusion/exclusion on definition or exact diagnosis of cellulitis

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Steady as She Goes: Osteopathic Manipulative Treatment in Individuals with Vertigo

Osteopathic Manipulative Treatment in Individuals with Vertigo and Somatic Dysfunction: A Randomized, Controlled, Comparative Feasibility Study

Fraix M, Badran S, Graham V, et al. Osteopathic manipulative treatment in individuals with vertigo and somatic dysfunction: a randomized, controlled, comparative feasibility study. *J Osteopath Med*. 2021; 121(1):71–83. doi:10.7556/jaoa.2020.147

KEY TAKEAWAY: Osteopathic manipulative treatment with vestibular rehabilitation therapy may reduce vertigo impairment, but larger studies are necessary to assess efficacy.

STUDY DESIGN: Randomized, controlled, comparative, feasibility study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Vertigo negatively affects patient quality of life. Osteopathic philosophy teaches that form and function are reciprocally related. Therefore, vestibular rehabilitation combined with osteopathic treatment should improve quality of life in vertigo patients. This study aimed to determine feasibility of future research.

PATIENTS: Adults 29–67 years old with vertigo

INTERVENTION: Vestibular rehabilitation therapy and/or osteopathic manipulative treatment

CONTROL: No intervention

OUTCOME: Feasibility of vertigo evaluation/treatment in a community setting using an interdisciplinary team

METHODS (BRIEF DESCRIPTION):

- Inclusion criteria: 18–79 years old, vertigo symptoms greater than 3 months, tolerance of 30 minutes sitting/standing, transfer ability for sitting/standing, therapy/exercise tolerance, comprehension of English or Spanish, presence of somatic dysfunction
- After meeting inclusion criteria, patients were assigned to one of the following:
    - Control: No intervention
    - OMT: Osteopathic manipulative treatment, a method of treating somatic dysfunction
    - VRT: Vestibular rehabilitation therapy, an individualized vertigo treatment regimen
    - Combination OMT/VRT
- Pre-exam by OMT-certified DO, DPT, and optometrist. Evaluators blinded to assignments.
- Second physician performed all osteopathic diagnosis/OMT (total 3 sessions), blinded to initial osteopathic assessment. Patients assessed by initial DPT and treated by second, blinded PT.
- Outcome recording was blinded.
- Primary outcomes measures: Sensory Organization Test (SOT) with Computerized Dynamic Posturography (CDP), compiled into Composite Score (CS) scaled 0–100; higher scores indicate less postural sway. Dizziness Handicap Index (DHI), a validated questionnaire of symptoms scored 0-100; higher scores indicate worse vertigo.
- Outcome Scoring: CS, DHI, osteopathic exam (somatic dysfunction), and optometric evaluation (vergence skills/ocular alignment) measured prior to treatment, 3 weeks post-treatment, and again 3 months post-treatment.

INTERVENTION (# IN THE GROUP): 19

- OMT: 7
- VRT: 6
- OMT and VRT: 6

COMPARISON (# IN THE GROUP): 7

FOLLOW UP PERIOD: 3 months

RESULTS:

- There was a measurable improvement in the symptoms of vertigo. The intervention demonstrated feasibility of protocol and coordination between specialists.
    - OMT & VTR group experienced a decrease in DHI mean score at 3 months post-treatment compared to baseline (Mean Score 15.3; 95% CI, 2.4–28).
    - OMT group experienced a decrease in CS score at:
        - Immediately post-treatment compared to baseline (Decrease of 4.0; 95% CI, 1.3–6.7)
        - 3 months post-treatment compared to baseline (Decrease of 5.0; 95% CI, 1.0–9.0)
- Metrics not relevant to feasibility: Somatic dysfunction, vergence dysfunction, vertical heterophoria, and monocular visual acuity

LIMITATIONS:

- Preliminary study, focused on feasibility/methods rather than outcomes.
- Studying vergence, visual acuity, and vertical heterophoria are not common/accepted criteria.
- Small sample size

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Does Pre-Pregnancy Contraception Use Affect Future Fertility?

Pregravid Contraceptive Use and Fecundability: Prospective Cohort Study

Yland JJ, Bresnick KA, Hatch EE, et al. Pregravid contraceptive use and fecundability: prospective cohort study. *BMJ*. 2020; 371:m3966. doi:10.1136/bmj.m3966.

KEY TAKEAWAY: Injectable contraception delayed the return of fertility longer than any other hormonal birth control method (BCM), but there are little or no lasting effects on future fertility with long-term use.

STUDY DESIGN: Prospective cohort study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Long-acting reversible contraception has become increasingly popular. Research has mainly focused on oral contraception and its effects on future fertility. This study focuses on a variety of BCMs and their effects on fecundability.

PATIENTS: Women 18–49 years old trying to conceive

INTERVENTION: Hormonal birth control methods, intrauterine devices, and natural methods as last used birth control method

CONTROL: Barrier method as last used birth control method

OUTCOME: Pregnancy within 12 cycles

METHODS (BRIEF DESCRIPTION):

- Pooled data from three prospective cohort studies of participants planning pregnancies.
- Participants were recruited via social media and health-related website advertising.
- Each participant was self-assigned into groups based upon the last BCM used prior to trying to conceive.
  - PRESTO participants additionally reported the total number and length of contraceptive methods they had used in their lifetime.
- Exclusion criteria included insufficient menstrual cycle data, pregnancy, fertility treatments, attempts to conceive for more than six menstrual cycles at study entry, and current contraception use.
- Participants answered follow-up questionnaires every two months for 12 months or until a pregnancy was reported, whichever came first.

INTERVENTION (# IN THE GROUP): 12,457

COMPARISON (# IN THE GROUP): 5,497

FOLLOW UP PERIOD: 12 cycles or until reported pregnancy (whichever occurred first)

RESULTS:

- Injectable contraception delayed return of fertility longer than any other BCM (5–8 cycles), (fecundability ratio 0.65; 95% CI, 0.47–0.89)
- Hormonal IUD delayed return of fertility 2 cycles (fecundability ratio 1.1; 95% CI, 1.0–1.2)
- Oral contraceptive pills delayed return of fertility 3 cycles (fecundability ratio 0.94; 95% CI, 0.90–0.98)
- Long-term use of hormonal BCMs had no lasting effect on fecundability
- Increased fecundability with long-term use of oral contraceptive pills for 4–5 years

LIMITATIONS:

- Study population was racially homogenous (92%non-Hispanic White)
- Selection bias may have resulted from self-selection of cohorts, the volunteer nature of the study, and because women who conceive immediately following contraception discontinuation might be less likely to enroll.
- Time-to-pregnancy was based on cycle length and reported last menstrual period, which may have resulted in cycle misclassification. Additionally, data was not collected regarding last injection date for women using injectable contraception.

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