GOOD EVIDENCE MATTERS

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Adult Weight Loss: Is Semaglutide More Effective in Those with or Without Diabetes?

Weight Loss Effects of Once-Weekly Semaglutide 2.4 mg in Adults with and Without Type 2 Diabetes: A Systematic Review and Meta-Analysis

Hong B, Kim H, Lee D, Kim K. Weight Loss Effects of Once-Weekly Semaglutide 2.4 mg in Adults with and without Type 2 Diabetes: A Systematic Review and Meta-Analysis. *Pharmaceuticals (Basel)*. 2025;18(7):1058. Published 2025 Jul 18. doi:10.3390/ph18071058

KEY TAKEAWAY: Semaglutide 2.4 mg increases weight loss in adults with obesity, but people without diabetes lose nearly twice as much weight as those with diabetes.

STUDY DESIGN: Systematic review and meta-analysis of 10 randomized controlled trials (RCTs) (N=5,339)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Semaglutide is widely used for weight management, and prior trials have shown it to be effective in adults with obesity. It has been observed that individuals with diabetes may lose less weight on this medication, but the degree of difference has not been clearly defined. This study aimed to quantify and compare the magnitude of weight loss achieved with once weekly semaglutide 2.4 mg in adults with overweight or obesity who have type 2 diabetes compared to those without type 2 diabetes.

PATIENTS: Adults with overweight or obesity, with or without type 2 diabetes

INTERVENTION: Semaglutide 2.4 mg weekly

CONTROL: Placebo

PRIMARY OUTCOME: Percent change in body weight

METHODS (BRIEF DESCRIPTION):

- Studies with adults with overweight or obesity (diagnosis defined by a body mass index [BMI] ≥27 kg/m² with a weight-related comorbidity or BMI ≥30 kg/m²) were included in the systematic review.
- The study included only RCTs lasting 40–70 weeks and using semaglutide 2.4 mg and excluded studies with overlapping populations, prediabetes-only groups, and non-RCT designs.
- Semaglutide 2.4 mg, subcutaneous injection, once weekly was used.
- Trials generally incorporated concurrent lifestyle modification such as hypocaloric diet, increased physical activity, or behavioral counseling.
- Matching placebo injections were used and administered at the same frequency as semaglutide, with identical background lifestyle counseling when applicable.
- Participants included multinational, overweight or obese adults enrolled in RCTs.
  - Both sexes were included, with the mean age range in the 40–60s.
- The primary outcome was measured as percent change in body weight from baseline.
- Outcome type: Continuous (percentage change)

INTERVENTION (# IN THE GROUP): 3,167

COMPARISON (# IN THE GROUP): 2,172

FOLLOW-UP PERIOD: 51–111 weeks

RESULTS:

Primary Outcome –

- Once weekly semaglutide 2.4 mg produced significantly greater weight loss compared to placebo:
  - Adults without diabetes (6 studies, n=3,841; weighted mean difference [WMD] –12%; 95% CI, −13 to −10; I^2=63%).
  - Adults with diabetes (3 studies, n=1,407; WMD 6.3%; 95% CI, −7.0 to −5.7; I^2=0%).

LIMITATIONS:

- The study relied on post hoc subgroup analyses from several trials and therefore randomization may not have been preserved within these subgroups, and important confounders may not have been evenly distributed, which increases the risk of bias and overinterpretation.
- Variations in the intensity of lifestyle interventions, treatment duration, and type of behavioral support across trials contributed to heterogeneity.
- Some placebo groups were pooled with other dose arms, which may have introduced comparison bias.
- The meta-analysis involved small number of studies, thus reducing the statistical power.

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To Doxy or Not to Doxy? Doxycycline's Role in STI Prophylaxis in Women

Doxycycline Prophylaxis to Prevent Sexually Transmitted Infections in Women

Stewart J, Oware K, Donnell D, et al. Doxycycline Prophylaxis to Prevent Sexually Transmitted Infections in Women. *N Engl J Med*. 2023;389(25):2331-2340. doi:10.1056/NEJMoa2304007

KEY TAKEAWAY: Doxycycline prophylaxis does not statistically improve the prevention of any sexually transmitted infections (STIs), chlamydia only, or gonorrhea only compared to women receiving standard care.

STUDY DESIGN: Open label trial randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Worldwide the incidents of sexually transmitted infections of *Chlamydia trachomatis*, *Neisseria gonorrhea*, and *Treponema pallidum* are rising. While studies of cisgender men and transgender women taking doxycycline post exposure prophylaxis (PEP) have proven effective in decreasing STIs from the above bacteria, data on its effectiveness in cisgender women is lacking. This study aimed to provide more data on the effectiveness of doxycycline PEP to prevent the contraction of bacterial STIs in cisgender women.

PATIENTS: Cisgender women 18–30 years in Kisumu, Kenya receiving preexposure prophylaxis against STIs

INTERVENTION: Doxycycline PEP

CONTROL: No prophylactic medication

PRIMARY OUTCOME: Incidence of any STIs, incidence of chlamydia only, and gonorrhea only

METHODS (BRIEF DESCRIPTION):

- Participants recruited from Kenya population who were receiving tenofavir disoproxil fumarate (300 mg) - emtricitabine (200 mg) once daily for HIV PrEP from the Ministry of Health.
- Patients who were pregnant were excluded. Doxycycline was withdrawn if patient became pregnant, but patient could remain in the study.
- Patients were randomized into a treatment and control group by a computer-based system.
- Participants in the intervention group were told to take 200 mg of doxycycline hyclate within a 72-hour window after condomless sex.
- Patients followed up for quarterly testing.
- Patients received weekly short message service (SMS) surveys asking about sexual exposures, and participants in the doxycycline group were asked to report doxycycline use.
- Endocervical swabs collected quarterly and tested for chlamydia and gonorrhea using nucleic acid amplification testing (NAAT), and evaluations of results from the endocervical swabs occurred quarterly.
- Plasma samples were also tested on a quarterly basis using the BD Macro-Vue test to determine new incidents of syphilis contraction.
- Treatment regimens:
  - Chlamydia: 1 g oral azithromycin
  - Gonorrhea: 500 mg intramuscular ceftriaxone, or 400 mg oral cefiximine
  - Treponema: 2.4 million units of intramuscular penicillin G benzathine
  - Test of cure completed after treatment
- Hair strands were collected from participants with the 1 cm segmented closest to the root being tested for doxycycline presence (representing about a month of time). A percentage of randomly selected hair strands were then tested from each group.
- The endocervical swabs that were positive for gonorrhea were purified and the bacteria DNA extracted and tested for the tetracycline resistant gene tet(M).
- Designed for 80% power in the detection of 50% decrease with doxycycline PEP.
- STI incidence between the test and control group was estimated by using the relative risk of having at least one STI per quarterly visit, and then a modified Poisson model was used.
- Two-sided alpha level set at 0.05 for statistical significance; and a 95% confidence interval.

INTERVENTION (# IN THE GROUP): 216

COMPARISON (# IN THE GROUP): 221

FOLLOW-UP PERIOD: Once every three months over one year

RESULTS:

Primary Outcome –

- Doxycycline PEP did not significantly reduce the risk of any STI compared to the control (relative risk [RR] 0.88; 95% CI, 0.60–1.3).
- Doxycycline PEP did not significantly reduce the risk of any chlamydia only compared to the control (RR 0.73; 95% CI, 0.47–1.1).
- Doxycycline PEP did not significantly reduce the risk of any gonorrhea only compared to the control (RR 1.6; 95% CI, 0.78–3.5).

LIMITATIONS:

- The most significant limitation is adherence to the medication regimen post-sexual activity.
- Hair analysis suggests that up to 44% of participants assigned to take doxycycline post-sex never took the medication.
- Only tested for vaginal infections with STIs, not pharyngeal or rectal STI infections.

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Does Therapeutically Increasing Potassium Level Benefit Patients at Risk of Ventricular Arrythmia?

Increasing the Potassium Level in Patients at High Risk for Ventricular Arrhythmias

Jøns C, Zheng C, Winsløw UCG, et al. Increasing the Potassium Level in Patients at High Risk for Ventricular Arrhythmias. *N Engl J Med*. 2025;393(20):1979-1989. doi:10.1056/NEJMoa2509542

KEY TAKEAWAY: For patients with cardiovascular disease (CVD) at high risk for ventricular arrhythmia and with an implantable cardioverter-defibrillator (ICD) in-situ, therapeutically increasing potassium levels with diets and medications significantly lowers risk of appropriate ICD therapy, unplanned hospitalization from arrhythmia or heart failure (HF), and all-cause mortality.

STUDY DESIGN: Multicenter, open-label, randomized superiority trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Hypokalemia is associated with increased incidence of ventricular and supraventricular arrhythmia. In patients with CVD at risk of tachyarrhythmias, even low-normal levels (<4.0 mmol/L), is associated with all-cause mortality. However, the impact of therapeutically increasing potassium levels in this cohort has never been directly assessed in a clinical trial.

PATIENTS: Patients with CVD with an ICD in-situ

INTERVENTION: Therapeutically increasing potassium levels

CONTROL: Current standard of care

PRIMARY OUTCOME: Composite endpoint of sustained ventricular tachycardia (>120 bpm), appropriate ICD therapy, unplanned hospitalization due to arrhythmia or HF, and all-cause mortality

Secondary Outcome: All-cause mortality; hospitalization for HF, arrhythmia, kidney failure or electrolyte disturbances; both appropriate and inappropriate ICD therapy

METHODS (BRIEF DESCRIPTION):

- Participants were drawn from three different tertiary academic hospitals in Denmark.
- Inclusion criteria included adults ≥18 years old with an ICD or a cardiac-resynchronization therapy defibrillator (CRT-D) in-situ, and with a baseline potassium level of ≤4.3 mmol/L.
- Exclusion criteria included estimated glomerular filtration rate (eGFR) <30 ml/min/1.7m^2, pregnancy, inability or refusal to consent.
- Participants were randomly assigned 1:1 to receive treatment to increase potassium (high-normal potassium group) in addition to standard care or to receive standard care only (standard care group).
    - High-normal potassium group received counseling on potassium-rich diets, increased potassium by using potassium supplements (administered as potassium chloride tablets 750 mg or about 10 mmol), mineralocorticoid receptor antagonists (MRA) (daily doses being 100 mg for spironolactone and 50 mg for eplerenone) or both or, if needed, adjusting existing thiazide or loop diuretics, to reach and maintain target potassium level of 4.5 to 5.0 mmol/L.
    - Standard care: Both groups received appropriate care according to standard guidelines.
- Participants in treatment arm had biweekly clinic visits with blood tests until potassium targets were reached and then seen every six months.
- Data on components of primary outcome and secondary outcomes were obtained from ICD interrogations and hospital records, all hosted in an electronic research database server.

INTERVENTION (# IN THE GROUP): 600

COMPARISON (# IN THE GROUP): 600

FOLLOW-UP PERIOD: Variable, with median being 40 months (interquartile range 26–49 months)

RESULTS:

Primary Outcome –

- Therapeutically increasing potassium significantly decreased the risk of the composite outcome of ventricular tachyarrhythmia events, unplanned hospitalization for arrhythmia or HF, appropriate ICD therapy or death from any cause compared to the control (hazard ratio [HR] 0.76; 95% CI, 0.61–0.95; NNT=12).

Secondary Outcome –

- Therapeutically increasing potassium levels, compared to the control, significantly decreased:

    - Incidence of appropriate ICD therapy or ventricular tachycardia (15% vs 20%, respectively; HR 0.75; 95% CI, 0.57–0.98)
    - Unplanned hospitalization for cardiac arrhythmia (HR 0.63; 95% CI, 0.42–0.93)
- Therapeutically increasing potassium levels, compared to the control, did not decrease unplanned hospitalization for HF, all-cause mortality, or the incidence of inappropriate ICD therapy.
- Therapeutically increasing potassium levels, compared to the control, did not increase hospitalization for kidney failure or electrolyte disturbances.

LIMITATIONS:

- This study only looked at patients with ICD in place, so no inference can be made for other high-risk patients who do not have an ICD in place.
- The trial was performed in only one country with a homogenous population, thus limiting the generalizability of the findings.
- The participants were not blinded.
- Several of the subgroups were small, and no adjustments were made for multiplicity, limiting validity of findings from the subgroup analyses.
- Adherence to dietary interventions was not measured or accounted for.
- Use of MRA's in the intervention group could confound the results.

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Effects of X-Ray-Based Diagnosis and Explanation of Knee Osteoarthritis on Patient Beliefs About Osteoarthritis Management: A Randomized Clinical Trial

Lawford BJ, Bennell KL, Ewald D, et al. Effects of X-ray-based Diagnosis and Explanation of Knee Osteoarthritis on Patient Beliefs about Osteoarthritis Management: A Randomized Clinical Trial. *PLoS Med*. 2025;22(2):e1004537. Published 2025 Feb 4. doi:10.1371/journal.pmed.1004537

KEY TAKEAWAY: An x-ray-based explanation of knee osteoarthritis (OA), whether by describing the radiograph findings to the patient or showing the images to patients increases patient belief in the need for surgery but does not alter patient's perceptions on the benefit of physical activity.

STUDY DESIGN: Three-arm randomized control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Although x-rays are not recommended or necessary to diagnosis knee OA, they are often performed due to clinicians and patients' belief they are necessary. This study examined whether using a clinical explanation of knee OA compared to using an x-ray-based approach OA influenced patient's beliefs concerning management.

PATIENTS: Adults with and without chronic knee pain

INTERVENTION: Patients receiving radiographic explanations but not shown x-rays and patients receiving radiographic explanation and shown x-rays

CONTROL: Patients receiving clinical explanations without x-ray

PRIMARY OUTCOME: Belief of patient that knee replacement was necessary and perception that exercise and physical activity were helpful

Secondary Outcome: Belief medication is helpful, belief exercise and physical activity would damage the knee, level of concern, fear of movement

METHODS (BRIEF DESCRIPTION):

- Adults ≥45 years old (half with knee pain and half without) were recruited online.
- Participants were excluded if they had consulted a physician for chronic knee pain, were unable to read/understand English.
- Participants were randomized into three groups, and each group was assigned to watch one of the following video-recorded explanations of knee OA delivered by a general practitioner:
  - Clinical explanation without x-rays (n=208)
  - Explanation incorporating an x-ray report without images (n=203)
  - Explanation incorporating x-ray images (n=206)
- At conclusion of the video patients were asked "Based on the video you watched:"
  - Do you think joint replacement surgery would be necessary for your hypothetical knee OA?
  - Do you think exercise and physical activity would be helpful to manage your hypothetical knee OA?
- Responses were measured on an 11-point numeric rating scale (NRS) ranging from zero indicating "definitely not necessary/helpful" to 10 indicating "definitely necessary/helpful."
- Participants were paid for completing the survey.
- Secondary outcomes were each based on a NRS score of 0–10.
  - Beliefs on medication helpfulness: Score of zero indicating definitely not helpful and a score of 10 indicating definitely helpful.
  - Belief damage made worse by activity: Score of zero indicating definitely not damage and a score of 10 indicating definitely would damage.
  - Concern that OA would worsen. Score of zero indicating not concerned and a score of 10 indicating very concerned.
  - Fear of movement was graded on four-point scale ranging from a score of one indicating "strongly disagree" to a score of four indicating "strongly agree."

INTERVENTION (# IN THE GROUP):

- Explanation of x-rays: 203
- Viewed x-rays: 206

COMPARISON (# IN THE GROUP): 208

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- Patients receiving radiographic explanation and shown x-ray were more likely to believe surgery was

necessary than those receiving a clinical explanation without x-rays (mean difference [MD] 1.1; 95% CI, 0.5–1.8).

- Patients receiving radiographic explanations but not shown x-rays were more likely to believe surgery was necessary than those receiving a clinical explanation without x-rays (MD 0.6; 95% CI, 0.1–1.1).
- There were no significant differences between any of the groups on the perception of the helpfulness of exercise and physical activity.
- Patients receiving radiographic explanations and shown x-ray compared to those receiving a clinical explanation without x-rays (MD –0.4; 95% CI, –0.9 to 0.1).
- Patients receiving radiographic explanations and not shown x-ray compared to those receiving a clinical explanation without x-rays (MD –0.2; 95% CI, –0.6 to 0.1).

Secondary Outcome –

- Patients receiving radiographic explanation and shown x-ray were more likely to believe exercise would further damage the knee compared to than those receiving a clinical explanation without x-rays (MD 0.6; 95% CI, 0.2–1.1).
- There was no significant difference in the belief exercise would further damage the knee for patients receiving radiographic explanations but not shown x-rays compared to those receiving a clinical explanation without x-rays.
- There were no significant differences between the groups regarding their beliefs about the helpfulness of medication.
- Patients receiving radiographic explanation and shown x-ray had a higher level of concern compared to those receiving a clinical explanation without x-rays (MD 1.0; 95% CI, 0.5–1.5).
- Patients receiving radiographic explanation and not shown x-ray had a higher level of concern compared to those receiving a clinical explanation without x-rays (MD 0.7; 95% CI, 0.20–1.2).
- Patients receiving radiographic explanation and shown x-ray had an increased fear of movement compared to those receiving a clinical explanation without x-rays (MD 1.0; 95% CI, 0.3–1.7).
- There was no significant difference in the fear of movement for patients receiving radiographic explanations but not shown x-rays compared to those receiving a clinical explanation without x-rays.

LIMITATIONS:

- The survey was utilized in a hypothetical scenario, which may not correlate with real world clinical outcomes.
- Patients were paid to complete survey which may have compromised their diligence in completing survey.
- Unknown if any of the participants had knee OA.

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Dose-Dependent Lysergide (MM120) for Generalized Anxiety Disorder Improvement

Single Treatment with MM120 (Lysergide) in Generalized Anxiety Disorder: A Randomized Clinical Trial

Robison R, Barrow R, Conant C, et al. Single Treatment with MM120 (Lysergide) in Generalized Anxiety Disorder: A Randomized Clinical Trial. *JAMA*. 2025;334(15):1358-1372. doi:10.1001/jama.2025.13481

KEY TAKEAWAY: A single dose of MM120 (lysergide-D-tartrate) reduces anxiety symptoms in adults with moderate to severe generalized anxiety disorder (GAD) in a dose-dependent manner.

STUDY DESIGN: Multicenter, double-blinded, randomized, placebo-controlled trial

LEVEL OF EVIDENCE: STEP 3 (downgrade due to small sample size and short study duration)

BRIEF BACKGROUND INFORMATION: GAD is a common and chronic mental health condition characterized by excessive and persistent worry, often inadequately managed with current first-line treatments such as selective serotonin reuptake inhibitors (SSRIs). This study aimed to evaluate a dose dependent reduction in the Hamilton Anxiety Rating Scale (HAM-A) scale for GAD after a one-time dose of MM120 in 12 weeks.

PATIENTS: Adults with GAD

INTERVENTION: MM120 (lysergide D-tartrate)

CONTROL: Placebo

PRIMARY OUTCOME: GAD symptoms at four weeks

METHODS (BRIEF DESCRIPTION):

- The study was conducted at 22 outpatient psychiatric research sites across the United States from August 2022 to August 2023.
- Adults 18–74 years old with a primary diagnosis GAD confirmed by DSM-5 criteria and the Mini-International Neuropsychiatric Interview (MINI) were included.
    - The mean age of patients was 41 years old. This includes 57% were female, 83% were White, 7.7% Black or African Americans, and 3.6% were Asian.
- All participants had moderate to severe anxiety, defined by a HAM-A score >20 at both screening and baseline.
- HAM-A score is 14 questions, scoring 0–3 each item with a total score of 0–56. Interpretation is <7 mild anxiety and >24 severe anxiety.
- Minimally clinically important difference (MCID) was 2.5 points.
- Regarding medication status, 84% required tapering of prohibited psychotropic medications before enrollment; most commonly SSRIs/SNRIs (up to 78%) and benzodiazepines (up to 35%).
- 18% were receiving psychotherapy at enrollment and maintained stable session frequency throughout the trial.
- Participants were randomized to receive a single oral dose of MM120 at 25 µg, 50 µg, 100 µg, or 200 µg, or placebo.
    - Each participant was continuously monitored for at least 12 hours after administration in comfortable, private room with trained monitors.
    - No psychotherapy was provided during or after dosing sessions to mitigate the pharmacological effects.
    - Follow up at day two, weeks one, two, four, eight, and 12.
- Primary Outcome: Change in anxiety symptoms measured by the HAM-A.
- Independent, blinded raters conducted all HAM-A assessments via structured interviews.
- The primary outcomes measured the changes in anxiety for each MM120 dose group, including 25 µg, 50 µg, 100 µg, and 200 µg compared to control.

INTERVENTION (# IN THE GROUP): 159

COMPARISON (# IN THE GROUP): 39

FOLLOW-UP PERIOD: 12 weeks

RESULTS:

Primary Outcome –

- MM120 doses 100 µg, and 200 µg significantly reduced HAM-A scores at four weeks, compared to placebo.
    - 100 µg (least-squares mean difference [LSMD] –5.0; 95% CI, –9.6 to –2.0)
    - 200 µg (LSMD –6.0; 95% CI, –9.8 to –2.0)

- MM120 dose 25 µg and 50 µg did not significantly reduce HAM-A scores at four weeks, compared to placebo.

LIMITATIONS:

- Trial was funded and conducted by MindMed, the company developing MM120 with several study authors being tied to the company. This shows potential for design bias.
- Short follow-up duration of 12 weeks prevented evaluation of long-term benefits with repeated administration.
- Participants excluded with recent psychedelic use, limiting applicability of the results to those populations.
- The trial did not include an active comparator (e.g., SSRI or benzodiazepine), making it difficult to evaluate its place in therapy.
- This study only evaluates effects after a singular dose and not if multiple treatments would be more effective or safer.
- The small sample size limits the ability to detect rare side effects.
- HAM-A scale relief on participant reporting, this can introduce a subjective bias. People may have expectations that may influence how symptoms are reported.

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Can Antioxidant Vitamin Supplementation Reduce Endometriosis-Related Pain?

Antioxidant Vitamins Supplementation Reduce Endometriosis Related Pelvic Pain in Humans: A Systematic Review and Meta-Analysis

Zheng SH, Chen XX, Chen Y, Wu ZC, Chen XQ, Li XL. Antioxidant Vitamins Supplementation Reduce Endometriosis Related Pelvic Pain in Humans: A Systematic Review and Meta-analysis. *Reprod Biol Endocrinol*. 2023;21(1):79. Published 2023 Aug 29. doi:10.1186/s12958-023-01126-1

KEY TAKEAWAY: Antioxidant vitamins supplementation significantly reduces the severity of chronic pelvic pain, dysmenorrhea, and dyspareunia and the levels of inflammatory biomarkers caused by endometriosis.

STUDY DESIGN: Systematic review and meta-analysis of 13 randomized controlled trials (RCTs) (N=589)

LEVEL OF EVIDENCE: STEP 3 (downgraded due to small sample size and heterogeneity of included studies)

BRIEF BACKGROUND INFORMATION: Endometriosis is an inflammatory condition that can cause chronic pelvic pain, dysmenorrhea, or dyspareunia in women. The effectiveness of antioxidant therapy such as higher consumption of antioxidant diet, citrus fruits, or garlic extract has been shown to improve endometriosis. Vitamins such as vitamin C, D, and E have antioxidant effects that may reduce the symptoms of endometriosis by mitigating the inflammatory mechanisms involved. However, more clarity is needed on the potential effects of antioxidant vitamins supplementation on endometriosis due to the inconsistency in study outcomes.

PATIENTS: Women with endometriosis

INTERVENTION: Vitamin C/E/D supplementation with no limits on the dose or frequency

CONTROL: Placebo pills, oral contraceptive (Yasmin), or non-treatment

PRIMARY OUTCOME: Chronic pelvic pain, dysmenorrhea, dyspareunia

Secondary Outcome: Oxidative stress markers

METHODS (BRIEF DESCRIPTION):

- Relevant Chinese and English studies were located from electronic databases such as Web of Science, PubMed, Cochrane Library, Scopus, and China National Knowledge Infrastructure from inception through March 16, 2023.
- 940 patients with endometriosis were included:
  - Pre-post change in pain scores using the Visual Analogue Scale (VAS) was analyzed in seven RCTs (n=370).
  - Pre-post change in number of patients with decreased pain scores was analyzed in three RCTs (n=219).
  - Pre-post change in plasma Malondialdehyde (MDA) levels and other markers of oxidative stress, was analyzed in six RCTs (n=520).
- The mean age of patients ranged from 19–41 years old.
- Across studies, the duration of the intervention ranged from six weeks to six months.
- Standard mean difference (SMD) and odds ratio (OR) and their respective 95% confidence intervals (95% CI) were used in the analysis of continuous and dichotomous outcome variables, respectively.
- The GRADE System was used to classify the quality of evidence in the review of the RCTs.

INTERVENTION (# IN THE GROUP): 505

COMPARISON (# IN THE GROUP): 435

FOLLOW-UP PERIOD: Six weeks to six months

RESULTS:

Primary Outcome –

- Compared to the placebo group, chronic pelvic pain was significantly alleviated by:
  - Vitamin E and C (4 RCTs; mean –1.8; 95% CI, –3.2 to –0.3; I^2=88%) and (odds ratio [OR] 12; 95% CI, 4.4–30; I^2=0%)
  - Vitamin E with or without vitamin C (7 RCTs; mean –2.7; 95% CI, –4.3 to –1.1; I^2=88%) and (OR 12; 95% CI, 4.4–30; I^2=0%)
  - Vitamin D showed a non-significant reduction in pelvic pain (2 RCTs).
  - The quality of evidence was low.
- Compared to the placebo group, dysmenorrhea was significantly reduced by vitamins E, C, or D (9 RCTs; mean –0.6; 95% CI, –1.0 to –0.2; I^2=0%) and (OR 3.0; 95% CI, 1.5–6.1; I^2=0%).
  - The quality of evidence was moderate.

- Compared to the placebo group, endometriosis-related dyspareunia was significantly improved with a combined vitamin E and C supplementation (3 RCTs; OR 6.4; 95% CI, 2.3–18; I^2=0%) and (1 RCT; mean –4.8; 95% CI, –6.2 to –3.4).
    - The quality of evidence was low.

Secondary Outcome –

- Compared to the placebo group:
    - MDA levels were reduced with a combined vitamin E and C supplementation (3 RCTs; mean –13; 95% CI, –20 to –5.6; I^2=81%).
    - Other oxidative stress markers included lipid hydroperoxides, reactive oxygen spices, high-sensitivity C-reactive protein, RANTES, interleukin-6, and monocyte chemotactic protein-1, were significantly reduced by vitamin supplementation (5 RCTs; *P*<.05).

LIMITATIONS:

- A limited number of studies and small sample sizes were included in the meta-analysis.
- Variability in vitamin dosage across the studies and confounding variables such as daily diet and sun exposure can influence the results of the meta-analysis.

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