GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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What's in this week's issue?

Week of February 5 - 9, 2024

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Antibiotic or Snot: Which Kids Should Be Treated for Acute Sinusitis?

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Identifying Children Likely to Benefit from Antibiotics for Acute Sinusitis: A Randomized Clinical Trial

Shaikh N, Hoberman A, Shope TR, et al. Identifying Children Likely to Benefit From Antibiotics for Acute Sinusitis: A Randomized Clinical Trial. *JAMA*. 2023;330(4):349-358. doi:10.1001/jama.2023.10854

KEY TAKEAWAY: In children with acute sinusitis, antibiotic treatment had minimal benefit for those with and without a bacterial nasopharyngeal pathogen or colored nasal discharge.

STUDY DESIGN: Multicentered, randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Studies suggest that children with acute sinusitis uncolonized with specific pathogens are less likely to benefit from antibiotic therapy. There is also literature suggesting purulence of nasal discharge may indicate the presence of bacteria. This study investigated the benefit of antibiotics for children with and without purulent discharge and the presence of bacterial pathogens on presentation.

PATIENTS: Children with acute sinusitis

INTERVENTION: Amoxicillin-clavulanate

CONTROL: Placebo

PRIMARY OUTCOME: Sinusitis symptoms

Secondary Outcome: Treatment failure, adverse events, resources used by families

METHODS (BRIEF DESCRIPTION):

- Patients 2–11 years old were recruited from primary care offices affiliated with six US institutions and met the criteria for persistent or worsening presentation of acute sinusitis.
- Inclusion criteria included sinusitis according to the clinical practice guidelines from the American Academy of Pediatrics (AAP), defined as persistent nasal symptoms, cough, or both for 11–30 days without improvement, worsening symptoms after initial improvement, or new onset of fever after presumed viral illness.
- Exclusion criteria included children with severe presentation diagnosed by colored nasal discharge and fever for ≥3 days, history of asthma or allergic rhinitis, or treatment with systemic antibiotics 15 days prior.
- The median age was five years old with 45% female in the antibiotics group and 48% female in the placebo group, 67% had colored nasal discharge in the antibiotic group and 66% in the placebo group, 70% had nasopharyngeal pathogens detected in the amoxicillin-clavulanate group vs 72% the placebo group.
- The antibiotic group received a 10-day course of oral amoxicillin 90 mg/kg/day with clavulanate 6.4 mg/kg/ day in two divided doses.
- The comparison group received 10 days of oral placebo in two divided doses.
- Nasopharyngeal cultures were obtained at study entry and visit at the end of the study.
- Symptom burden was measured via the pediatric rhinosinusitis symptom scale (PRSS) which includes eight rated symptoms (range 0–40 with higher scores indicating greater severity of symptoms, score ≤3 indicating symptom resolution) measured by parents every evening on days 2–11.
- Clinically significant diarrhea was defined as three or more watery stools for one day, or two watery stools for two consecutive days on days 2–11.
- Treatment failure is defined as an increase in a PRSS score of >20% from enrollment, a decrease of <2 points from enrollment to day three, a decrease in PRSS score <20% by day four and also on two consecutive days (day 5–11), or a decrease of less than 50% by the end of the study.
- Parents provided information on missed work alternative child-care arrangements, or visits to other clinicians.

INTERVENTION (# IN THE GROUP): 246

COMPARISON (# IN THE GROUP): 250

FOLLOW-UP PERIOD: 10 days

RESULTS:

Primary Outcome –

- Patients treated with antibiotics had lower symptom severity scores at 10 days than those treated with placebo (9.0 vs 11 points, between-group mean difference [MD] –1.69; 95% CI, –2.07 to –1.31).

Secondary Outcome –

- Patients treated with antibiotics had slightly greater symptom improvement as compared to those treated with placebo:
  - With detected nasopharyngeal pathogens: (MD –1.95; 95% CI, –2.4 to –1.5)
  - Without detected nasopharyngeal pathogens: (MD –0.88; 95% CI, –1.6 to –0.12)
  - Questionable clinical significance noted.
- Patients with colored or clear nasal discharge showed similar improvement in symptoms in:
  - Antibiotic group (MD –1.6; 95% CI, –2.1 to –1.2)
  - Placebo group (MD –1.7; 95% CI, –2.4 to –1.0)
  - Questionable clinical significance noted.
- Patients treated with antibiotics had more diarrhea compared to placebo (MD 6.3%; 95% CI, 0.3–12%).
- Treatment failure was lower in the antibiotic group (NNT 8; risk ratio [RR] 0.69; 95% CI, 0.54–0.88).
- All reports of work missed, extra childcare, and health care visits were not significant.

LIMITATIONS:

- The target sample size was not reached due to a disruption in enrollment from COVID-19.
- There was a lack of data regarding treatment failures.
- Children with severe sinusitis were excluded and they may be the most likely to benefit from antibiotics.
- The study did not include the gold-standard testing of sinus aspiration.

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Insulin with Breakfast, Lunch, and Dinner? Tirzepatide is the Winner!

Tirzepatide vs Insulin Lispro Added to Basal Insulin in Type 2 Diabetes: The SURPASS-6 Randomized Clinical Trial

Rosenstock J, Frías JP, Rodbard HW, et al. Tirzepatide vs Insulin Lispro Added to Basal Insulin in Type 2 Diabetes: The SURPASS-6 Randomized Clinical Trial [published correction appears in JAMA. 2023 Oct 26:]. *JAMA.* 2023;330(17):1631-1640. doi:10.1001/jama.2023.20294

KEY TAKEAWAY: Once weekly tirzepatide is superior to prandial insulin as an adjunct therapy to basal insulin in hemoglobin A1c (HbA1c) reduction in patients with inadequately controlled type 2 diabetes with the benefit of greater weight loss and less hypoglycemia.

STUDY DESIGN: Randomized, open-label phase 3b clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Insulin is a common treatment option for those with inadequately controlled diabetes. Recent guidelines have recommended the use of glucagon-like peptide receptor agonists (GLP-1 RA) to treat diabetes when oral agents are not producing satisfactory results. Previous studies have shown improved glycemic control and weight loss with the use of GLP-1 RAs. Tirzepatide is a glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 RA that was shown to vastly reduce HbA1c and body weight in all patients in all stages of diabetes treatment. This study evaluates the efficacy and safety of using tirzepatide as an adjunct to basal insulin versus three times a day (TID) prandial insulin.

PATIENTS: Adults with inadequately controlled type 2 diabetes

INTERVENTION: Tirzepatide

CONTROL: Insulin lispro

PRIMARY OUTCOME: HbA1c reduction

Secondary Outcome: Body weight reduction, HbA1c of <7.0

METHODS (BRIEF DESCRIPTION):

- Adults who are on no more than two diabetic therapies were included.
- Participants had HbA1c between 7.5–11% and a BMI between 23–45 kg/m2.
- Participants were excluded if they had a diagnosis of type 1 diabetes, history of pancreatitis, diabetes-related eye complications, severe hypoglycemia, or had an eGFR of 30 (45 if on metformin).
- Prior to randomization, trial participants ceased their diabetes medications and were standardized on insulin glargine that was titrated to a blood glucose level between 100–125 mg/dL.
- Participants with an HbA1c of 7.5% or greater were randomized via computer-generated sequence into a group that either receives TID prandial insulin lispro or a once-weekly subcutaneous injection of either 5 mg, 10 mg, or 15 mg of tirzepatide.
- Tirzepatide was started at 2.5 mg weekly and titrated up every four weeks until the randomized goal dose was reached.
- Lispro started at four units before meals. Lispro doses were modified twice weekly until the 24th week. Lispro doses were then adjusted once weekly for the remainder of the study to achieve a blood glucose target of 100–125 mg/dL before lunch, dinner, and bedtime.
- To decrease hypoglycemia risk, basal insulin was decreased by 30% during randomization and titrated weekly.

INTERVENTION (# IN THE GROUP): 716

- 5 mg tirzepatide: 243
- 10 mg tirzepatide: 238
- 15 mg tirzepatide: 236

COMPARISON (# IN THE GROUP): 708

FOLLOW-UP PERIOD: 56 weeks

RESULTS:

Primary Outcome –

- Tirzepatide decreased HbA1c more than insulin lispro (mean difference [MD] –0.98%; 95% CI, –1.2% to –0.79%).

Secondary Outcome –

- More participants receiving tirzepatide reached the target HbA1c of <7.0 compared to those receiving insulin lispro (odds ratio [OR] 4.2; 95% CI, 3.2–5.5).
- At week 52, tirzepatide resulted in more weight loss than insulin lispro (MD –12 kg; 95% CI, –13 to –11).

LIMITATIONS:

- There was no blinding or masking of the treatments due to the dosing frequency, dosing delivery, and dosing titration of the medications.
- The standardized insulin algorithm and blood glucose targets are not necessarily feasible or realistic outside of use in this trial.
- Patients using sodium-glucose cotransporter 2 (SGLT-2) inhibitors were excluded from this study.

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Effects of Early Sport Specialization on Quality of Life

The Association of Sport Specialization and Concussion History on Self-Reported Depressive Symptoms and Quality of Life Among High School Athletes

Chou TY, Biese K, Leung W, Bell D, Kaminski T, McGuine T. The Association of Sport Specialization and Concussion History on Self-Reported Depressive Symptoms and Quality of Life Among High School Athletes. *Clin J Sport Med*. 2023;33(2):139-144. doi:10.1097/JSM.0000000000001092

KEY TAKEAWAY: Early sports specialization may increase depressive symptoms and decrease quality of life compared to multisport adolescent athletes. A subset of single-sport athletes may require increased surveillance of depressive symptoms.

STUDY DESIGN: Cross-sectional study

LEVEL OF EVIDENCE: STEP 3

BRIEF BACKGROUND INFORMATION: Although sports are generally beneficial for most adolescents, early sport specialization continues to be an area of concern. Despite evidence indicating early specialization contributes to overuse injury, burnout, and decreased quality of life, more students are becoming sport-specialized at a younger age.

PATIENTS: High school student-athletes

INTERVENTION: Early sport specialization or history of concussion

CONTROL: Multisport athletes or no history of concussion

PRIMARY OUTCOME: Depressive symptoms, health-related quality of life

METHODS (BRIEF DESCRIPTION):

- Interscholastic high school students across 31 Wisconsin high schools were the target population for this study.
- Inclusion criteria: Member of an interscholastic athletics team, be in grade 9–12, and be fully able to participate in their sport on the day of selection.
- Single and multisport athletes were designated by the number of organized sports they reported playing in the past year before filling out the survey.
- Eligible athletes were asked about their demographics including sports participation, number of sport-related concussions, and medical history, and filled out a patient health questionnaire (PHQ-9) and the pediatric quality of life core scale.
- The PHQ-9 is a common screening tool for depression with scores 0–27, a higher score indicating a higher likelihood of depression.
- The pediatric quality of life core scale is a 23-question survey to assess overall health and quality of life. Questions assess physical, emotional, social, and school functioning with a score range of 0–100 with higher scores indicating an overall high quality of life.
- Statistical analysis included utilization of a beta coefficient which is used to show the correlation between a continuous variable like PHQ-9 and quality of life scores and a discrete variable like single vs multisport athletes.
    - A positive beta coefficient means an outcome is more likely to happen with the predictor variable while a negative beta coefficient means an outcome is less likely to happen with the predictor variable.

INTERVENTION (# IN THE GROUP): 1,395

COMPARISON (# IN THE GROUP): 1,058

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- Single-sport athletes reported more depressive symptoms than multisport athletes (odds ratio [OR] 1.5; 95% CI, 1.1–2.0).
- Single-sport athletes reported a lower quality of life than multisport athletes (β=–0.056, *P*=.012).
- Previous concussions did not have a significant correlation with depressive symptoms and quality of life (OR 1.17; 95% CI, 0.69–2.1; *P*=.55 and *P*>.05).
- Sport specialization of choice and concussion did not have a statistically significant correlation between depressive symptoms and quality of life scores (OR 0.94; 95% CI, 0.49–1.84; *P*=.87 and *P*>.05).

LIMITATIONS:

- This study was limited by recall bias and did not account for the effect of non-sport extracurricular activities on mental health.

- Schools without an onsite athletic trainer were not studied.
- Schools outside of Wisconsin were not included which may have a geographic bias.

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Ablation and Heart Break

Atrial Fibrillation Catheter Ablation vs Medical Therapy and Psychological Distress: A Randomized Clinical Trial

Al-Kaisey AM, Parameswaran R, Bryant C, et al. Atrial Fibrillation Catheter Ablation vs Medical Therapy and Psychological Distress: A Randomized Clinical Trial. *JAMA*. 2023;330(10):925-933. doi:10.1001/jama.2023.14685

KEY TAKEAWAY: Among patients with atrial fibrillation, catheter ablation improved anxiety and depression more than medical therapy alone.

STUDY DESIGN: Multicenter, randomized, investigator-initiated trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to unblinded design)

BRIEF BACKGROUND INFORMATION: Prior studies that have investigated the relationship between atrial fibrillation and mental health demonstrated the superiority of catheter ablation compared to medical therapy in relieving the physical symptoms of atrial fibrillation. Previous studies have also looked at the positive impact of catheter ablation on psychological distress such as anxiety and depression. This study set out to investigate the effect of catheter ablation on markers of psychological distress.

PATIENTS: Adults with atrial fibrillation

INTERVENTION: Catheter ablation

CONTROL: Medical therapy

PRIMARY OUTCOME: Anxiety and depression

Secondary Outcome: Severe distress, individual anxiety, depression scores, atrial fibrillation symptoms/reccurence

METHODS (BRIEF DESCRIPTION):

- Patients 18–80 years old were recruited from two specialty atrial fibrillation centers in Australia.
- Patient demographics:
  - The mean age of participants was 59 years old.
  - 32% identified as women.
  - 49% had persistent atrial fibrillation.
  - 53% of the ablation group had hypertension vs 55% in the medical group.
  - 27% of the ablation group had vascular disease vs 15% in the medical group.
- Patients diagnosed with paroxysmal or persistent atrial fibrillation, who failed one antiarrhythmic drug, and were eligible for treatment with two drugs were included in this study.
- Patients were excluded if they received treatment for severe depression, had severe valvular disease, or had contraindications to systemic anticoagulation.
- The treatment group received catheter ablation within one month of randomization.
- The comparison group received optimization for the antiarrhythmic drug to maintain sinus rhythm. If failed, then tried a second antiarrhythmic drug.
- Primary outcomes were measured via the Hospital Anxiety and Depression Scale (HADS) using a scale of 0–42, with scores ≥7 suggesting the presence of depression (minimum clinically important difference of 1.7) at baseline, three, six, nine, and 12 months.
- Secondary outcomes included:
  - Severe depression measured as HADS ≥15.
  - Anxiety and depression were individually scored using HADS (0–21 with a score ≥7 indicative of symptoms).
  - Symptoms of atrial fibrillation via Atrial Fibrillation Symptom Severity Score (AFSSS) on a scale of 0–35, a higher score indicating more severe physical symptoms.
  - Atrial fibrillation recurrence identified by atrial fibrillation and duration via recording device or Holter monitor.

INTERVENTION (# IN THE GROUP): 49

COMPARISON (# IN THE GROUP): 47

FOLLOW-UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- Patients who received catheter ablation had decreased rates of anxiety and depression symptoms compared to placebo at 12 months (between-group difference –4.2; 95% CI, –7.04 to –1.3).

Secondary Outcome –

- Severe distress was lower in the ablation group compared to the medical group at 12 months (10.2% vs 31.9%, respectively; *P*=.01).

- Anxiety was lower in the ablation group compared to the medical group at 12 months (4.5 vs 6.6, respectively; *P*=.01).
- Depression was lower in the ablation group compared to the medical group at 12 months (3.1 vs 5.2, respectively; *P*=.004).
- Atrial fibrillation symptoms were lower in the ablation group compared to the medical group at 12 months (7.7 vs 12, respectively; *P*=.004).
- Atrial fibrillation recurrence was lower in the ablation group compared to the medical group at 12 months (47% vs 96%, respectively; *p*<.001).

LIMITATIONS:

- There were more patients with stroke, persistent atrial fibrillation, and heart failure in the ablation group compared to the medical group.
- Participants were not blinded to assignment and no sham procedure was conducted, raising concern for possible placebo effect.
- There was a limited sample size and recruiting participants from a larger multicenter would improve the power of the study.

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