GOOD EVIDENCE MATTERS

GEMs of the Week

SPOTLIGHT

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A Spoonful of TXA Keeps the Hemorrhage Away

Meta-Analysis: The Prophylactic Use of Tranexamic Acid to Reduce Blood Loss During Caesarean Delivery

Guinness F, Hanley C, Spring A. Meta-analysis: the prophylactic use of tranexamic acid to reduce blood loss during caesarean delivery. *Ir J Med Sci*. 2025;194(1):311-322. doi:10.1007/s11845-024-03834-y

KEY TAKEAWAY: Prophylactic tranexamic acid (TXA) at time of cesarean section reduces the likelihood of postpartum hemorrhage (PPH). The risk reduction was greatest in patients at high risk of hemorrhage (NNT=14).

STUDY DESIGN: Systematic review and meta-analysis of 61 randomized studies (N=25,098)

LEVEL OF EVIDENCE: STEP 2 (downgraded due to high heterogeneity of included studies)

BRIEF BACKGROUND INFORMATION: PPH has major impacts on maternal morbidity and mortality. Decreasing significant PPH, particularly in high-risk patients, decreases morbidity and mortality. Though the antifibrinolytic drug TXA has become standard for treatment of PPH, the optimal use of TXA for prophylaxis at time of cesarean delivery has been unclear. This information will be of benefit to family physicians who perform cesarean sections and those who provide prenatal care.

PATIENTS: Pregnant women undergoing cesarean section

INTERVENTION: Prophylactic TXA

CONTROL: No intervention or placebo

PRIMARY OUTCOME: PPH >1 L

Secondary Outcome: Estimated mean blood loss, blood transfusion, drop in hemoglobin, need for additional uterotonics or surgical intervention

METHODS (BRIEF DESCRIPTION):

- Included studies evaluated women undergoing elective or urgent/emergent cesarean delivery that must be published, randomized trials.
- Studies with and without placebo were included and required that both groups received standard prophylactic uterotonic at time of delivery.
- Studies were assessed for risk of bias using the Cochrane Collaboration's risk of bias tool, and 37 studies (26% of included patients) were at high risk of bias in ≥1 domains. 12 studies (68% of included patients) were at low risk of bias across all domains.
- Studies were identified using an online systematic review management program and selected by two independent reviewers.
- Intervention studied was administration of prophylactic intravenous TXA (95% of patients received 1 g and 5% received 10 mg/kg) given prior to (within 30 minutes) or during cesarean section within three minutes after delivery, compared with placebo or no intervention.
- The primary outcome was PPH >1 L measured via quantitative blood loss calculation.
- The secondary outcomes measured estimated blood loss, blood transfusion within 48 hours, drop in hemoglobin within 48 hours, need for additional uterotonics, need for additional interventions such as Bakri, B-lynch, hysterectomy or embolization.

INTERVENTION (# IN THE GROUP): 12,446

COMPARISON (# IN THE GROUP): 12,472

FOLLOW-UP PERIOD: Varied (usually 48 hours or until hospital discharge)

RESULTS:

Primary Outcome –

- Prophylactic TXA reduced the risk of PPH >1 L compared to placebo or usual care (24 studies, n=19,949; relative risk [RR] 0.47; 95% CI, 0.38–0.59; NNT=14; I^2=67%).
- In high-risk patients, TXA reduces the risk of PPH >1 L compared to placebo or usual care (RR 0.3; 95% CI, 0.21–0.41).

Secondary Outcome –

- Prophylactic TXA decreased cumulative mean blood loss compared to placebo or usual care (mean difference [MD] 186 mL; 95% CI, 159–213).
- Prophylactic TXA reduced likelihood of requiring a blood transfusion compared to placebo or usual care (30 studies, n=20,207; RR 0.42; 95% CI, 0.39–0.57).
- Prophylactic TXA decreased the need for additional uterotonics compared to placebo or usual care (28 studies, n=20,159; RR 0.47; 95% CI, 0.39–0.57).
- Prophylactic TXA decreased the need for additional surgical measures to control bleeding compared to placebo or usual care (8 studies, n=16,430; RR 0.54; 95% CI, 0.30–0.95).

LIMITATIONS:

- High heterogeneity due to differing practice and surgical expertise
- Limited time window, unable to evaluate risk for post hospital complications
- Variable risk in recruited patients across the studies
- 37 of the included studies were considered at high risk of bias.
- Limited data on adverse effects was included in the studies
- 57 of the 61 included trials were conducted in emerging or developing countries, which may limit application of results in developed countries

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From Sugar to Steatosis: Can Beinaglutide Break the Link?

Efficacy of Beinaglutide in the Treatment of Hepatic Steatosis in Type 2 Diabetes Patients with Nonalcoholic Fatty Liver Disease: A Randomized, Open-Label, Controlled Trial

Fan Y, Xia M, Yan H, Li X, Chang X. Efficacy of beinaglutide in the treatment of hepatic steatosis in type 2 diabetes patients with nonalcoholic fatty liver disease: A randomized, open-label, controlled trial. *Diabetes Obes Metab*. 2024;26(2):772-776. doi:10.1111/dom.15359

KEY TAKEAWAY: Beinaglutide is an effective treatment for nonalcoholic fatty liver disease (NAFLD) in patients with type 2 diabetes (T2DM); however, this change appears to be primarily mediated by weight loss.

STUDY DESIGN: Open label (non-blinded) randomized controlled trial (RCT)

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

BRIEF BACKGROUND INFORMATION: NAFLD is the leading cause of liver cirrhosis and hepatocellular carcinoma. This is the first open-label RCT to evaluate the efficacy of beinaglutide, a recombinant human glucagon-like petide-1 receptor agonist (GLP-1 RA), for the treatment for NAFLD in patients with T2DM.

PATIENTS: Adults with T2DM and NAFLD

INTERVENTION: Beinaglutide

CONTROL: Lifestyle interventions

PRIMARY OUTCOME: Intrahepatic triglyceride (IHTG) levels

Secondary Outcome: Liver stiffness, weight, waist circumference, glycemic control, lipids

METHODS (BRIEF DESCRIPTION):

- The study was an open-label RCT of Chinese adults ≥18 years old and included adults with T2DM and magnetic resonance spectroscopy (MRS)-confirmed NAFLD defined as IHTG content >15% within one month of screening on MRS.
- Patients were randomized in a 1:1 ratio to receive beinaglutide 0.1 mg three times daily injections or lifestyle interventions for 24 weeks.
- The lifestyle intervention group followed recommendations based on the 2018 American Diabetes Association Standards of Medical Care, including diet and physical activity guidance.
- The primary outcomes measured IHTG using proton MRS (H-MRS) and FibroScan.
  - FibroScan defined improvement in overall liver stiffness as an improvement in at least one liver stiffness stage.
- Secondary outcomes included changes in body weight (kg), waist circumference (cm), glycemic control, blood lipids, and serum liver enzymes from baseline to week 24 of the intervention.

INTERVENTION (# IN THE GROUP): 25

COMPARISON (# IN THE GROUP): 25

FOLLOW-UP PERIOD: 24 weeks of intervention with a telephone visit on week 28

RESULTS:

Primary Outcome –

- Participants in the beinaglutide group achieved a >50% reduction in IHTG compared to lifestyle interventions (unadjusted odds ratio [uOR] 4.4; 95% CI, 1.1–17).
  - After adjusting for weight change, this difference was no longer statistically significant (adjusted OR 3.7; 95% CI, 0.87–16).

Secondary Outcome –

- Beinaglutide increased weight loss compared to lifestyle interventions (−5.5 vs −1.5 kg; *P*=.008)
- Beinaglutide reduced waist circumference compared to lifestyle interventions (−6.0 vs. 0.0 cm; *P*=.018).
- Clinically meaningful weight loss occurred more frequently in the beinaglutide group compared to lifestyle interventions:
  - >5% weight loss (60% vs 21%; *P*=.005)
  - >10% weight loss (28% vs 4.2%; *P*=.024)
- Beinaglutide did not significantly improve fasting plasma glucose, post-prandial glucose, HbA1c levels, liver enzymes, or cholesterol compared with lifestyle intervention.
- Participants in the beinaglutide group had lower serum triglycerides compared to the lifestyle intervention group (2.0 mmol/L vs 1.4 mmol/L; *p*=.023).

LIMITATIONS:

- This study was open label, meaning that both participants and researchers were aware of the treatment interventions, which may introduce bias.
- The methods of assessing the primary outcomes were noninvasive measures, which could affect validity and reliability of the results.
- The sample size was relatively small, and the intervention period was short (24 weeks), which may limit the generalizability of the findings.
- The study population was limited to individuals in China, which may restrict the applicability of the findings to other populations.

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Home Oxygen Matters: Long Term Oxygen Therapy Reduces COPD Exacerbations and Hospitalizations

Effects of Long-term Oxygen Therapy on Acute Exacerbation and Hospital Burden: The National DISCOVERY Study

Khor YH, Palm A, Wong AW, et al. Effects of Long-term Oxygen Therapy on Acute Exacerbation and Hospital Burden: The National DISCOVERY Study. *Thorax*. 2025;80(6):378-384. Published 2025 May 20. doi:10.1136/thorax-2023-221063

KEY TAKEAWAY: Long-term oxygen therapy (LTOT) reduces the rate of acute exacerbations in patients with chronic obstructive pulmonary disease (COPD), but not for interstitial lung disease (ILD) and pulmonary hypertension (PH).

STUDY DESIGN: Longitudinal cohort study

LEVEL OF EVIDENCE: STEP 4 (downgraded due to self-controlled study design)

BRIEF BACKGROUND INFORMATION: LTOT reduces mortality in COPD patients with severe hypoxemia, but it is unknown if LTOT has any effect on frequency of exacerbations in patients with COPD, ILD or PH. This study sought to evaluate the effect of LTOT on the frequency of exacerbations and outpatient visits in patients with COPD, ILD, and PH.

PATIENTS: Adults ≥18 years with COPD, ILD, or PH treated with LTOT

INTERVENTION: LTOT

CONTROL: No LTOT

PRIMARY OUTCOME: Total acute exacerbations, hospitalizations, and length of stay of hospitalizations due to exacerbations

Secondary Outcome: Hospitalizations for all causes, length of stay (LOS), outpatient visits

METHODS (BRIEF DESCRIPTION):

- Patients were selected through Swedish National Registries and the study included Swedish adults (≥18 years old) with COPD, ILD, or PH who were started on LTOT between 2000–2018.
- Patients were evaluated the year prior to starting LTOT and up to 12 months after LTOT was started.
- If follow up was <12 months, data was annualized.
- Hospitalized acute exacerbations, all cause hospitalizations and LOS were determined using ICD codes from the Swedish National Patient Registry.
- Outpatient exacerbations were determined based on medication changes recorded in National Prescribed Drugs Registry.
- COPD and ILD exacerbations were determined based on new prescriptions for or an increased in the dosage of maintenance oral corticosteroid.
- PH exacerbations were determined based on increased dosing of diuretics.

INTERVENTION (# IN THE GROUP): 13,491

COMPARISON (# IN THE GROUP): 13,491

FOLLOW-UP PERIOD:

- COPD: Median 1.8 years
- ILD: Median 1.1 years
- PH: Median 1.3 years

RESULTS:

Primary Outcome –

- For patients with COPD, LTOT decreased the incidence of:
  - Total acute exacerbations (incidence rate ratio [IRR] 0.78; $p<.001$).
  - Hospitalized acute exacerbations (IRR 0.75; $p<.001$).
  - Length of hospital stay for acute exacerbations (IRR 0.63; $p<.001$).
- For patients with ILD, LTOT increased the incidence of:
  - Total acute exacerbations (IRR 1.3; $p<.001$).
  - Hospitalized acute exacerbations (IRR 1.2; $p<.001$).
  - For patients with ILD, LTOT did not significantly affect the length of hospital stay for acute exacerbations (IRR 1.1; $p=.30$).
- For patients with PH, LTOT increased the incidence of:
  - Total acute exacerbations (IRR 1.3; $p<.001$).
  - Hospitalized acute exacerbations (IRR 1.2; $p<.003$).
- For patients with PH, LTOT did not significantly affect the length of hospital stay for acute exacerbations (IRR 0.88; $p=.20$).

Secondary Outcome –

- For patients with COPD, LTOT decreased the incidence of:
  - All cause hospitalizations (IRR 0.84; $p<.001$).

- LOS (IRR 0.69; $p<.001$).
- For patients with COPD, LTOT increased the incidence of outpatient clinic visits (IRR 1.1; $p<.001$).
- For patients with ILD, LTOT increased the incidence of:
  - All cause hospitalizations (IRR 1.3; $p<.001$).
  - LOS (IRR 1.2; $p<.03$).
  - Outpatient clinic visits (IRR 1.1; $p<.001$).
- For patients with PH, LTOT increased the incidence of:
  - All cause hospitalizations (IRR 1.2; $p<.001$).
  - Outpatient clinic visits (1.3; $p<.001$).
- For patients with PH, LTOT did not significantly affect LOS.

LIMITATIONS:

- Definitions for non-hospitalized and hospitalized acute exacerbations were based on medication prescription records and ICD codes, respectively, which can cause diagnostic inaccuracy with either underestimation or overestimation due to misattribution of medication indication or hospital diagnosis.
- Annualized rates of events of interest were calculated and estimated for patients with a follow-up duration of less than 12 months. This includes patients lost due to discontinuation of LTOT and death.
- Patients with ILD and PH had decreased follow-up durations due to increased attrition. This increased attrition could influence exacerbation rate and all-cause hospitalizations.
- The DISCOVERY cohort does not measure adherence to LTOT therapy.
- The study is vulnerable to time-variant confounders. Patients in this study are used as their own control group, comparing events from the previous year to events one year after initiation of LTOT. This is due to the ethical implications of not prescribing LTOT to patients who meet prescribing requirements for LTOT.
- This study performed many sub analyses, which will inflate the number of false positives.

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