GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

Volume 1 - Issue 17

FPIN
Family Physicians Inquiries Network

What's in this week's issue?

Week of April 26 - 30, 2021

SPOTLIGHT: Digoxin and Bisoprolol have similar patient reported quality of life for rate control in atrial fibrillation

Digoxin and Bisoprolol have similar patient reported quality of life for rate control in atrial fibrillation

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Effect of Digoxin vs Bisoprolol for Heart Rate Control in Atrial Fibrillation on Patient-Reported Quality of Life

Kotecha D, Bunting KV, Gill SK, et al. Effect of Digoxin vs Bisoprolol for Heart Rate Control in Atrial Fibrillation on Patient-Reported Quality of Life: The RATE-AF Randomized Clinical Trial. *JAMA*. 2020; 324(24):2497–2508. doi:10.1001/jama.2020.23138

KEY TAKEAWAY: Digoxin and bisoprolol have equivalent clinical outcomes for atrial fibrillation (AF). Bisoprolol has a slight, but significant advantage for vitality compared to digoxin, while digoxin has a lower risk of adverse events (AEs) compared to bisoprolol.

STUDY DESIGN: Multisite, open label, blinded end-point RCT

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Heart failure patients with AF are usually rate controlled with digoxin, a beta-blocker, or a combination of the two. However, there is minimal high quality evidence to support clinical decision making for rate control in AF for cardiac function or the impact on patient reported quality of life (PRQOL).

PATIENTS: Elderly patients with permanent AF

INTERVENTION: Bisoprolol

CONTROL: Digoxin

OUTCOME: PRQOL

Secondary: Quality of Life (QOL), symptoms, cardiac function, unblended NYHA classification, 6-minute walk distance, heart rate and 24 hour ambulatory echocardiogram

METHODS (BRIEF DESCRIPTION):

- Patient Information:
  - Inclusion Criteria: >60 years old, permanent AF in need of rate control, breathlessness NYHA ≥ class II
  - Exclusion: Indication for bisoprolol (i.e. recent MI), contraindication to bisoprolol or digoxin, baseline bradycardia, base line second- or third-degree heart block myocarditis, pericarditis, hypertrophic cardiomyopathy, planning heart transplant, pacemaker dependency, terminal illness, recent major surgery
- Patients were randomized to one of two groups:
  - Bisoprolol: 1.3–15 mg/d (mean 3.2 mg/d)
  - Digoxin: 63–250 mcg/d (mean 161 mcg/d)
- Outcome measurements:
  - Quality of life: patient reported SF-36 domains, analyzing health and wellbeing at 6 and 12 months (0–100; high scores were more favorable)
  - Symptoms: modified EHRA functional classification scores measuring impact of AF on QOL at 6 and 12 months (range 1–4, 1=no impact, 4=severely disabling)
  - Cardiac function: NT-proBNP levels
  - Cardiac function: blinded echocardiogram at 12 months

INTERVENTION (# IN THE GROUP): 80

COMPARISON (# IN THE GROUP): 80

FOLLOW UP PERIOD: 12 months

RESULTS:

Primary Outcome: Bisoprolol and digoxin had similar effects on PRQOL at 6 months (adjusted mean difference [AMD] 2.4; 95% CI, 1.1 to 3.8)

Secondary Outcomes:

- At 12 months, patients taking bisoprolol compared to those taking digoxin reported significantly better scores for QOL using SF-36 domains:
  - Vitality (AMD 3.9; 95% CI, 0.8 to 7)
  - General health (AMD 2.8; 95% CI, 0 to 5.6)
  - Physical functioning (AMD 3.4; 95% CI, 0 to 6.9)
- Patients taking digoxin fared significantly better than those taking bisoprolol in the following areas:
  - Improved symptoms indicated by at least a 2 class improvement in EHRA classification score (adjusted odds ratio 10.3; 95% CI, 4.0–27)
  - Adverse events (25% vs 64% ≥1 AE; X2=24.91; *P*<.001)
- At 12 months, bisoprolol and digoxin had similar effects in systolic and diastolic function.

LIMITATIONS:

- Open label study design (though blinded endpoints helped mitigate bias)
- Not enough power to compare major cardiovascular events
- Study does not apply to patients with severely reduced LVEF

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Intrapartum Oxygen Administration for Category II Fetal Monitoring Patterns, Is it Helping?

The effect of intrapartum oxygen supplementation on category II fetal monitoring

Raghuraman N, López JD, Carter EB, et al. The effect of intrapartum oxygen supplementation on category II fetal monitoring. *Am J Obstet Gynecol.* 2020; 223(6):905.e1–7.

KEY TAKEAWAY: Intrapartum oxygen (O_2) administration for category II electronic fetal monitoring (EFM) patterns does not improve high-risk category II EFM features, eliminate recurrent decelerations, or hasten the resolution of recurrent decelerations.

STUDY DESIGN: Secondary analysis of a randomized noninferiority clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Maternal O_2 supplementation is one of the most commonly used techniques for intrauterine resuscitation. Studies suggesting that maternal hyperoxia improved fetal oxygenation and alleviated fetal heart rate decelerations were published over 40 years ago. These studies did not compare O_2 administration to room air and were published when there was no standardized EFM nomenclature. Given literature reporting harm associated with hyperoxygenation (associated with increases in systemic vascular resistance in pregnant patients and higher rates of respiratory morbidity amongst neonates), it is imperative that this technique be investigated.

PATIENTS: Pregnant patients at ≥37 weeks gestation, with category II EFM patterns

INTERVENTION: 10 L/min of oxygen via face mask

CONTROL: Room air (RA)

OUTCOME: composite of high-risk category II features (recurrent variable decelerations, recurrent late decelerations, prolonged decelerations, tachycardia, or minimal variability) 60 minutes after randomization

Secondary: individual components of the composite high-risk category II features, resolution of recurrent decelerations within 60 minutes of randomization, and total deceleration area (TDA – sum of the area within all decelerations)

METHODS (BRIEF DESCRIPTION):

- Patients at ≥37 weeks gestation admitted for spontaneous or induction of labor were enrolled.
- Randomization to 10 L/min of oxygen via face mask or RA if at any point in the active phase labor (≥6 cm dilated) when a category II pattern was identified necessitating any form of intrauterine resuscitation.

INTERVENTION (# IN THE GROUP): 57

COMPARISON (# IN THE GROUP): 57

FOLLOW UP PERIOD: There was no follow up.

RESULTS:

Primary Outcome

- Similar rate of high-risk category II features between the O_2 and the RA groups (42.1% vs 47.4%; RR 0.9; 95% CI, 0.6–1.3)

Secondary Outcomes

- No difference in the individual high-risk category II features noted between the groups or in the resolution of recurrent decelerations.
- O_2 administration did not decrease time to resolution of recurrent decelerations or improve the TDA.
- Most recurrent decelerations resolved without supplemental O_2.

These results suggest that intrapartum O_2 supplementation does not improve high-risk category II EFM features and its liberal use for intrapartum resuscitation should be reevaluated.

LIMITATIONS:

- The sample size was small.
- Data was only collected for 60 minutes after the intervention.

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Is laughter the best medicine?

Feasibility of a group-based laughter yoga intervention as an adjunctive treatment for residual symptoms of depression, anxiety and stress in people with depression

Bressington D, Mui J, Yu C, et al. Feasibility of a group-based laughter yoga intervention as an adjunctive treatment for residual symptoms of depression, anxiety and stress in people with depression. *J Affect Disord*. 2019; 248:42–51.

KEY TAKEAWAY: Laughter yoga improves depressive symptoms and quality of life immediately after 4 weeks of biweekly sessions. There is no difference between laughter yoga and usual care after 3 months. Laughter yoga has no effect on anxiety, stress, or physical health.

STUDY DESIGN: Single site, non-blinded parallel-group randomized control trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Depression is a common mental health disorder affecting about 350 million people worldwide. Multiple therapies for depression and anxiety exist, with first-line antidepressant drugs only leading to remission in 1 in 3 patients. This has attracted the use of adjunctive therapies including exercise, light therapy, mindfulness-based meditation, omega-3 fatty acids, and yoga.

PATIENTS: Community dwelling people diagnosed with depressive disorder

INTERVENTION: Laughter yoga + usual depression treatment

CONTROL: Usual depression treatment

OUTCOME: Depression, anxiety, and stress scores per the DASS21

METHODS (BRIEF DESCRIPTION):

- Patients were selected from community-dwelling people
  - Inclusion criteria: depressive disorder diagnosis with baseline residual depressive, anxiety, or stress symptoms, ages 18–60, able to attend yoga sessions, no plans to change medication regimen
  - Exclusion criteria: history of bipolar disorder or schizophrenia, confounding comorbid conditions, or current use of alternate active therapies
- Participants were randomly assigned to Laughter Yoga (LY) vs. Treatment as Usual (TAU)
  - Laughter Yoga (LY) is a group-based intervention involving simulated laughter, gentle stretching, rhythmic breathing and meditation.
  - The intervention group completed 4 weeks of biweekly laughter yoga sessions
- Participants completed surveys at baseline (T0), post-intervention (T1), and at 3 months follow-up (T2)
  - The DASS is the Depression Anxiety Stress Scale (DASS–21) with 21 items scored 0–3 with higher scores indicating more severe levels of distress.
  - The Short Form 12 item (version 2) Health Survey (SF12v2) measured patients' physical and mental quality of life with higher scores indicating better quality of life.
  - The intervention group completed Client Satisfaction Questionnaire (CSQ8) at T1 measuring satisfaction with scores ranging from 8–32 and higher scores indicating higher satisfaction

INTERVENTION (# IN THE GROUP): 23

COMPARISON (# IN THE GROUP): 27

FOLLOW UP PERIOD: 3 months

RESULTS:

- The Laughter Yoga group experienced a **5.1 times greater decrease** in depression compared the control group after 4 weeks of biweekly sessions (beta coefficient [B] =–5.1; 95% CI, –9.5 to –0.72).
- The Laughter Yoga group experienced a **4.4 times greater improvement** in mental health related quality of life compared to the control group after 4 weeks of biweekly sessions (B=4.386; 95% CI, 0.34–8.4).
- At 3 months follow up there was no statistically significant difference in depression or mental health related quality of life.
- The laughter yoga and usual care group never experienced differences in anxiety, stress, or physical health.

LIMITATIONS:

- No blinding
- Self-reported data
- Reliance on community diagnoses of psychiatric disorders to assess eligibility (rather than diagnostic interview)

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