GEMs
GOOD EVIDENCE MATTERS

GEMs of the Week

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FPIN
Family Physicians Inquiries Network

What's in this week's issue?

Week of May 10 - 14, 2021

SPOTLIGHT: New Monthly Injection for HIV Maintenance Treatment

- Antihypertensive Medication Reduction vs Usual Care on Patients Aged 80 Years and Older

New Monthly Injection for HIV Maintenance Treatment

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Long Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression

Swindells S, Andrade-Villanueva JF, Richmond GJ, et al. Long-Acting Cabotegravir and Rilpivirine for Maintenance of HIV-1 Suppression: A Randomized Controlled Trial. *N Engl J Med*. 2020; 382:1112–23.

KEY TAKEAWAY: Standard oral therapy and long-acting monthly injections of cabotegravir and rilpivirine are noninferior treatment options for maintenance of HIV. Participants preferred the injections but reported more adverse events.

STUDY DESIGN: Multicenter, parallel-group, open-label RCT

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Oral maintenance therapies have been the standard HIV treatment. New monthly injections aim to provide simplified treatment with increased compliance and satisfaction.

PATIENTS: Patients with HIV-1

INTERVENTION: Cabotegravir/rilpivirine IM

CONTROL: Standard once-daily oral HIV-1 medcations

OUTCOME: Plasma HIV-1 RNA levels, virologic failure and resistance, CD4 counts, and adverse events

METHODS (BRIEF DESCRIPTION):

- Patient population: 33% female, 32% nonwhite, average age 42 years old, 74% had CD4 counts >500
- Inclusion Criteria: >18 years old that have been on antiretroviral drug regimen without changing meds for the last 6 months, HIV-1 RNA level <50 copies at randomization, as well as 6–12 months before the start of screening
- Exclusion Criteria: Active hepatitis B infection; virologic failure; INSTI or NNRTI resistance mutations; antiretroviral regimen interruptions within 6 months of screening; lapse in therapy >1 month at any time; patients taking abacavir, dolutegravir, or lamivudine
- Treatment arm: 30 mg of oral cabotegravir and 25 mg of oral rilpivirine once daily for 1 month, then received 900 mg rilpivirine / 600 mg cabotegravir IM once, and finally received 600 mg rilpivirine / 400 mg cabotegravir IM every 4 weeks

INTERVENTION (# IN THE GROUP): 308

COMPARISON (# IN THE GROUP): 308

FOLLOW UP PERIOD: 52 weeks

RESULTS:

Those receiving monthly injections had no statistically significant differences in plasma RNA levels at 48 weeks compared to the oral-therapy group:

- 1.6% injectable group vs 1.0% oral-therapy group had plasma RNA levels >50 copies per millimeter (adjusted difference 0.6%; 95% CI, –1.2 to 2.5)
- 92.5% injectable group vs 95.5% oral-therapy group had HIV RNA levels <50 copies per millimeter (adjusted difference –3%; 95% CI, –6.7 to 0.7)

Adverse Events:

- Participants receiving monthly injections were more likely to experience mild or moderate (grade 1–2) adverse events compared to the oral therapy group (29% vs 3%; no p-value provided)
- Adverse events in the monthly injections group:
  - Injection site reaction pain (75%)
  - Nodules (12%)
  - Induration (10%)
  - Swelling (7%)
  - 4% withdrew from the study as a result of injection site reactions
  - No life-threatening reactions reported in this group

Monthly injections compared to oral-therapy had a similar rate of virologic failure (3 participants vs 4 participants respectively).

86% of the long-acting therapy group reporting preferring monthly injectable treatment to their previous daily oral therapies.

LIMITATIONS:

- The results are not applicable to all individuals living with HIV, as the study only enrolled stable, adherent HIV-1 patients with no history of treatment failure
- No placebo injections or medications were used to compare injection site-reactions or medication compliance

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Antihypertensive Medication Reduction vs Usual Care on Patients Aged 80 Years and Older

Effect of Antihypertensive Medication Reduction vs Usual Care on Short-term Blood Pressure Control in Patients with Hypertension Aged 80 Years and Older

Sheppard JP, Burt J, Lown M, et al. Effect of Antihypertensive Medication Reduction vs Usual Care on Short-term Blood Pressure Control in Patients With Hypertension Aged 80 Years and Older: The OPTIMISE Randomized Clinical Trial. *JAMA*. 2020; 323(20):2039–2051.

KEY TAKEAWAY: Among frail older patients taking multiple antihypertensive medications, reduction of medication does not lead to significant elevation in blood pressure and is noninferior to usual care in short-term blood pressure control.

STUDY DESIGN: Randomized, unblended, parallel group, noninferiority design

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: For frail older patients treated with multiple antihypertensive medications, current deprescribing guidance lacks evidence and is largely based on expert opinion. This randomized clinical trial aims to evaluate a short-term strategy that can safely and effectively guide providers in reducing antihypertensive medication.

PATIENTS: Elderly patients taking >2 antihypertensive medications

INTERVENTION: Medication reduction strategy

CONTROL: Usual care

OUTCOME: SBP maintained <150 mmHg

Secondary: frailty, quality of life, serious adverse events, changes in systolic and diastolic blood pressures

METHODS (BRIEF DESCRIPTION):

- Patients were selected from 69 primary care clinics in Britain
    - Inclusion criteria: >80 years old, taking >2 antihypertensive medications for >12 months, baseline SBP <150 mmHg
- Patients were randomized to strategic or non-strategic medication reduction.
- Treatment Guidelines:
    - Antihypertensive treatment guided by National Institute for Health and Care Excellence (NICE) treatment step (C+A+D): CCB (C), ACEi (A), Thiazide or thiazide like diuretics (D).
    - Contraindicated medication identified using the STOPP criteria were removed.
    - Identify 4th, 3rd or 2nd line of therapies according to the NICE algorithm, remove based on clinical judgment.
- If patients experienced changes in systolic blood pressure their medications were modified:
    - If <150/90 mmHg, continue lowering dose
    - If 150/90–180/110 mmHg, restart original dose
    - If >200/120 or >180/110 mmHg with symptoms, restart original dose and seek expert advice

INTERVENTION (# IN THE GROUP): 282

COMPARISON (# IN THE GROUP): 287

FOLLOW UP PERIOD: 4 and 12 weeks

RESULTS:

Primary Outcome:

- Reducing antihypertensive medication was noninferior to usual care in maintaining SBP <150 mmHg (86% in reduced medication group vs 88% in usual care group; adjusted RR 0.98; meeting the noninferior margin of a RR of 0.9)

Secondary Outcome:

- The SBP and DBP of the medication reduction group were higher at 12 weeks compared to the usual care group after correcting for baseline blood pressure
    - SBP: adjusted mean difference [MD] 3.4 mmHg; 95% CI, 1.0–5.8; PNI=.005
    - DBP: adjusted MD 2.2 mmHg; 95% CI, 0.9–3.6; PNI=.001
- The medication reduction group and the usual care group had no significant difference in the following outcomes:
    - Frailty
    - Quality of life
    - Adverse events

LIMITATIONS:

- Selection bias: physicians selected participants that were likely to benefit from intervention

- The intervention group had 1 more clinic visit than the control group, potentially providing an additional opportunity to detect adverse events
- 13 participants from the control group reduced medication during follow up
- Short follow up period
- Noninferiority margin was based on physician opinion

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