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RESEARCH THAT MATTERS

Safety of Long-Acting Injectable Buprenorphine for Opioid Use Disorder

Authors: Lintzeris et al., 2021
Article: JAMA Network Open

Research Summary

Long-acting injectable buprenorphine (LAIs) has been demonstrated as a safe treatment for opioid use disorder (OUD), with mostly mild side effects. A 2021 randomized clinical trial comparing weekly or monthly depot buprenorphine to daily sublingual buprenorphine found that while LAIs had more adverse drug reactions (ADRs), they significantly improved treatment satisfaction, which may contribute to better long-term adherence and reduced relapse rates.

Study Design:

- **Design:** Open-label, randomized clinical trial
- **Participants:** 119 adults with opioid dependence
- **Intervention:** Weekly or monthly depot buprenorphine vs. daily sublingual buprenorphine
- **Duration:** 24 weeks
- **Setting:** Six outpatient addiction treatment centers in Australia (October 2018–September 2019)
- **Primary Outcome:** Global treatment satisfaction at week 24, assessed by the Treatment Satisfaction Questionnaire for Medication (TSQM)
- **Safety Outcomes:** Monitored ADRs and treatment-emergent adverse events (TEAEs)

Study Findings:

1. Safety Profile:

- Depot buprenorphine group: 65.0% (39 participants) experienced ADRs, mostly mild injection site reactions.
- Sublingual buprenorphine group: 20.3% (12 participants) reported ADRs.
- TEAEs: 90.0% in the depot group vs. 83.1% in the sublingual group, primarily mild injection site reactions.
- Severe TEAEs: 5.0% in the depot group (including one case of suicidal ideation that resolved after dose adjustment); 6.8% in the sublingual group (none drug-related).
- No deaths or withdrawals due to adverse events.

2. Unexpected Detail:

- Despite the higher incidence of ADRs in the depot buprenorphine group, patients reported significantly greater treatment satisfaction (mean TSQM score: 82.6 vs. 72.9 for sublingual). This improvement in satisfaction suggests potential benefits for long-term adherence and relapse prevention.

Additional Safety Evidence from Reviews & FDA Evaluations:

- **2022 Systematic Review:** Long-acting injectable buprenorphine was associated with improved social inclusion and employment outcomes, with no major safety concerns. (ScienceDirect)
- **2023 Systematic Review:** LAIs share systemic adverse effects with oral buprenorphine but may have fewer due to reduced peak-to-trough fluctuations. Caution is advised for patients with respiratory conditions. (PMC)
- **FDA Approval of Brixadi (2024):** Safety data from a randomized, double-blind, active-controlled trial in 428 adults reported common adverse reactions (injection site pain, headache, nausea) occurring in ≥5% of patients, with no life-threatening events. (FDA)

Study Limitation & Future Directions:

Limitations:

- The open-label design may introduce bias, and the study's setting in Australia may limit generalizability

Future Directions:

- Long-term studies beyond 24 weeks are needed to assess sustained efficacy and safety. Studies should also focus on special populations, such as pregnant individuals and those with comorbid conditions.

Clinical Implications of the Research

Clinical Implications for Payers:

- Expanding coverage for LAIs could lead to cost savings by reducing relapse-related healthcare utilization.
- Higher patient satisfaction may contribute to improved adherence and long-term treatment success.

Clinical Implications for Provider Organizations & Health Systems:

- Training programs should be implemented for depot administration, given the mild injection site reactions.
- Health systems should advocate for increased access to LAIs, particularly for populations with poor adherence to daily medications.

Clinical Implications for Clinical Professionals:

- Providers should educate patients on the benefits of LAIs, including convenience and safety, while monitoring for adverse events.
- LAIs should be considered for patients with difficulty adhering to daily buprenorphine.

Clinical Implications for Consumers:

- LAIs provide a stable, long-term treatment option that minimizes the burden of daily medication adherence.
- Patients should discuss with their provider the potential benefits and risks, especially those with conditions like liver disease or pregnancy, where safety data is limited.

Administrative & Business Implications

Administrative Implications for Payers:

- Coverage expansion for LAIs could reduce opioid-related emergency department visits and hospitalizations.
- Value-based reimbursement models should incentivize the use of long-acting formulations.

Administrative Implications for Provider Organizations & Health Systems:

- Tracking patient outcomes related to LAIs can support policy advocacy and quality improvement initiatives.
- Investments in infrastructure and staff training for depot administration are necessary.

Administrative Implications for Clinical Professionals:

- Providers should advocate for improved insurance coverage and patient assistance programs for LAIs.
- Expanding knowledge on LAIs can enhance their integration into standard OUD treatment protocols.

Other Considerations

- **Integration into Broader Treatment Models:** LAIs should be incorporated into comprehensive care plans, including behavioral health and primary care.
- **Quality Metrics & Reporting:** Healthcare systems should track utilization and safety outcomes for LAIs to inform future policies.
- **Patient Engagement & Education:** Increased awareness of LAIs could reduce stigma and improve treatment adherence.

Conclusion

The 2021 randomized clinical trial by Lintzeris et al. provides strong evidence supporting the safety of long-acting injectable buprenorphine, with primarily mild adverse effects and no serious safety concerns leading to withdrawal. This is reinforced by systematic reviews and FDA data. The improved patient satisfaction and potential for better long-term adherence highlight LAIs as a promising treatment option for OUD. Future studies should further explore long-term outcomes, cost-effectiveness, and safety in diverse populations.