

Peer Review

Review of: "L-Type Calcium Channel Blockers, Extrapyramidal Symptoms, and Delirium: A Systematic Review of Case Reports"

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This systematic review examines the potential link between L-type calcium channel blockers (CCBs) and extrapyramidal symptoms (EPS) or delirium. The study systematically analyzes 23 reported cases from published literature, highlighting the demographics, symptom onset, drug interactions, and outcomes. Findings suggest that older patients, particularly females, are more susceptible to EPS, while males are more prone to delirium. Most adverse effects were associated with dihydropyridine-class CCBs, with symptoms typically resolving after drug discontinuation. The study calls for larger prospective studies and randomized controlled trials to confirm these findings.

Positive Comments:

1. The study highlights a possible link between L-type calcium channel blockers (CCBs) and movement disorders, which is relevant for clinicians prescribing antihypertensives.
2. The manuscript clearly states its objective of analyzing CCB-induced extrapyramidal symptoms (EPS) and delirium.
3. The study follows a structured PRISMA approach, ensuring a transparent selection of cases from reputable databases.
4. The manuscript provides in-depth case analyses, including demographics, drug interactions, and outcomes, which enhance its credibility.
5. The PRISMA flowchart and tables summarizing case data improve readability and aid quick interpretation.

6. The study explores plausible biological mechanisms linking CCBs to EPS and delirium, grounding findings in pharmacology.
7. The discussion acknowledges both supportive and conflicting evidence, ensuring an objective analysis.
8. The study suggests that clinicians should be aware of potential neurological side effects in elderly patients on CCBs.
9. The manuscript follows a logical flow, making it easy to follow for both researchers and clinicians.
10. The manuscript declares no conflicts of interest and acknowledges research support, reinforcing its integrity.

Negative Comments:

1. The study includes only 23 cases, limiting its generalizability and making conclusions less robust.
2. Without a control group, it is difficult to determine if CCBs directly cause EPS or delirium or if other factors contribute.
3. Many patients were on multiple medications, making it unclear whether CCBs alone were responsible for the symptoms.
4. The reliance on published case reports introduces bias, as only severe or unusual cases are likely to be reported.
5. EPS and delirium were reported within 1 day to 8.5 years, making it difficult to establish a clear causal relationship.
6. A statistical meta-analysis of case data could have strengthened the conclusions and provided quantitative risk estimates.
7. The study identifies a risk but does not provide specific recommendations for patient monitoring or management.
8. Some references are decades old, raising concerns about whether findings remain relevant given changes in drug formulations and patient care.
9. While mechanisms are discussed, there is no in-vitro or in-vivo data to support the hypothesis that CCBs induce EPS or delirium.

10. The study could discuss other potential causes of EPS/delirium, such as pre-existing neurodegenerative disorders.

Final Decision:

Minor Revisions Required.

While the manuscript is well-structured and provides valuable insights, its conclusions would be stronger with additional discussion on confounding factors, alternative explanations, and potential clinical guidelines. Including a meta-analysis (if possible) would further enhance its impact.

Declarations

Potential competing interests: No potential competing interests to declare.