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Efficacy and Safety of Intravenous Calcium Pretreatment Prior to Nondihydropyridine Calcium Channel Blockers in Atrial Fibrillation or Flutter: A Meta-Analysis

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KEY WORDS Calcium channel blockers; Calcium pretreatment; blood pressure; hypotension; meta-analysis

Background

Intravenous nondihydropyridine calcium channel blockers (CCBs), such as diltiazem and verapamil, are standard agents for acute rate control in atrial fibrillation (AF) and atrial flutter (AFL). However, their use can be limited by drug-induced hypotension. Pretreatment with intravenous calcium has been proposed to attenuate this effect without compromising rate-control efficacy, but evidence remains limited and heterogeneous

Methods

A systematic review and meta-analysis was conducted according to PRISMA guidelines using a PubMed search through December 2024. Of 222 records identified, two reviewers independently screened and extracted data; nine underwent full-text review, and four met inclusion criteria (two RCTs, one prospective comparative study, one multicenter cohort). Five were excluded (abstract-only, commentary, review, and single-arm cohorts).

A total of 521 patients were analyzed—177 received intravenous calcium (chloride, gluconate, or sulfate) prior to a nondihydropyridine CCB (Diltiazem or Verapamil), and 344 received CCB alone. The primary endpoint was change in systolic blood pressure (SBP) and heart rate (HR) after drug administration. Timing of measurement varied—Az (2025) and Miyagawa (1993) assessed outcomes at 15 min, Rossi (2023) at 60 min, while Haft (1986) did not specify timing but measured BP via arterial line monitoring.

Secondary outcomes included bradycardia, nausea, urticaria, flushing, and conversion to normal sinus rhythm (NSR) after calcium alone

Results

Calcium pretreatment was associated with a consistent trend toward smaller SBP reductions in all studies except Rossi et al.; however, pooled estimates were not statistically significant as the 95% credible interval crossed zero (mean difference +10 mm Hg, 95% CrI –1 to +16). The change in HR was nonsignificant across studies, and calcium did not reduce rate-control efficacy, except for a modest attenuation noted in Az et al. (2025).

Adverse events were rare and mild (nausea, flushing, urticaria), and several early-era patients cardioverted to NSR after calcium alone

Conclusions

Intravenous calcium pretreatment prior to nondihydropyridine CCBs appears to lessen CCB-induced hypotension without materially affecting rate-control efficacy. Although findings did not reach statistical significance, the direction of effect was consistent. Limitations include the small number of studies, variation in timing of BP/HR measurement, differences in calcium formulation and dosing, and significant heterogeneity.

Larger randomized trials are warranted to clarify the optimal calcium dose and clinical benefit.Data Availability: All data analysed in this meta-analysis are available in the published source articles cited in the Reference section. No new primary data were generated for this study

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