CONCEPTS IN HYPERTENSION

A Journal Article-Based Approach to Understanding the Clinical Aspects of Hypertension

Volume 3 Issue 4 April 2018

Article of Interest

Faulkner J, et al. The pharmacokinetics of amlodipine in healthy volunteers after single intravenous and oral doses and after 14 repeated oral doses given once daily. British J Clin Pharmacology. 1986. (Click to Access)

Context and Study Objective

Among hospitalized patients, dihydropyridine calcium channel blockers (CCBs) such as extended-release nifedipine and amlodipine are frequently the class of choice as they lack the renal and metabolic considerations attendant to other classes. Yet CCBs are not interchangeable; each possesses distinct attributes. In this article, Faulkner sought to categorize the pharmacologic properties of amlodipine, characteristics which inform its suitability for inpatient medicine.

Design, Setting, and Participants

In a double-blind fashion, 56 healthy men received either amlodipine 15mg or placebo daily for two weeks. Volunteers were admitted to a research ward; capsules were administered under direct supervision at 9 am each day. Blood pressure (BP) was checked twice/day. Blood work was drawn at pre-specified intervals to determine the agent's pharmacokinetic profile.

Results

-Study characteristics: 28 men per arm. Mean age 26; mean weight 68kg. All "healthy." No further baseline characteristics were provided.
-No meaningful changes in BP occurred.
-Time of peak: The time for amlodipine to reach peak plasma concentration was nearly 9 hours.
-Half-life: 35-45 hours were required for the plasma concentration of amlodipine to fall by 50%.
-Steady state: After the seventh dose, the plasma concentration of amlodipine stabilized.
-Trough-to-peak ratio: After a given dose, the lowest and highest plasma concentrations of amlodipine were relatively similar.

Pharmacokinetic Properties of Amlodipine by Day of Administration

	Day 1	Day 14
Time of Peak (hrs)	8.9	8.7
Average Concentration (ng/mL)	4.5	14.5
Half-life (hrs)	36	45

Clinical Perspective

-The above pharmacologic profile allows for an appreciation of the anti-hypertensive characteristics of amlodipine, how it differs from other CCBs, and why it is a poor choice for inpatient therapy.
-Given the 9 hour lag between agent ingestion and peak concentration (time of peak), meaningful declines in BP will not occur for 6-12 hours. Consequently, it should be avoided if BP reduction is sought within hours.
-Since the full anti-hypertensive effect will not be realized for more than a week (the amount of time required to achieve a steady state), dose escalation within 1-2 days of initiating therapy will not hasten BP control but only serve to magnify the risk of hypotension in the following weeks.
-In contrast, amlodipine's long half-life and modest variation in plasma concentration (trough-to-peak ratio) ensure a continuous and uniform anti-hypertensive effect throughout the day. Thus, it is an ideal outpatient therapy.
-Given half-lives of 4-5 hours, isradipine and extended release nifedipine act within 4-6 hours and achieve near full effect within days. In the absence of contraindications, these remain my inpatient agents of choice.
-*N.B.*: While a medication's effect on BP and its time to onset cannot generally be determined from drug concentrations, studies of amlodipine indicate that serum concentrations are a credible indicator of time to anti-hypertensive effect.
-Disclosures: I have no conflicts to declare. My thanks to Sean Kane, Pharm.D. of ClinCalc for this article.