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

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Article of Interest

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 prespecified 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.

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 46 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.

Pharmacokinetic Properties of Amlodipine by Day of Administration

<table>
<thead>
<tr>
<th>Pharmacokinetic Property</th>
<th>Day 1</th>
<th>Day 14</th>
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<tbody>
<tr>
<td>Time of Peak (hrs)</td>
<td>8.9</td>
<td>8.7</td>
</tr>
<tr>
<td>Average Concentration (ng/mL)</td>
<td>4.5</td>
<td>14.5</td>
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<tr>
<td>Half-life (hrs)</td>
<td>36</td>
<td>45</td>
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