

## **Does aspirin use have an increased benefit in patients with ischemic heart disease (IHD) taking angiotensin-converting enzyme (ACE) inhibitors?**

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In theory, based on their mechanisms of action, it has been proposed that concomitant use of aspirin may *interfere* with the efficacy of ACE inhibitors.<sup>1</sup> Angiotensin-converting enzyme inhibitors are thought to be efficacious in treatment of patients with IHD in part due to their effects on kinins. Specifically, ACE inhibitor use is associated with increased kinin levels, which may be mediated by the release of vasodilator prostaglandins. Aspirin is known to inhibit prostaglandin synthesis and therefore thought to interfere with ACE inhibitor efficacy. In fact, a cursory search of several databases for interactions between aspirin and ACE inhibitors (e.g., enalapril), including Micromedex,<sup>2</sup> Clinical Pharmacology,<sup>3</sup> and Facts and Comparisons,<sup>4</sup> corroborates this, classifying the drug interactions as mild<sup>4</sup> to moderate<sup>2,3</sup> in severity, with substantial documentation.

A search of the literature revealed several studies addressing this interaction and possible decrease in ACE inhibitor efficacy. In a review, Park summarizes that the data from these studies are conflicting and there are several limitations to the studies cited.<sup>5</sup> For example, she cites a study in which 18 patients with chronic, stable but severe heart failure with mean left ventricular ejection fraction (LVEF) of 23.9% were given enalapril prior to, concomitantly, or the day after a 350 mg dose of aspirin. The investigators found that co-administration of enalapril on the day of or day after aspirin was associated with a negative hemodynamic effect. Park notes the limited external validity of this study and other similar studies based on their small population, endpoints, and short duration. She includes the results of larger scale trials such as the Studies of Left Ventricular Dysfunction (SOLVD) trials, which demonstrated a reduction in benefit of enalapril among patients taking aspirin (as observed by an absolute decrease in mortality of 9% in patients taking enalapril alone compared to an absolute increase in mortality of 4% in patients taking both enalapril and aspirin<sup>6</sup>), and the Heart Outcomes Prevention Evaluation (HOPE) study, which did not reveal any negative interactions between ramipril and aspirin.<sup>7</sup> She notes that these, too, are limited in their clinical application, the former lacking data on dosage and duration of therapy with aspirin, and the latter excluding patients with reduced systolic function.<sup>5,7</sup> Based on these findings, Park recommends that clinicians take into consideration the severity of heart failure when placing patients with IHD and on an ACE inhibitor on aspirin therapy, stating that the more severe the heart failure, the greater likelihood of an observable interaction between aspirin and ACE inhibitor.<sup>5</sup>

Therefore, although inconclusive, it appears that concomitant use of aspirin with ACE inhibitor therapy may lead to decreased ACE inhibitor efficacy. No studies were found suggesting that the use of aspirin would potentiate the effects of ACE inhibitor therapy in patients with IHD.

### References:

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