Journal of Clinical and Basic Cardiology

An Independent International Scientific Journal

Journal of Clinical and Basic Cardiology 2004; 7 (1-4), 1

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Indexed in
Chemical Abstracts
EMBASE/Excerpta Medica

Krause & Pachernegg GmbH · VERLAG für MEDIZIN und WIRTSCHAFT · A-3003 Gablitz/Austria

Editorial: VALIANT, a Whiter Shade of Pale …

N. Bareza, S. Gasser, W. Klein(†), R. Gasser

Abstract

More and more patients survive myocardial infarction, but one third die within a year after heart attack. Different studies indicated an improvement of prognosis by ACE-inhibitors after myocardial infarction (MI). The VALIANT-study [1] compared the effects of Captopril and the ATII-receptor blocker Valsartan and the combination of both on post-MI patients with decreased systolic function, in view of a more specific and effective blockade of ACE at the receptor level. However, both were of equal effect, also the combination did not improve outcome. There was no marked difference in total mortality and in the combined arm with additional β-blocker treatment, however, hospitalisation rate has been reduced significantly. More adverse effects were found in the captopril-group and even more in the combination-group. Valsartan, hence, constitutes an effective alternative to conventional treatment with ACE-inhibitors. In the light of earlier studies on the effect of ATII-receptors on CHF (c.f. CHARM, ValHEFT) and β-blockade post MI (c.f. ISIS II), VALIANT has brought about interesting results.

Introduction

More and more patients survive myocardial infarction, but prognosis is still not always satisfactory. One third die within a year after heart attack. Studies like SAVE [2], AIRE [3] or TRACE [4] indicated, that ACE-inhibitors improve prognosis of post-infarct patients. ACE-inhibitors led to a 25 % decrease in total mortality, hospitalisation rate and reduced the risk of re-infarction in patients with reduced systolic function. Angiotensin II exerts negative effects upon the cardiovascular system. ACE-inhibitors decrease the concentration of angiotensin II by blocking ACE and thus the Renin-Angiotensin-system. Direct blockade of the Angiotensin II-receptor, on the other hand, is more specific and effective for a number of reasons. The clinical benefit of ATII receptor blockade in the setting of post-MI has not been completely established as yet.

Results

VALIANT compared the effects of captopril with valsartan and the combination of both on post-MI patients with left ventricular systolic dysfunction: Within ten days after acute myocardial infarction, patients were randomly assigned to each treatment group. The patient number was large. The first group (4909 patients) received 160 mg Valsartan bid, the second group (4909 patients) 50 mg Captopril three times a day and the third group (4885 patients) a combination of 50 mg captopril three times a day plus 80 mg Valsartan bid. The dosage used had been derived from SAVE and Val-HeFT [5].

Discussion

The results surprise, since captopril was as effective as valsartan and the combination of both did not improve the outcome compared with monotherapy either. There was no marked difference in total mortality between the three groups. In the valsartan-group 979 patients died, in the combined group 941, and in the captopril-group 958. No therapeutic regimen was superior concerning the re-infarction risk and decrease of NYHA stage. In the light of Val-HeFT [5] and CHARM [6], these results are difficult to interpret. However, there were more adverse effects in the captopril-group than in the valsartan-group and even more in the combination-group. There also has been seen a slight gender difference: while women generally have a lower risk of MI and a worse prognosis, here, the clinical benefit of ATII-receptor blockers was higher for them.

Conclusion

In post-MI patients, valsartan constitutes an effective alternative to conventional treatment with ACE-inhibitors. While VALIANT apparently could prove the clinical relevance for valsartan in secondary prevention on the one hand, it has, on the other, shown results which have to be interpreted with caution, especially when compared to CHARM and the large trials on β-blockade post MI as well as CHF (like e.g. ISIS I [7], BBPP [8], MERIT-HF, CIBIS-II and COPERNICUS). Ultimately, we know that we have done well in treating patients with ACE-inhibitors after MI with systolic dysfunction and that, in the light of rising costs, we may continue to do so: a whiter shade of pale …

The alternative view would be to use valsartan as first choice, since it is as effective as ACE-inhibitors, but shows less side effects.

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