Point of View

Do Angiotensin II Receptor Blockers (ARB-II) Increase the Incidence of Myocardial Infarction?

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The editorial written by Verma and Strauss in *British Medical Journal* of 27th November, 2004, (349:1248) puts the possibility that angiotensin II receptor blockers may be associated to the increase of acute myocardial infarction (AMI) rate. Clinical assays used to base such hypothesis were VALUE study[1] and CHARM-alternative[2]. In both there was a statistically significant increase in the incidence of myocardial infarctions, with 19% (CI 95% from 2 to 38%) and 52% (CI 95% from 6 to 118%), respectively. However, the two greatest comparative studies with cardiovascular outcomes between ARB-II and angiotensin converter enzyme inhibitors (ACEI) were put aside, which means, OPTIMAAL[3] and VALIANT[4] studies.

In OPTIMAAL study, 5,477 post-AMI and left ventricular dysfunction patients were randomized for losartan (50 mg/day) or captopril (150 mg/day). After a 2.7-year follow-up, there was an excess of mortality in losartan group, but without reaching statistical significance (18% vs. 16%, p=0.07) and AMI incidence between groups was the same (14%).

In VALIANT study, 14,703 post-AMI individuals were randomized for valsartan, captopril or the combination of both. Results were shown neutral within limits of primary outcome (death) among the three groups. The number of AMI individuals was similar between valsartan (820) and captopril (840) groups, therefore, without statistically significant indication (16.7% vs. 17.1%) of excess between the groups.

Therefore, the hypothesis shown by the authors on mortality excess due to AMI associated to the use of ARB-II does wrong from tendenciousness and incomplete analysis. The ideal scenery to test such hypothesis would be the one of a clinical assay to detect clinically relevant differences, in the specific case, the incidence of fatal and non-fatal myocardial infarctions, in the comparison between ARB-IIs and ACEIs. Results from ONTARGET and TRANSCEND[5] studies are expected to clarify that matter even more. By then, a decent alternative would be a meta-analysis[6] with all available studies, in an impartial and non-oblique way.

ACEIs have a long positive history of positive results and great clinical relevance, including the reduction of acute myocardial infarction incidence among high cardiovascular risk patients. ARB-IIs, so far, have not shown superiority when compared to ACEIs in this and in other contexts, such as in heart failure. In the presence of such facts, ACEIs are still the best option when it comes to inhibit rennin-angiotensin system searching for relevant results for the patient. ARB-IIs are useful in cases of intolerance (especially cough and angioedema) to ACEIs. Those cases occur from 5 to 20% of the cases of first exposure to ACEIs, that is, at least 80% of the individuals are tolerant to ACEIs, and they can use them chronically. The affirmative that ARB-IIs are not alternative anymore, but "substitutes" for ACEIs, has no sound scientific basis. Besides, cost-effectiveness aspects must be considered in a country like Brazil, and also in this item, ACEIs remain superior to ARB-IIs and, therefore, the first choice.

References

1. Julius S, Kjeldsen SE,Weber M et al. VALUE Trial Group. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial. Lancet 2004; 363: 2022-31.
2. Granger CB, McMurray JJ, Yusuf S et al. CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the CHARM-alternative trial. Lancet. 2003; 362: 772-6.
3. Dickstein K, Kjekshus J. OPTIMAAL Steering Committee of the OPTIMAAL Study Group. Effects of losartan and captopril on mortality and morbidity in high-risk patients after acute myocardial infarction: the OPTIMAAL randomised trial. Optimaal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan. Lancet. 2002; 360: 752-60.
4. Pfeffer MA, McMurray JJ, Velazquez EJ et al. Valsartan, captopril or both in myocardial infarction complicated by heart failure, left ventricular dysfunction or both. N Engl J Med. 2003; 349: 1893-906.
5. Teo K, Yusuf S, Anderson C et al. Rationale, design and baseline characteristics of 2 large, simple, randomised trials evaluating telmisartan, ramipril and their combination in high-risk patients: the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial/Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease (ONTARGET/TRANSCEND) trials. Am Heart J. 2004; 148: 52-61.
6. Lee VC, Rhew DC, Dylan M, Badamgarav E, Braustein GD, Weingarten SR. Meta-analysis: Angiotensin-Receptor blockers in chronic heart failure and high-risk acute myocardial infarction. Ann Intern Med. 2004; 141: 693-704.

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