Point of View

# Do Angiotesin II Blockers Increase the Incidence of Myocardial Infarction?

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In a recent BJM editorial, vol. 329, Nov. 2004, p. 1248-49, signed by Marty Strauss from North York General Hospital, North York, Canada, a larger incidence of myocardial infarctions in angiostesin II blockers was discussed.

First there was a citation of VALUE study[1], where valsartan produced a significant statistical increase of 19% in the myocardial infarction (MI) incidence, fatal and non-fatal. Actually, this study compared valsartan with amlodipine and, in the occurrence of MI, there was really a significant advantage (p=0.02) over amlodipine. Nevertheless, this was a secondary goal. N this sense, the first observation we should make is that the study did not compare drug x placebo, but drug x drug. In the first composed outcome there was no difference between the two drugs. In the valsartan group there was gain in relation to the diabetic subgroup (p<0.0001) and in the occurrence of cardiac failure (CF), in this case without significance (p=0.12).

Later there was a citation of the alternative-CHARM study[2], with an increase of 36% in MI incidence in the group using candersartan. In this group that compared candersartan x placebo, the primary goal was an outcome composed of obit due to cardiovascular causes or hospitalization due to CF. In this study there was a risk reduction of 23% in the candersartan group (p<0.0004). In the CHARM-plus, the primary outcome was also significant with the risk reduced in 15% (p=0.011), with a 23 NNT. In the CHARM-preserved there was no significant difference 9p=0.18).

The explanation for the larger incidence of MI that could be related to higher risk and higher blood pressure patients would only sustain itself with a new and deeper study of this aspect.

In the LIFE study[3] comparing iosartan to atenolol, with the same levels of blood pressure reduction, there was no difference between the two groups in the occurrence of fatal and non-fatal MI. On the other hand, there were advantages with significance in favor of iosartan in the primary composed outcome (p=0.021) in the reduction of fatal and non-fatal stroke (p=0.001). There was no significant advantage for atenolol in cardiovascular mortality (p=0.21).

We would have to consider it a good result for iosartan the equal reduction of in the occurrence of MI, once it was compared to a drug that was considered standard for such cases.

The RENAAL study[4] comparing iosartan x placebo in diabetic patients with nephropathy, showed a significant risk reduction in the primary outcomes of serum creatine duplication, terminal kidney failure and death. In this study, iosartan exercised renoprotection and proved to be a useful drug.

The IDNT study[5] comparing ibersatan x amlodipine, also in diabetic patients with nephropathy, there was significant risk reduction in the ibersartan group in the primary outcome, besides duplication of serum creatine, kidney failure and death (p=0.001) There was non-significant worsening with the use of amlodipine.

Two other studies, IRMA II[6] and MARVAL[7] were done in diabetes with microalbuminuria patients. In the IRMA II ibesartan x placebo were compared in a two year sequence, with significant reduction to mormoalbuminuria of 33% in the ibesartan group (p<0.01). In the MARVAL, valsartan and amlodipine were compared, with very significant reduction of albuminuria in the valsartan group.

In the article we comment it is mentioned that there was no reduction in the incidence of MI, stroke or cardiovascular death in the comparing of ibesartan to amlopidine[8-9].

Closing these comments, we may conclude that the antagonists to angiotensin II have its use well established, once in diabetic patients with nephropathies or microalbuminuria, it presents large disadvantages[10]. Patients with MI or ejection fraction below 40%[11,12] are also important. These are drugs which were considered alternatives to ECA inhibitors, but which have proved the can be used as first choice.

About the reports of larger MI incidence in relation to the use of angiostesin II, I believe we do not yet have elements to counter-recommend their use. In all the studies cited the increase of MI incidence was an occasional finding or secondary outcome. Such indications are an alert about this fact, to which primary outcomes of future studies should be directed to definitely clarify these findings.

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Enviado em 13/01/2005
Aceito em 26/01/2005

## 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. Dahlof B, Devereux RB, Kjeldsen SE et al. LIFE Study Group. Cardiovascular morbidity and mortality in the losartan intervention for endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet 2002; 359: 995-1003.
4. Brenner BM, Cooper ME, de Zeeuw D et al. RENAAL Study Investigators. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001; 345: 861-9.
5. Brenner BM, Cooper ME, de Zeeuw D. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001; 345: 861-9.
6. Lewis EJ, Hunsicker LG, Clarke WR. Renoprotective effect of the angiotensin-receptor antagonist ibesartan in patients with nephropathy due type 2 diabetes. N Engl J Med 2001; 345: 851-60.
7. Viberti G, Whoeldon N. Microalbuminuria Reduction with Valsartan (MARVAL) trial. Circulation 2002; 106: 672-8.
8. Lewis EJ, Hunsicker LG, Clarke WR et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001; 345: 851-60.
9. Levy BI. Can angiotensin II type 2 receptors have deleterious effects in cardiovascular disease? Implications for therapeutic blockade of the renin-angiotensin system. Circulation 2004; 109: 8-13.
10. Strippoli GF, Craig M, Deeks JJ, Schena FP, Craig JC. Effects of angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists on mortality and renal outcomes in diabetic nephropathy: systematic review. Br Med J 004; 329: 828.
11. Yusuf S, Pfeffer MA, Swedberg K et al. CHARM Investigators and Committees. Effects of candesartan in patients with chronic heart failure and preserved left-ventricular ejection fraction: the CHARM-preserved trial. Lancet 2003; 362: 777-81.
12. 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.