Point of View

Do Angiotensin 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 angiotensin II blockers was discussed.

First there was a citation of VALUE study¹, 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. In 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 study², with an increase of 36% in MI incidence in the group using candesartan. In this group that compared candesartan 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 candesartan 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 (p=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 study³ comparing isosartan 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 isosartan 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 isosartan the equal reduction of in the occurrence of MI, once it was compared to a drug that was considered standard for such cases.

The RENAAAL study⁴ comparing isosartan 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, isosartan exercised renoprotection and proved to be a useful drug.

The IDNT study⁵ comparing ibersartan 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 II⁶ and MARVAL⁷ 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 amlodipine⁸⁻⁹.

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 disadvantages¹⁰. 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 angiotensin 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.
References