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Letter to the Editor

Metabolic agents in the management of diabetic coronary patients: A new era

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Abstract

The modulation of cardiac metabolism with Trimetazidine is very important for the control of myocardial ischemia and for the preservation of left ventricular function. The optimization of cardiac metabolism should also include improvement of cardiac insulin resistance with insulin sensitizer agents and the optimization of Kreb's Cycle with essential amino acids. Regarding new drugs that may act inhibiting free fatty acid oxidation we have to underline that to date it is not clear whether Ranolazine has an effect on cardiac metabolism. We agree instead that metabolic agents like Dichloroacetate, Perhexiline and Etomoxir have an antiischemic effect, while their administration requires adjustment of dose and careful monitoring of side effects.

Keywords: Metabolic agents; Coronary artery disease; Diabetes

Dear Prof. Coats,

We have read with interest the letter from Dr. Celik and co-workers on the effect of metabolic agents in the management of coronary diabetic patients [1]. We share with them the opinion on the importance of modulation of cardiac metabolism with Trimetazidine both for the control of myocardial ischemia and for the preservation of left ventricular function. We believe that optimization of cardiac metabolism should also include improvement of cardiac insulin resistance with insulin sensitizer agents and the optimization of Kreb's Cycle with essential amino acids.

Regarding new drugs that may act inhibiting free fatty acid oxidation we have to underline that to date it is not clear whether Ranolazine has an effect on cardiac metabolism. Studies have shown that the effect of Ranolazine on free fatty acid oxidation is observed at concentrations higher than those obtained in clinical trials [2]. This evidence has prompted to a shift in the suggested mechanism of action from fatty acid inhibition to an effect on late sodium current [3,4]. This later effect may have just a cosmetic effect on the ECG and not a direct effect on the improvement of myocardial ischemia. Therefore, we believe that Ranolazine cannot be considered a metabolic agent with anti-ischemic effects. Furthermore, the effect of Ranolazine on the electrocardiographic signs of myocardial ischemia is small [5,6] when compared to that obtained with Trimetazidine in the Trimpol I [7] and II [8] studies.

We agree that metabolic agents like Dichloroacetate, Perhexiline [9] and Etomoxir have an anti-ischemic effect. However, their administration requires adjustment of dose and careful monitoring of side effects that are seldom seen with Trimetazidine.

In conclusion, we do believe that Trimetazidine is today the only true metabolic drug with anti-ischemic effect that can be safely and easily administered in patients with all forms of ischemic heart disease. The drug is very effective in combination with haemodynamic drugs and possibly its effect can be potentiated by concurrent manipulation of

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cardiac metabolism with insulin sensitizers and selected amino acids.

References

[1] Celik T, Kursakliogu H, Iyisoy A, Jata B. Metabolic agents in the management of diabetic coronary patients: A new era. Int J Cardiol 2008;127:133–4.
[2] MacInnes A, Fairman DA, Binding P, et al. The antianginal agent trimetazidine does not exert its functional benefit via inhibition of mitochondrial long-chain 3-ketoacyl coenzyme A thiolase. Circ Resp 2003;93:E26–32.
[3] Antzelevitch C, Belardinelli L, Zygmunt A, et al. Electrophysiological effects of ranolazine, a novel antianginal agent with antiarrhythmic properties. Circulation 2004;110:904–10.
[4] Undrovinas AL, Undrovinas NA, Belardinelli L, et al. Ranolazine inhibits late sodium current in isolated left ventricular myocytes of dogs with heart failure. J Am Coll Cardiol 2004;43(Suppl 1):A178.
[5] Chaitman BR, Skettino SL, Parker JO, et al. Anti-ischemic effects and long-term survival during ranolazine monotherapy in patients with chronic severe angina. J Am Coll Cardiol 2004;43:1375–82.
[6] Chaitman BR, Pepine CJ, Parker JO, et al. Effects of ranolazine with atenol, amlodipine, or diltiazem on exercise tolerance and angina frequency in patients with severe chronic angina: a randomized controlled trial. JAMA 2004;291:309–16.
[7] Szwed H, Pachocki R, Domzal-Bochenska M, et al. Efficacy and tolerance of trimetazidine, a metabolic antianginal, in combination with a hemodynamic antianginal in stable exertion angina. TRIMPOL I, a multicenter study –– Presse Med., vol. 29 (10); Mar 18 2000. p. 533–8.
[8] Ruzyllo W, Szwed H, Sadowski Z, et al. Efficacy of trimetazidine in patients with recurrent angina: a subgroup analysis of the TRIMPOL II study. Curr Med Res Opin Sep 2004;20(9):1447–54.
[9] Sudre Y, Becq-Giraudon B, Pouget-Abadie JF, Demange J, Boutaud P. Hypoglycemic complications in the course of treatment with perhexilline maleate and beta-blocking agents. Coeur Med Interne Apr–Jun 1977;16(2):279–84.