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Effect of colestimide therapy for glycemic control in type 2 diabetes mellitus with hypercholesterolemia

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Many important clinical trials demonstrated in the last years the benefit of statins treatment in type 2 diabetic patients, especially by the effects on LDL cholesterol. Statins, as a class, are a first therapeutical choice for metabolic control in diabetic patients, yet, there are reports about different effects on blood glucose control among different statin agents. On the other hand, bile acid sequestrants, also very effective in reducing LDL levels, are not widely used because of diabetic patients' predisposition to hypertriglyceridemia and the poor tolerance of the drug. In Japan, colestimide, a new anion exchange resin, replaced recently cholestiramine in the treatment of hypercholesterolemia, being very well tolerated and showing strong hypolipidemic effects. There are reports about colestimide effects on blood glucose reduction, but there were no studies concerning the glycemic control in diabetic patients.

In this paper, the authors intended to compare the effects of colestimide and pravastatin (which seems to be a "favorable" statin for blood glucose) on glycemic control at 70 type 2 diabetic patients. Randomization was made so that patients received either 10 mg of pravastatin or 3 g of colestimide for 3 months, with no changes in their oral agents or insulin doses. After this period, fasting plasma glucose, body weight, serum total cholesterol, HDL, LDL and triglycerides were determined to compare the effects of the two treatments. Fasting plasma glucose was reduced at 1 month of treatment in the colestimide group and the reduction maintained after 3 months ($p<0,01$), while in the pravastatin group no change was noticed. Also, HbA1c decreased after 1 month of colestimide treatment and at 3 and 6 months the decrease was significant (by 8% of the baseline value, $p<0,01$) while pravastatin had no effect. As for the other parameters, body weight and HDL remained unchanged, LDL decreased significantly in both groups, triglycerides increased slightly but not significantly in the colestimide group. Both medications were very well tolerated. The study also concluded that the blood glucose reduction was independent from the lipid-lowering effect in the colestimide group, because the HbA1c reduction/LDL reduction ratio was highly superior in this group; it is suggested that the mechanism might be, at least in part, an improvement in insulin sensitivity.

The importance of these findings is related to UKPDS study data, showing that reductions in HbA1c levels can lower the risk of microvascular complications in diabetics. Unlike sulphonylureas or metformin, colestimide seems to be safe for patients at risk of hypoglycemia, renal or hepatic insufficiency.

In conclusion, a new agent having beneficial effects both on hyperglycemia and hypercholesterolemia and a very good tolerance profile could be an important achievement for a large population worldwide. To which extent the comparison with statins (known to be a life-prolonging medication class for these patients by many non-lipidic effects) stands in terms of survival outcome needs to be further investigated.

Comment on the paper:

Yamakawa T, Takano T, Utsunomiya H et al – Effect of colestimide therapy for glycemic control in type 2 diabetes mellitus with hypercholesterolemia. *Endocrine Journal* 2007, 54(1):53-58