Abstract

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Effects of short-term treatment with metformin on serum concentrations of homocysteine, folate and vitamin B12 in type 2 diabetes mellitus: a randomized, placebo-controlled trial.

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OBJECTIVE: Metformin is a key treatment option in type 2 diabetes. However, metformin may decrease vitamin B12 levels and increase levels of homocysteine, a cardiovascular risk factor. We investigated whether 16 weeks of treatment with metformin affects serum concentrations of homocysteine, folate and vitamin B12 in subjects with type 2 diabetes treated with insulin.

DESIGN: Placebo-controlled, randomized trial. Measurements: at baseline and 16 weeks later.

SETTING: This trial was conducted in the outpatient clinics of three general hospitals in The Netherlands.

SUBJECTS: A total of 745 patients with type 2 diabetes, treated with insulin and not known with a contraindication for the use of metformin, were approached; 390 gave informed consent and entered the study. Thirty-seven subjects dropped out (12 placebo and 25 metformin users).

INTERVENTION: Addition of metformin or placebo to insulin therapy.

PRIMARY OUTCOME PARAMETERS: Serum homocysteine, folate, vitamin B12, indices of glycaemic control and body weight.

RESULTS: Amongst those who completed 16 weeks of treatment, metformin use, as compared with placebo, was associated with an increase in homocysteine of 4% (0.2 to 8; P=0.039) and with decreases in folate [-7% (-1.4 to -13); P=0.024] and vitamin B12 [-14% (-4.2 to -24); P<0.0001]. In addition, the increase in homocysteine could be explained by the decreases in folate and vitamin B12.

CONCLUSION: In patients with type 2 diabetes, 16 weeks of treatment with metformin reduces levels of folate and vitamin B12, which results in a modest increase in homocysteine. The clinical significance of these findings remains to be investigated.

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