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Vitamin B_{12}-Mangel bei Typ 2-Diabetikern - Diagnostik und Zusammenhang zwischen Biomarkern, Metformin-Einnahme und diabetischen Neuropathien

Masterarbeit

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Betreuung

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Abstract

Background

Metformin is a known pharmacological cause of vitamin B_{12} (VB_{12}) deficiency among type 2 diabetic patients. Diagnosis of deficiency is mainly based on low serum VB_{12} levels whereas low holotranscobalmin (HoloTc) concentrations would be more sensitive (but not routinely used yet). Firstly, the effect on Metformin reflected by serum VB_{12} and HoloTc should be investigated in type 2 diabetic patients. Secondly, VB_{12} status was analyzed in non-diabetic patients in comparison to type 2 diabetic patients. In addition, the grade of diabetic neuropathy was estimated of each patient to investigate the relationship between severity and prevalence of neurological deficits.

Research design and methods

Blood samples were obtained from patients with type 2 diabetes while coming for a routine visit to their diabetologist (observational study). Comparisons between patients receiving metformin and the non-metformin group tended to investigate the effect on metformin exposure (> 6 months). Data irrespective of metformin intake was obtained in comparison with non-diabetic patients. Clinical, nutritional and demographic factors associated with vitamin B_{12} deficiency were assessed by a questionnaire. The severity of diabetic neuropathy status was determined using a generally accepted clinical scoring system (Neuropathy Disability Score, NDS).

Results

30 patients completed the study. Patients receiving metformin (n = 19) had slightly lower serum VB_{12} (median 229 vs. 245 pmol/l, p = 0.75) and unchanged HoloTc levels (median 85.1 vs. 84.6 pmol/l, p = 0.67) compared to non-metformin group (n = 11) (not significant). Diabetic patients (n = 9) compared to non-diabetic patients (n = 11) - both with VB_{12} deficiency (< 200 pmol/l) - showed significant higher HoloTc levels (median 50 vs. 40.7 pmol/l, p = 0.05); 90 % within normal ranges.

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The grade of neuropathy was predicted by traditional parameters such as duration of diabetes, age and HbA1c values. Furthermore, elevation of homocysteine (Hcy) was associated with the presence of neuropathy ($p = 0.05$). Beyond that there were significant correlations concerning the two elektrolytes Natrium (Na^+) ($p = 0.02$) and Potassium (K^+) ($p = 0.02$) and severity of diabetic neuropathy.

Discussion

Metformin-treated patients showed depressed serum VB_{12} levels (-5 %) in comparison to patients without metformin exposure. But the difference was not significant which might be due to the higher age in average of the non-metformin group (+ 10 years), because the older the population the higher the risk of achieving VB_{12}-deficiency. Furthermore, the active HoloTc remained unchanged in relation to metformin treatment. But there were significant higher HoloTc levels in type 2 diabetic patients in comparison to the non-diabetic group. These results suggest that Diabetes do have more influence on VB_{12} status than metformin intake itself.

Hcy might target nervous function by oxidative damage or by direct toxic effects. This could explain the higher Hcy levels found in more severe neurological deficits.

Conclusion

The possibility to measure HoloTc has provided convincing evidence that metformin isn't as bad as its reputation. Furthermore, HoloTc is not recommended to use alone when judging VB_{12} status among typ 2 diabetic patients (with or whitout metformin therapy).

Hcy is considered as potential predictor for diabetic neuropathy. Further prospective studies are warranted to clarify the role of Hcy as possible predictor of diabetic neuropathies.

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