Abstract

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Homocysteine, cystathionine, methylmalonic acid and B-vitamins in patients with renal disease.

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BACKGROUND: Moderate hyperhomocysteinemia is very frequent in renal patients. Aside from homocysteine (HCY) itself, the metabolites methylmalonic acid (MMA) and cystathionine (CYS) supply further information about disturbances in HCY metabolism.

METHODS: In two groups of renal patients, transplant and hemodialysis patients, we measured HCY, MMA and CYS and evaluated their diagnostic value for impaired HCY metabolism due to vitamin deficiency and renal insufficiency. We investigated serum samples from 63 transplant patients and 38 patients undergoing hemodialysis. HCY, MMA and CYS were assayed by gas chromatography-mass spectrometry, vitamin B6 by HPLC, B12 and folate by chemiluminescence immunoassay.

RESULTS: The determination of HCY, MMA, and CYS in renal patients provides specific information about intracellular disturbances of HCY metabolism. The frequency of increased metabolite levels in renal patients was much higher than the frequency of lowered vitamin concentrations in serum. Furthermore, the metabolite levels in transplant patients were only moderately increased, whereas they were strongly increased in patients on hemodialysis (HCY 19.2 vs. 28.8 micromol/l, MMA 292 vs. 1025 nmol/l, CYS 733 vs. 2711 nmol/l). Our findings may support the use of MMA determination in the diagnosis of vitamin B12 deficiency in renal patients. Compared to vitamin B12 deficiency, renal dysfunction itself appears to cause only a modest elevation in serum MMA. Regression analysis revealed that the moderate elevation of HCY and CYS in transplant patients is mainly a consequence of impaired remethylation of HCY to methionine with activated transsulfuration, whereas the mildly elevated MMA level is attributable to renal dysfunction. In patients on hemodialysis, all three metabolites were markedly elevated, indicating a strongly disturbed HCY metabolism. Based on a backward regression, we discovered that the HCY metabolism was strongly disturbed by renal insufficiency and vitamin deficiency. The markedly elevated HCY level was mainly attributable to functional vitamin B12 deficiency indicated by high MMA, and the strong CYS elevation was due to renal dysfunction and inhibition of this pathway by low levels of vitamin B6.

CONCLUSION: In conclusion, besides HCY, the determination of MMA and CYS levels supports an early diagnosis of B-vitamin deficiency in renal patients. MMA is a more sensitive indicator of intracellular vitamin B12 deficiency than vitamin B12 in serum.

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