

HOLOTRANSCOBALAMIN- A NOVEL MARKER FOR VITAMIN B12 DEFICIENCY- ? CLINICAL UTILITY

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Introduction: Low vitamin B12 is frequently seen in the elderly population but the presence of vitamin B12 deficiency is much lower and patients are frequently given B12 injections for life unnecessarily. HolotranscobalaminII (HTC) bound to vitamin B12 is the biologically active fraction of total vitamin B12 available for tissue uptake. Decreased HTC could be an early marker for cobalamin (B12) deficiency, and clinically useful. We analytically evaluated the pre-release AXIS-SHIELD automated HTC assay, which has been adapted for routine use on the Abbott AxSYM. We also investigated the clinical usefulness of HTC in diagnosing B12 deficiency in a cohort of patients with low B12 levels. We present the preliminary analysis here.

Methods: Following ethics approval, we prospectively identified and collected appropriate blood samples and blood films from patients (n=210), with cobalamin (B12) values <200 pmol/L. These samples were aliquoted and stored at -70°C. B12 and creatinine were analysed by the Abbott Architect, Hcy and HTC by the Abbott AxSYM, MMA (n= 80) by GCMS and intrinsic factor antibody (n=80) by ELISA. HTC values are reported after correction for the AXIS-SHIELD calibrator value reassignment. Blood films, clinical histories and laboratory data were independently reviewed by two clinical haematologists blinded for the HTC values, who determined, whether the patients were likely vitamin B12 deficient or not. Univariate and multivariate statistical analysis was performed using SAS software. A 5 day precision study for HTC was performed in accordance with the Clinical and Laboratory Standards Institute protocol, EP5-A2.

Results: The analytical evaluation of HTC on the Abbott AxSYM showed good precision, with intra -assay CV (4.5 – 8.2 %), HTC values 19/40 pmol/L, and inter-assay CV (7.3-9.5%), HTC values 21/41 pmol/L.

34/210 patients were likely B12 deficient on clinical review. On univariate analysis patients with B12 deficiency had lower B12 levels (69 vs 121 pmol/L), higher homocysteine levels (22 vs 15 µmol/L), higher MCV (94 vs 89 fl) and were older (77 vs 66 years) (p< 0.01 for all). The HTC levels were lower in the vitamin B12 deficient group than in the other patients with low B12 levels (22.4 vs 31.5 pmol/L, p< 0.001). In a multivariate analysis the HTC values provided additional independent information to the clinical diagnosis of B12 deficiency. Odds ratio estimates showed each unit of HTC decrease was associated with a 4.7% increase in risk of being B12 deficient (OR 0.953, 95%CI 0.908-1.0).

Conclusion: Serum HTC on the automated Abbott AxSYM is a rapid and precise assay. In our clinical setting a low HTC value has been shown to add independent value when diagnosing cobalamin(B12) deficiency. Further studies on the clinical usefulness of HTC are continuing.

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