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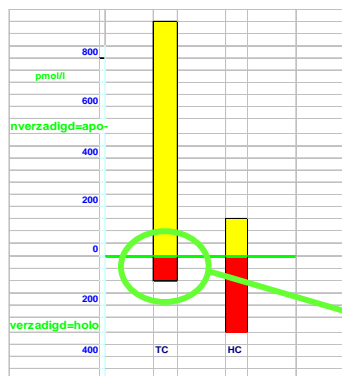
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Introduction

Vitamin B12 deficiency is a frequent problem, particularly among older persons. Because vitamin B12 deficiency can cause serious complications, accurate and early detection is needed. Total serum cobalamin is the standard method for detection of B12 deficiency, although it is known that it is composed of two fractions: the rapidly metabolized transcobalamin-bound B12 and the slowly cleared haptocorrin-bound fraction. It is generally assumed that only transcobalamin-bound B12 is available to the tissues.



ApoTC:

•m:480 -1335 pmol/l

•f: 570 -1400 pmol/l

ApoHC:

•m: 70 -175 pmol/l

•f: 75 -185 pmol/l

HoloTC= Active B12:

m/f: 20-120 pmol/l

Plasma distribution of cobalamin-binding protein fractions

From a physiological point of view it would be reasonable to assume that the HoloTC-fraction would be a better predictor of availability of vitamin B12 to the tissues than total B12. Several smaller studies with non-automated assays for HoloTC have more or less confirmed the potential value of this parameter. This multicenter study evaluated the diagnostic value of a new automated HoloTC assay (Abbott Active B12 assay for AxSYM).

Methods

Vitamin B12, HoloTC, Folate, Hb, MCV, WBC, platelets and creatinine were measured in 1725 samples from consecutive patients for whom a B12 test had been requested, by standard laboratory techniques. The HoloTC-assay itself was evaluated with respect to precision (within-and between run), sample requirement and stability, and accuracy in comparison with the HoloTC-RIA from AXIS-Shield.

Methylmalonic acid was measured in an subset of samples by LC-MS and used as a "gold standard" for establishing real vitamin B12 deficiency on the cellular level.

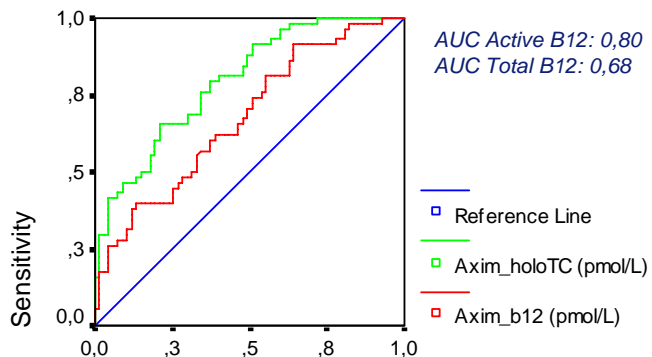
Results

Within and between run imprecision for the Active B12 assay ranged from 5% at 20 and 40 pmol/l to 10% at 80 pmol/l. Between center imprecision using 20 serum samples in the range from 20 to 120 pmol/l was on average 7,5%.

Samples above 120 pmol/l can be effectively diluted with saline up to 100-fold.

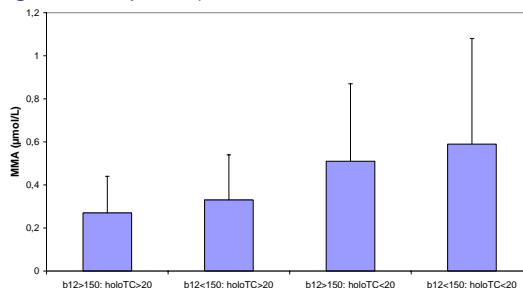
Serum and heparin samples give almost equal results; EDTA-plasma results in 40% higher values and is therefore unsuitable.

Reference values have been determined in 120 volunteer blood donors (50% men) and found to be from 20-122 pmol/l (95% interval) without a difference between sexes.



1 - Specificity

Using a methylmalonic acid level of 0.26 $\mu\text{mol/L}$ as cutoff and excluding patients with renal insufficiency, active B12 was a better predictor for vitamin B12 deficiency than total B12 (see ROC curve). Addition of total B12 to the linear regression model including active B12 did not increase predictive power (R^2 change 0.001, $p=0.8$)



MMA levels sorted by cutoff values for total and active B12

Conclusions

➤ The Active B12 assay demonstrates satisfactory analytical qualities

➤ Active B12 appears superior to total B12 in discriminating between deficient and sufficient vitamin B12 status >> "Active B12 is more than total B12"