COMPARATIVE STUDY OF VITAMIN B12 AND HOLOTRANSCOBALAMIN OR ACTIVE B12 AS A MARKER FOR VITAMIN B12 DEFICIENCY AT DR GEORGE MUKHARI HOSPITAL

By

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DECLARATION

I, Dr LM Murray, hereby declare that this work, unless where acknowledged, is my own. It is being submitted in partial fulfillment of MMed in Chemical Pathology, in the Department of Chemical Pathology, School of Pathology, Faculty of Health Sciences at the University of Limpopo, Medunsa campus.

................................................. ...........................................
Signature of candidate Date
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Abstract

Aim: This study was undertaken to compare the diagnostic sensitivity and specificity of total vitamin B12 analyses to active B12 (holoTC) analyses in a population of patients attending the Dr George Mukhari Hospital in Pretoria.

Methods: Routine serum folate, full blood count (FBC), thyroid function test, homocysteine, serum total vitamin B12 and active B12 analyses were performed on 30 samples.

Results: Serum folate was determined in all patients and 96% of the patients had a normal folate value. When looking at the FBC results it is important to note that three times as many males as females presented with anemia (36% versus 16%). Thyroid function tests were normal in 90% of patients. When the total vitamin B12 test was performed only 10% of patients tested positive for vitamin B12 deficiency, in contrast to the active B12 analyses where 16% of patients tested positive for vitamin B12 deficiency. Both tests had a diagnostic sensitivity of 50%. The diagnostic specificity for total vitamin B12 was 93% in comparison with the 86% obtained by the active B12 analyses; when homocysteine was used as the true marker for vitamin B12 deficiency.

Conclusion: Diagnostic sensitivity was the same and the total vitamin B12 test’s specificity was better in comparison to the active B12 analyses. Thus the active B12 assay cannot be recommended for routine use, since it has no benefit.
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**List of abbreviations**

CoA Coenzyme A
CLIA Clinical Laboratory Improvement Amendments
CV Coefficient of variation
Da Dalton
DGM Dr George Mukhari
DNA Deoxyribonucleic acid
dTMP Deoxythymidine monophosphate
dUMP Deoxyuridine monophosphate
<table>
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<tr>
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<th>Description</th>
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<tr>
<td>DxI</td>
<td>Beckman Coulter UniCel DxI 800 Immunoassay System</td>
</tr>
<tr>
<td>e.g.</td>
<td>exempli gratia (for example)</td>
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<tr>
<td>FBC</td>
<td>Full blood count</td>
</tr>
<tr>
<td>FN</td>
<td>False negative</td>
</tr>
<tr>
<td>FP</td>
<td>False positive</td>
</tr>
<tr>
<td>FT3</td>
<td>Free triiodothyronine</td>
</tr>
<tr>
<td>FT4</td>
<td>Free thyroxine</td>
</tr>
<tr>
<td>g/dl</td>
<td>gram per deciliter</td>
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<tr>
<td>GC-MS</td>
<td>Gas chromatography mass spectrometry</td>
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<tr>
<td>GUM</td>
<td>Guide to the Expression of Uncertainty in Measurement</td>
</tr>
<tr>
<td>Hb</td>
<td>Hemoglobin</td>
</tr>
<tr>
<td>HC</td>
<td>Haptocobalamin</td>
</tr>
<tr>
<td>Hct</td>
<td>Hematocrit</td>
</tr>
<tr>
<td>H⁺/K⁺ ATPase</td>
<td>Hydrogen potassium adenosine triphosphate enzyme(ase)</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>holoTC</td>
<td>Holotranscobalamin</td>
</tr>
<tr>
<td>IF</td>
<td>Intrinsic factor</td>
</tr>
<tr>
<td>IQC</td>
<td>Internal quality control</td>
</tr>
<tr>
<td>LC-MS/MS</td>
<td>Liquid chromatography tandem mass spectrometry</td>
</tr>
<tr>
<td>LDH</td>
<td>Lactate dehydrogenase</td>
</tr>
<tr>
<td>MCV</td>
<td>Mean cell volume</td>
</tr>
<tr>
<td>MEIA</td>
<td>Microparticle enzyme immunoassay</td>
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<tr>
<td>mg</td>
<td>milligram</td>
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mIU/l  milli International Units per litre
MU     Measurement of uncertainty
ng/l    nanogram per litre
NHANES National Health and Nutritional Examination Survey
NHLS   National Health Laboratory Services
NIST   National Institute of Standards and Technology
nmol/l nanomol per litre
pmol/l picomol per litre
RBC    Red blood cell
RDA    Recommended daily amount
RE     Random error
SD     Standard deviation
SE     Systematic error
SRM    Standard Reference Material
TC     Transcobalamin
TC-II  Transcobalamin II
TE     Total error
TFT    Thyroid function test
THF    Tetrahydrofolate
TN     True negative
TP     True positive
TSH    Thyroid stimulating hormone
µg     microgram
<table>
<thead>
<tr>
<th>Symbol</th>
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<tbody>
<tr>
<td>µg/100g</td>
<td>microgram per 100 gram</td>
</tr>
<tr>
<td>µg/day</td>
<td>microgram per day</td>
</tr>
<tr>
<td>µmol/l</td>
<td>micromol per litre</td>
</tr>
<tr>
<td>USA</td>
<td>United States of America</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
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