Treatment of Vitamin B12 deficiency

NHS
Bury Clinical Commissioning Group

Anaemia or clinical suspicion of deficiency
Check vitamin B12

*In this guidance vitamin B12 levels are reported as ng/L.
Reference range 200 – 800ng/L

Causes of vitamin B12 deficiency

- Pernicious anaemia
- Gastric causes – gastrectomy or resection
- Inadequate dietary intake of B12 e.g.vegan diet
- Intestinal causes e.g. malabsorption, ileal resection, Crohn's disease
- Medications e.g.colchicine, metformin, anticonvulsants, long term PPIs or H2blockers

Food based malabsorption associated with gastric atrophy (age related or associated with long term PPI use) is the likely cause of 30 to 50% of cases with sub-clinical B12 deficiency

Consider referral to dietician if diet is poor

B12 ≥200ng/L*
Possible deficiency

B12 <200ng/L*
Probable deficiency

If 150-200ng/L and no symptoms or anaemia recheck in 1 to 2 months

In reference range - no further investigation

Still low - check IFAB
Consider 4 weeks of low dose oral cobalamin 50mcg daily, and repeat B12 after 3 – 4 months

BUT Strong clinical suspicion e.g. macrocytic anaemia, Do not delay treatment if there is (or there is a suspicion of) neurological involvement

If <150ng/L or symptomatic e.g. neurological involvement

IFAB positive

IFAB negative and Vit B12 150 – 200ng/L confirm biochemical deficiency and may need to treat as pernicious anaemia

IFAB negative and Vit B12 >200ng/L – no further investigation. Consider low dose oral cobalamin, only if clinically indicated

Check intrinsic factor antibodies (specificity 95%, sensitivity 50%) (If B12 level <120ng/L lab automatically does test)

Positive

Initial Treatment

If neurological symptoms
IM hydroxocobalamin 1000mcg every 2nd day until no more improvement

If no neurological symptoms
IM hydroxocobalamin 1000mcg 3 times a week for 2 weeks

Maintenance treatment for those with neurological symptoms:
IM hydroxocobalamin 1000mcg every 2 months for life
Oral cobalamin is not recommended

Maintenance treatment for those without neurological symptoms
where the underlying cause is not dietary:
IM hydroxocobalamin 1000mcg every 3 months for life
Oral cobalamin is not recommended.

When the underlying cause is dietary, please see overleaf for maintenance treatment:

Test results

The clinical picture is the most important factor in assessing the results of the serum vitamin B12. Definitive cut off points for clinical and subclinical deficiency are not possible. Bear in mind:

- The test measures total, not metabolically active, vitamin B12.
- Normal range is 200 – 800ng/L
- The levels are not easily correlated with clinical symptoms, although people with vitamin B12 levels less than 100 ng/L usually have clinical or metabolic evidence of vitamin B12 deficiency.
- In most people with vitamin B12 deficiency, the serum vitamin B12 level is below 200ng/L
- Clinically significant vitamin B12 deficiency may be present even with vitamin B12 levels are in the normal range, especially in elderly people.

Investigation in particular patient groups

- **Pregnant women with low B12**

Serum B12 levels of 150 to 200 ng/l in pregnancy may be physiological, and other biochemical tests to determine tissue deficiency are unproven. Check anti-intrinsic factor antibodies and treat as pernicious anaemia if positive. If negative, in order to limit extensive investigation with resultant anxiety, three injections of hydroxocobalamin are suggested to cover the pregnancy, and serum B12 levels checked two months post-partum to ensure resolution to normal levels

- **Patients on oral contraceptive or hormone replacement therapy**

These therapies can result in a low B12 level that does not require further investigation and treatment unless there is a strong clinical suspicion of B12 deficiency

- **Patients with type 2 diabetes on Metformin for longer than 12 months**

These patients should have serum B12 monitored at 6 monthly intervals. If serum B12 levels fall, patients should have tests for anti-intrinsic factor antibody. If positive, they should have lifelong treatment with replacement hydroxocobalamin. If negative, the reduced level may be purely as a result of metformin. Treatment with three injections of hydroxocobalamin with subsequent monitoring of serum B12 at 6 monthly intervals is suggested.

Treatment

For patients with neurological symptoms

Initial treatment:

Intramuscular (IM) injections of hydroxocobalamin 1000mcg every second day until no further improvement

Maintenance:

IM injections of hydroxocobalamin 1000mcg every 2 months for life

For patients without neurological symptoms

Initial treatment:

Intramuscular (IM) injections of hydroxocobalamin 1000mcg 3times a week for 2 weeks

Maintenance:

Long-term treatment where the underlying cause is not dietary:
IM injections of hydroxocobalamin every 3 months for life

Oral cobalamin treatment is not currently recommended in the above.

Long-term treatment where the underlying cause is dietary:

- Advise either: oral cyanocobalamin tablets 50–150 micrograms daily between meals (in adults); or
- Twice-yearly hydroxocobalamin 1000mcg injection - may be preferable especially in the elderly who are more likely to have malabsorption
- In vegans, this treatment may need to be life-long
- In non-vegans treatment can be stopped once vitamin B12 levels have been corrected and diet has improved – but monitor B12 levels 6 monthly
- Advise consumption of foods rich in vitamin B12, eg: foods fortified with vitamin B12 - some soy products, and some breakfast cereals and breads, meat, eggs, and dairy products
- Further monitoring is generally considered unnecessary - exceptions are:
    - Suspected lack of compliance with treatment
    - Recurrence of anaemia

Assessing response to treatment

Initially a full blood count and reticulocyte count after 7 to 10 days of treatment is useful to document response, and a further check done after 8 weeks to confirm normal blood count. Cobalamin levels are not helpful because they increase with vitamin B12 influx regardless of the effectiveness of treatment.

References

- Hunt A, Harrington D, RobinsonS Vitamin B12 deficiency
- BMJ 2914;349: g5226 doi:10. 1136/bmj.g5226
- Devalia V et al Guidelines for the diagnosis and treatment of cobalamin and folate disorders Br J Haematology 2014;166: 496-513
- NICE/CKS Anaemia – B12 and folate updated Nov 2014 accessed January 2015

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