

BNP | Haemochromatosis | Vitamin D

Testing in Primary care

Quiz feedback



bpac nz
better medicine

Contents

| | |
|---|---|
| BNP Haemochromatosis Vitamin D Quiz..... | 2 |
| Quiz Feedback: Responses from Colleagues, GP Panel and Expert Review..... | 4 |

Please let us know if there is any way we can make our case studies more useful to you. We want our resources to be helpful with your day-to-day clinical practice. We would be pleased to receive any suggestions that you have.

If you have any questions please email these to us and we will answer via the 'Your Questions Answered' section of our web site.

bpac^{nz} GP Review Panel:

- Dr Janine Bailey, Motueka
- Dr Stephen Kuzmich, Wellington
- Dr Randall Sturm, Auckland
- Dr Neil Whittaker, Nelson

Panel discussion facilitated and summarised by:

- Rachael Clarke
- Sonia Ross
- Dr Trevor Walker

Acknowledgement:

bpac^{nz} would like to thank the GP review panel and Dr Edward Theakston (Diagnostic Medlab - Auckland), Dr Gerry Devlin (Waikato Hospital) and Professor John Campbell (University of Otago) for their expertise and guidance on the development of this resource.

Email: rachael@bpac.org.nz

Fax: 0800 bpac nz
0800 27 22 69

Phone: 03 477 5418

Website: www.bpac.org.nz

All information is intended for use by competent health care professionals and should be utilised in conjunction with pertinent clinical data.

BNP | Haemochromatosis | Vitamin D

Testing in Primary Care Quiz

1. An otherwise healthy 25 year-old woman has an older brother with hereditary haemochromatosis. She asks if she should be tested. Which of the following options do you recommend?

 - Advise her that iron takes several decades to accumulate, and she should wait until she is at least 40 to be checked
 - Request HFE gene testing
 - Request iron studies
 - Check for symptoms
2. Iron studies performed on a random blood sample from a 28 year-old man are all normal other than a transferrin saturation of 52%. Which of the following options do you recommend?

 - Repeat iron studies on a fasting sample when well
 - Request HFE gene testing
 - Follow up as recommended by the laboratory
 - Repeat when patient next visits
3. A 32 year-old female patient has previously been identified as homozygous for the C282Y mutation on the HFE gene. She asks about determining the HFE status of her two young children. Which of the following options do you recommend?

 - Suggest iron studies and HFE gene testing on both children
 - Recommend to defer testing until the children are >20 years old
 - Suggest HFE gene testing on the father of the children
 - Check the children for signs and symptoms of haemochromatosis
4. You suspect an 82 year-old female rest home patient may be vitamin D deficient. She has no relevant symptoms but does have low sun exposure. Which of the following options do you recommend?

 - Request vitamin D test
 - Request calcium, phosphate, and alkaline phosphatase tests
 - Prescribe vitamin D supplementation without vitamin D testing
 - Recommend a multivitamin
5. Which group(s) of people are most likely to benefit from vitamin D testing?

 - People with atypical osteoporosis
 - People with low sun exposure
 - People with pale complexions
 - People with either high alkaline phosphatase or low serum calcium or phosphate
 - People with hyperthyroidism
6. A 68 year-old man presents with breathlessness on exertion and you suspect chronic heart failure. Which of the following tests would you perform initially?

 - Chest xray
 - ECG
 - BNP
 - Echocardiography
7. A 69 year-old man has been on bendrofluazide and quinapril for the last three years. It was initiated by a previous GP because he was getting short of breath on a steep hill near his house. He has now moved from this location and feels well with no breathlessness. He asks if he can stop the medication. What role does BNP assay have in helping your decision?

 - BNP has no clear role yet in diagnosing heart failure in those already on therapy
 - BNP results may rule out the presence of systolic dysfunction
 - BNP results may confirm the presence of systolic dysfunction
 - BNP results may guide the need for echocardiography
8. A 72 year-old woman has acute dyspnoea with classical clinical features of acute heart failure. What effect would BNP levels have on your immediate management?

 - Would perform BNP testing and start treatment before results available
 - Would perform BNP testing and await results before starting treatment
 - Would delay BNP testing until after immediate management
 - Would not perform BNP testing at all

Quiz feedback

Responses from Colleagues, GP Panel and Expert Review

1. An otherwise healthy 25 year-old woman has an older brother with hereditary haemochromatosis. She asks if she should be tested. Which of the following options do you recommend?

| | You | Your Peers | GP Panel |
|--|-----|------------|----------|
| Advise her that iron takes several decades to accumulate, and she should wait until she is at least 40 to be checked | | 4 % | |
| Request HFE gene testing | | 85 % | + |
| Request iron studies | | 77 % | + |
| Check for symptoms | | 24 % | |

GP Panel

Most respondents recommended gene testing for this woman and the GP panel agreed. Many respondents also recommended iron studies. The panel felt this was a reasonable option although a female patient of this age is unlikely to have iron overload.

Expert comment

Most authorities recommend iron studies (including ferritin) and testing for HFE gene status in parents and siblings of affected persons after appropriate counseling.

A minor point to note is that it would be advisable to obtain details of the brother's exact diagnosis and HFE gene status (if possible) before testing the sister, in case he is one of the relatively rare cases of non-HFE haemochromatosis (more common in non-Caucasians), or a compound heterozygote.

Dr Edward Theakston

2. Iron studies performed on a random blood sample from a 28 year-old man are all normal other than a transferrin saturation of 52%. Which of the following options do you recommend?

| | You | Your Peers | GP Panel |
|---|-----|------------|----------|
| Repeat iron studies on a fasting sample when well | | 83 % | + |
| Request HFE gene testing | | 11 % | |
| Follow up as recommended by the laboratory | | 8 % | |
| Repeat when patient next visits | | 3 % | |

GP Panel

The panel agreed with the majority of respondents who would repeat the iron studies on a fasting sample when the man was well. This is because:

- This man's transferrin saturation is only just in the range that would trigger gene testing.
- There are significant day to day and within day variations in iron levels.
- Both ferritin and transferrin saturation are both temporarily affected by the inflammatory response.
- Results are affected by dietary and supplementary iron intake.
- When transferrin saturation is used for screening for haemochromatosis the fasting state has been shown to decrease the number of false positive tests.

The minimal amount of time needed to eliminate the effects of food and iron supplementation has not yet been established but may be as long as 24 hours.

If this man had a first-degree relative with hereditary haemochromatosis then gene testing would be appropriate.

Expert Comment

Agree with above. A fasting study avoids the effect of recent diet and diurnal variation, and eliminates 80% of false positive results.

Expert recommendations vary as to what level of fasting transferrin saturation should provoke genetic testing, ranging from 45–60%, with lower thresholds increasing sensitivity but reducing specificity. The former British Committee for Standards in Haematology Genetic Haemochromatosis Guideline (currently under revision) suggested fasting levels of 50% or more in women and 55% or more in men, recognising these as compromise values.

Dr Edward Theakston

3. A 32 year-old female patient has previously been identified as homozygous for the C282Y mutation on the HFE gene. She asks about determining the HFE status of her two young children. Which of the following options do you recommend?

| | You | Your Peers | GP Panel |
|---|-----|------------|----------|
| Suggest iron studies and HFE gene testing on both children | | 10 % | |
| Recommend to defer testing until the children are >20 years old | | 81 % | + |
| Suggest HFE gene testing on the father of the children | | 35 % | + |
| Check the children for signs and symptoms of haemochromatosis | | 4 % | |

GP Panel

The most favoured option is to delay gene testing until the children are older. Biochemical changes of hereditary haemochromatosis do not usually appear until well into adult life. Therefore there is no point in involving the children in the trauma of blood testing and explaining the reasons for the tests would not be easy.

The tests are probably best left until the children are adults, although the panel did point out that by the time the children are 20 years they may have lost contact with their family and the opportunity for testing.

The panel would discuss the option of gene testing the children's father. If he is not carrying the gene there is no chance the children can be homozygous for it. It is a decision for the family to make.

Expert comment

HFE homozygosity is not usually associated with a rapid iron loading tendency and so there is no need to identify affected offspring at an early age. It is generally recommended that testing be deferred until patients are able to provide informed consent.

Testing of the father is also a potential strategy, but it makes assumptions about the paternity of the offspring which are not always warranted. Estimates of "paternal discrepancy" in unselected populations range from 2-10%, depending on the population studied.

Dr Edward Theakston

4. You suspect an 82 year-old female rest home patient may be vitamin D deficient. She has no relevant symptoms but does have low sun exposure. Which of the following options do you recommend?

| | You | Your Peers | GP Panel |
|---|-----|------------|----------|
| Request vitamin D test | | 2 % | |
| Request calcium, phosphate, and alkaline phosphatase tests | | 9 % | |
| Prescribe vitamin D supplementation without vitamin D testing | | 94 % | + |
| Recommend a multivitamin | | 7 % | |

GP Panel

Nearly everyone would supplement once per month without testing.

The panel discussed the Number Needed to Treat (NNT). Almost all 82 year-old rest home patients are vitamin D deficient and supplementation will return nearly all of these to normal vitamin D levels. The NNT to get a person back to normal vitamin D levels therefore must be close to one.

The question of NNT to prevent one clinical event such as a fracture or proximal limb pain is more difficult as studies reach different conclusions.

Expert Comment

The prescription of once a month cholecalciferol 1.25mg (50,000 units) is appropriate. The prevalence of Vitamin D deficiency in rest homes, especially in winter and early spring, is so high that supplementation for all residents is justified. The low vitamin D levels result from lack of sunlight exposure, not an inadequate diet, so that once daily multivitamins are unnecessary.

Professor John Campbell

5. Which group(s) of people are most likely to benefit from vitamin D testing?

| | You | Your Peers | GP Panel |
|--|-----|------------|----------|
| People with atypical osteoporosis | | 89 % | + |
| People with low sun exposure | | 10 % | |
| People with pale complexions | | 1 % | |
| People with either high alkaline phosphatase or low serum calcium or phosphate | | 89 % | + |
| People with hyperthyroidism | | 2 % | |

GP Panel

Nearly everyone appropriately chose to test vitamin D levels in people with atypical osteoporosis, for example in men or pre-menopausal women, and in people with suggestive changes to serum calcium, phosphate or alkaline phosphatase.

One of our panel members has recently started seeing rickets in his practice. This has been in children of immigrants from the Indian sub-continent.

Expert comment

I would also check the Vitamin D level in a patient whose symptoms of limb girdle pain and weakness may be due to Vitamin D deficiency and osteomalacia.

Hyperthyroidism is not associated with osteomalacia but is associated with osteoporosis. There is increased bone turnover, release and loss of calcium and, with the lowered PTH levels, decreased conversion of Vitamin D to the active 1,25 dihydroxycholecalciferol. Bone conserving measures should be considered in patients with hyperthyroidism, those with a history of hyperthyroidism have an increased risk of fracture.

Professor John Campbell

6. A 68 year-old man presents with breathlessness on exertion and you suspect chronic heart failure. Which of the following tests would you perform initially?

| | You | Your Peers | GP Panel |
|------------------|-----|------------|----------|
| Chest xray | | 47 % | |
| ECG | | 63 % | + |
| BNP | | 61 % | + |
| Echocardiography | | 5 % | |

GP Panel

The responses to this question depended on local availability of the tests.

The ECG appears to be the first choice because it is usually available immediately in the practice setting and is likely to be abnormal if heart failure is present although ECG changes are not specific enough to make a diagnosis.

Some clinicians are using BNP when the diagnosis is in doubt. A low BNP gives them confidence not to keep trialing increasing doses of frusemide.

A CXR is not sensitive enough to rule out heart failure but can be useful to check for other pathology especially as it is often difficult to be sure of the diagnosis at initial presentation.

Expert Comment

ECGs are invariably abnormal in heart failure. The changes may however be quite subtle. The use of BNP to rule out heart failure in people with suspicious symptoms is a valuable aide in primary care .

Whilst the high negative predictive value of B-type natriuretic peptides assays enables general practitioners to effectively rule out heart failure, patients with elevated natriuretic peptides should be referred to a specialist for further assessment particularly to ascertain the aetiology of heart failure

Dr Gerry Devlin

7. A 69 year-old man has been on bendrofluazide and quinapril for the last three years. It was initiated by a previous GP because he was getting short of breath on a steep hill near his house. He has now moved from this location and feels well with no breathlessness. He asks if he can stop the medication. What role does BNP assay have in helping your decision?

| | You | Your Peers | GP Panel |
|---|-----|------------|----------|
| BNP has no clear role yet in diagnosing heart failure in those already on therapy | | 92 % | + |
| BNP results may rule out the presence of systolic dysfunction | | 4 % | |
| BNP results may confirm the presence of systolic dysfunction | | 3 % | |
| BNP results may guide the need for echocardiography | | 8 % | |

GP Panel

Most respondents understand that there is, as yet, no clear role for BNP in the diagnosis of heart failure for those already on therapy. BNP levels are influenced by many of the drugs, which are used for heart failure and it has not yet been established how this should be taken into account when interpreting results.

It will be interesting to see how our knowledge in this area evolves in the near future.

Expert comment

BNP must be interpreted cautiously in patients on diuretics. BNP can be reduced by diuretics and patients with “normal BNP” in this setting may have important LV dysfunction. Consider stopping the diuretic and repeating the assay in 4–6 weeks or referring for specialist opinion if confident of the diagnosis.

Dr Gerry Devlin

8. A 72 year-old woman has acute dyspnoea with classical clinical features of acute heart failure. What effect would BNP levels have on your immediate management?

| | You | Your Peers | GP Panel |
|--|-----|------------|----------|
| Would perform BNP testing and start treatment before results available | | 44 % | |
| Would perform BNP testing and await results before starting treatment | | 1 % | |
| Would delay BNP testing until after immediate management | | 1 % | |
| Would not perform BNP testing at all | | 54 % | + |

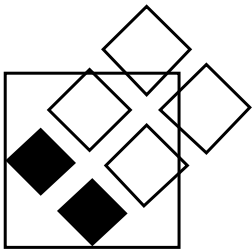
GP Panel

Respondents were somewhat divided on this question. The GP panel would not perform BNP testing for someone who was clearly in acute heart failure. They would however be highly suspicious of an acute cause, such as acute myocardial infarction, and would ensure that underlying pathology was managed. This may well mean hospital admission.

Expert Comment

I would perform a CXR to confirm the clinical suspicion of heart failure. Whilst BNP adds prognostic information in this setting (patients with very high levels do badly) current management strategies are not altered with the level and I would not routinely perform if the CXR shows pulmonary oedema.

Dr Gerry Devlin



bpac^{nz}
better medicine

www.bpac.org.nz

