Waitematā
District Health Board
Best Care for Everyone

Provider Healthcare Services
North Shore Hospital Campus
Shakespeare Road, Takapuna
Private Bag 93-503, Takapuna
Auckland 0740
Telephone: 09 489 0527
Facsimile: 09 486 8339

25 June 2020

[redacted]

Dear [redacted]

Re: OIA request - Haemochromatosis

Thank you for your Official Information Act request received 9 June 2020 seeking information about the access criteria for venesection in patients with haemochromatosis from Waitematā District Health Board (DHB).

Before responding to your specific questions, it may be useful to provide some context about our services.

Waitematā DHB serves a population of more than 630,000 across the North Shore, Waitakere and Rodney areas, the largest and one of the most rapidly growing DHBs in the country. We are the largest employer in the district, employing around 7,500 people across more than 80 locations.

In addition to providing services to our own population, we are also the metropolitan Auckland provider of forensic psychiatry, child disability services, child community dental services and community alcohol and drug services.

In response to your request, we can provide the following information:

1. **The criteria that is used to assess patients with haemochromatosis for venesection and separately for referral to a haematologist from 2010 to the present.**

The Auckland Regional HealthPathways website provides guidance on the assessment and management of patients with haemochromatosis. These guidelines were first published in December 2015 and remain current. The guidelines also include recommendations on when to refer to a haematologist. Prior to the publication of these guidelines, decisions about treatment or referral were made at the discretion of the individual clinician.

A copy of the current guidelines is attached for your reference – **Attachment 1**. You can also access this information online at: https://aucklandregion.healthpathways.org.nz/index.htm

2. **The dates the assessment criteria has changed**

The current guidelines for Haemochromatosis and Raised Ferritin were updated and published in December 2015.

3. If it has changed the reason for that change at each date

Our guidelines were reviewed and changed in 2015 to align with international guidelines. An abstract of the literature which prompted this review is presented below:

> *Waalen J, Felitti VJ, Gelbart T, Beutler E. Screening for haemochromatosis by measuring ferritin levels: A more effective approach. Blood. 2008;111(7):3373-3376.*
>
> *Because the penetrance of HFE haemochromatosis is low, traditional population screening measuring the transferrin saturation is unlikely to be cost-effective because the majority of subjects detected neither have clinical disease nor are likely to develop it. Three independent studies show that only patients with serum ferritin concentrations more than 1000 microg/L are at risk for cirrhosis, one of the main morbidities of haemochromatosis. Among 29,699 white subjects participating in the Scripps/Kaiser haemochromatosis study, only 59 had serum ferritin levels more than 1000 microg/L; 24 had homozygous mutant or compound heterozygous mutant HFE genotypes. In all but 5 of the other subjects, the causes of elevated ferritin were excessive alcohol intake, cancer, or liver disease. Screening for haemochromatosis with serum ferritin levels will detect the majority of patients who will be clinically affected and may detect other clinically significant disease in patients who do not have haemochromatosis genotypes. Because the ferritin level of the majority of adult homozygotes for HFE mutations does not rise over long periods of time, excluding subjects with serum ferritin levels less than or equal to 1000 microg/L should not result in missed opportunities for early treatment of patients who could benefit.*

4. The thresholds for venesection, including but not limited to whether any other conditions or predisposing conditions are reviewed or looked into, including pseudogout, whether the symptoms of iron overload such as extreme fatigue, joint pain, increasing frequency of calcium pyrophosphate deposition disease (CPPD) flares are put weighted or any other symptoms or conditions put forward by the referring physician are reviewed and taken into account and, if so, what factors are given what weight when deciding whether to either be seen by a haematologist, or whether they can have a venesection.

The Haemochromatosis and Raised Ferritin Guidelines on HealthPathways provide general information about the management of patients. All referrals to the haematology service are assessed by a consultant haematologist. Decisions about treatment are made by that clinician based on a combination of their clinical expertise, the information provided by the referring clinician and the clinical particulars of the individual patient.

5. I also want to know if the WDHB has any regard for the levels of iron saturation and serum iron put forward by Leukaemia and Blood Cancer New Zealand?

In response to your request, our Clinical Director has reviewed the information published by Leukaemia and Blood Cancer New Zealand. We are confident that our current HealthPathways guideline operates along the same general principles put forward by Leukaemia and Blood Cancer New Zealand.

6. I also request, the research papers/information that inform the venesection level and whether any regard has been had to overseas literature particularly in regard to iron saturation and serum ferritin levels.

Our current guidelines are based on published literature; the references for these are included in the guideline. We are operating as per international guidelines.

7. In essence I request a complete rundown on what the threshold is for being referred to a venesection in 2020 and how this has changed since 2010.

The access criteria for venesection and how this has changed since 2010 is detailed in the responses above. I trust that this information is helpful.

Waitematā DHB supports the open disclosure of information to assist community understanding of how we are delivering publicly funded healthcare. This includes the proactive publication of anonymised Official Information Act responses on our website from 10 working days after they have been released.

If you consider there are good reasons why this response should not be made publicly available, we will be happy to consider your views.

Yours sincerely

Mark Shepherd
Director Provider Healthcare Services
Waitematā District Health Board

HealthPathways

Haemochromatosis and Raised Ferritin

Background

About haemochromatosis

About haemochromatosis

- Hereditary haemochromatosis (HH) usually means the homozygous inheritance of the C282Y polymorphism of the HFE genes. A small number of patients are compound heterozygotes with the HFE C282Y and HFE H63D polymorphisms.
- 5% of people of North European descent are heterozygous for HFE C282Y (termed carriers).
- Heterozygotes do not develop haemochromatosis.
- 50% of patients with ferritin > 1000 micrograms/L do not have iron overload.
    - Other causes include fatty liver disease, high alcohol intake, and inflammatory conditions.
- In true iron overload, the transferrin saturation is significantly elevated, sometimes approaching 100%.
- In those with HH:
    - < 10% present with excessive iron absorption and iron deposition in the liver, pancreas, heart, endocrine glands, and joints causing organ damage.
    - as a group they do not experience any more symptoms than those without HH (although individuals can present with insidious, non-specific symptoms), and life expectancy is not shortened provided iron-overload is avoided or treated.
    - Ferritin levels of < 1000 is a good predictor for absence of organ damage from iron overload.

Assessment

Practice Point!

Genetic haemochromatosis is now frequently identified in asymptomatic patients and presymptomatic relatives of patients known to have the disease. Patients who do not fall into this category will only be identified if iron overload is detected and further investigated.

Investigation of Iron Overload

1. Measure ferritin. This provides some indication of the degree of iron loading, although it is an acute phase protein, and therefore may be elevated in inflammatory conditions.
    - If mildly elevated, < 400 micrograms/L in women and < 500 micrograms/L in men, consider infection, inflammation, malignancy, or liver disease, including fatty liver. If ferritin higher than these levels and is unexplained then arrange investigations as noted below.
        - Ferritin > 1000 micrograms/L in patients with haemochromatosis makes end organ damage more likely, especially cirrhosis.
        - Levels < 1000 micrograms/L are a good predictor for absence of cirrhosis, one of the main co-morbidities in haemochromotosis.
        - If ferritin is not > 1000 micrograms/L by the age of 50, it is unlikely that the patient will ever develop end organ damage.

2. Measure fasting transferrin:
    - Fasting transferrin saturation < 50% is not consistent with haemochromatosis and gene testing is usually not indicated.
    - A fasting transferrin saturation of > 50% needs further investigation.

Fasting transferrin saturation > 55%

Local physicians consider a 55% cut off to be an appropriate level to arrange further investigations. Guidelines have differing levels and may vary between men and women.

55% is considered a reasonable compromise between sensitivity and specificity.

        - Request HFE gene analysis if the patient is fit for management by venesection therapy and/or family screening is appropriate if a defect is found. Heterozygotes (carriers) may have slightly elevated transferrin but it is usually < 60%.
    - If normal transferrin saturation and elevated ferritin, look for other causes of elevated ferritin such as fatty liver, excess alcohol, and increased acute phase proteins, and treat the underlying cause, e.g., malignancy, infection, and inflammation.
    - A small number of patients with HH do not have the HFE gene mutation, and a liver biopsy might be required for diagnosis in patients with evidence of iron overload and hepatic damage. An alternative to liver biopsy is a MRI ferriscan which can accurately assess liver iron content.
3. Check liver function.

Management

1. Monitor mild elevations of ferritin on an occasional basis to observe the rate of increase, if any e.g., 6 to 12 monthly.
    - Heterozygotes (including compound heterozygotes) rarely have problems and do not need regular monitoring.
2. Venesection is not indicated where ferrritin remains < 800 to1000 micrograms/L as cirrhosis or other significant complications are extremely rare in such patients.[1,2]
    - Venesection is also extremely unlikely to relieve any non specific symptoms.
3. Therapeutic venesection is simple and effective and is indicated if ferritin is over 1000 micrograms/L

Therapeutic Venesection

If the patient meets the criteria for being a blood donor, venesected blood may be used in the donor pool.

Initially

1. Venesection every 1 to 2 weeks until the ferritin is in the normal range. Aim for a target level of ferritin ≤ 100.
2. Check CBC before each venesection and aim to keep Hb ≥ 110 g/L in men and ≥ 100 g/L in women. Ferritin levels at the time of venesection are useful for the patient to see that the levels are coming down.
3. The relevant service will monitor ferritin levels as appropriate.

Maintenance and monitoring

In many patients, maintenance venesections are not required, but they do require ongoing monitoring of the ferritin every 4 months. Re-venesection may be required if the ferritin is climbing over 600 to 700, although in many patients it takes years for this to occur.

To arrange therapeutic venesection, request as below.

- Commencing (or continuing) therapeutic venesection is appropriate in those patients with haemochromatosis who have a chance to prevent end organ damage from iron overload.
- As end organ damage occurs after many years of iron toxicity (very high ferritin e.g., ≥ 1000 micrograms/L), a patient with less iron overload or short life expectancy will not benefit from venesection.
- Some homozygous HH may not require venesection but need 6 monthly to annual ferritin and transferrin.

4. For patients with ferritin > 1000 micrograms/L, monitor for end organ damage e.g., diabetes, liver damage, arthritis, and heart disease.
5. Advise patients to avoid iron supplements and/or vitamin C supplements.
6. Genetic counselling is important.

Genetic counselling

- Haemochromatosis is an autosomal recessive disorder.
  - Siblings of an index case have a 1 in 4 chance of having the same genotype.
  - If the partner of an index case is an HFE carrier the offspring have a 1 in 2 chance of having haemochromatosis, otherwise they will be obligate HFE carriers but not develop iron overload.
- Screen all adult first degree relatives for HH, with blood tests for serum ferritin and transferrin saturation. Do not screen children or adolescents, as iron overload damage does not occur at this age group (except in the very rare cases of juvenile haemochromatosis due to mutations in the hepcidin gene or haemojuvelin gene).
- Only arrange HFE gene study in relatives if the transferrin is > 55% or ferritin ≥ 200 micrograms/L in women or ≥ 500 micrograms/L in men. As 1 in 9 people are carriers of haemochromatosis and have no health implications and only 2% of homozygotes have any clinical effect, it is important to only do HFE gene testing in patients who are more likely to have clinical implications.
- Provide advice to homozygotes and heterozygotes regarding the inheritance of HH.

- It is not clear why two first degree relatives, both with HH, may have significantly different levels of iron overload.
- Even if the index case is not heavily iron overloaded, offer biochemical screening of ferritin and transferrin saturation to all first degree relatives.

7. Patients who have an elevated ferritin but are negative for the haemochromatosis genes do not need venesection but should be investigated for other causes of an elevated ferritin. Discussion with an appropriate specialist may be indicated.

Request

- Request therapeutic venesection as indicated, from the relevant service. The majority of patients can be venesected by the New Zealand blood service.
- Refer all homozygous HH with iron related tissue damage to the appropriate service, e.g.:
  - Gastroenterology Department if liver dysfunction
  - Cardiology Department if cardiac dysfunction
  - Rheumatology Department if arthritis
- Consider haematologist assessment for homozygous HH with iron overload if the management plan is not clear or if negative HFE gene with raised transferrin and ferritin.
- Urgent or written advice is available.

Information

Clinical Resources

- Waitemata DHB – Haemochromatosis Protocol
- Patient – Hereditary Haemochromatosis
- NSW Health Centre for Genetics Education – Hereditary Haemochromatosis
- Bacon BR, Adams PC, Kowdley KV, Powell, LW, Tavill AS. Diagnosis and Management of Hemochromatosis:2011 Practice Guideline by the American Association for the Study of Liver Diseases. Hepatology. 2011;54(1):328-343

BMJ Learning – The Royal New Zealand College of General Practitioners Modules [requires registration]

- Haemochromatosis: a guide to diagnosis and treatment

Patient Information

Patient – Haemochromatosis

Sources

References

1. Waalen J, Felitti VJ, Gelbart T, Beutler E. Screening for hemochromatosis by measuring ferritin levels: A more effective approach. Blood. 2008;111 (7):3373-3376.
2. Adams PC, Barton JC. How I treat hemochromatosis. Blood. 2010;116(3).

Page Information | People

Information about this HealthPathways document (190402):

Last Updated: December 2015
Last Reviewed: December 2015
Keywords:

Have you read the disclaimer?

© 2008-2020 Counties Manukau DHB on behalf of the metro Auckland DHBs

No content in this website may be reproduced or transmitted in any form or by any means, electronic, mechanical, recording, or otherwise, without the prior written approval of Counties Manukau DHB on behalf of the metro Auckland DHBs and Canterbury District Health Board (where the original source of the content was from Canterbury District Health Board).

For information on obtaining permission for reproduction or transmission of the content please contact copyright@healthpathwayscommunity.org.