The iron salute

By Sue Carson

Medication reviews can be completed successfully, resulting in safe medication use and patient wellbeing, in rural areas where there is not an accredited pharmacist.

Mr B, in this case, lives in a small coastal community, approximately 90 km from a major town. The accredited pharmacists in the major town are few, swamped with home medication reviews (HMRs) in their own community, and cannot travel the distance to provide HMRs for people such as Mr B.

So as to provide an HMR service to patients in Mr B’s township and to maintain an excellent relationship with the general practitioners (GPs) in that community, the local pharmacist conducts the HMR interview. The interviewing pharmacist uses a pro forma medication history form provided by the accredited pharmacist to prompt questioning and gather information for the comprehensive medication history required for writing the report. This information is provided to an accredited pharmacist more than 450 km away, who then compiles the HMR report.

GPs, patients, community pharmacies and accredited pharmacists all agree that this process can work in areas where patients do not have access to an accredited pharmacist.

(Of course, the accredited pharmacist takes responsibility for the recommendations and information in the HMR report. An agreement defining responsibilities should be in place between the two parties involved.)

The patient

Mr B is a 72-year-old gentleman who is referred by his GP for an HMR. Mr B takes multiple medications and is complaining of inexplicable fatigue and dizziness. The referral for the HMR is made by a new medical practitioner, as Mr B’s regular GP has moved practices.

Current medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>Thiamine</td>
<td>100 mg each morning</td>
</tr>
<tr>
<td>Calcium</td>
<td>600 mg each morning</td>
</tr>
<tr>
<td>Folic acid</td>
<td>5 mg each morning</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1,500 mg three times daily</td>
</tr>
</tbody>
</table>

Amlodipine + atorvastatin
5/40 mg each morning

Metoprolol 50 mg twice daily

Clopidogrel 75 mg each morning

Pantoprazole 40 mg each morning

Valproate 500 mg each night.

Medical history

- Cerebral vascular accident (CVA) 12 months ago
- One seizure 10 months ago
- Paroxysmal atrial fibrillation
- Haemochromatosis
- Prostate cancer five years ago.

Additional information

The medication history interview revealed that Mr B experienced dizziness after taking his morning tablets. The ‘giddiness’ (as Mr B describes it) can last for an hour or, at times, can trouble Mr B throughout the day. Mr B currently smokes cigarettes and has smoked 20 cigarettes a day for approximately 50 years. He has more than three standard serves of alcohol per day. His body mass index is normal.

Learning objectives

After reading this article you should be able to:

- discuss the aetiology and symptoms of haemochromatosis
- describe the genetic link associated with haemochromatosis
- suggest management approaches for this condition
- explain the consequences of inappropriate management of haemochromatosis.

Competencies addressed:

3.1.1, 3.1.2, 3.1.3, 3.1.4, 3.2.1, 3.2.2, 3.2.3

Sue Carson is a Lecturer at James Cook University and a consultant pharmacist based in Townsville in Queensland.
Mr B has trouble sleeping at night and he has tried oxazepam without success. He is extremely fatigued during the day and has frequent naps. Mr B could not recall exactly when thiamine, calcium, folic acid and magnesium were initiated but estimated it was around the time of his CVA or seizure. He remembered that the valproate was introduced after his single seizure.

Pathology information
Electrolytes and creatinine (0.10 mmol/L) were within the normal reference ranges. Neither liver function test results nor iron study information was available.

Venesection had not been performed for at least 12 months. Venesection implies the withdrawal of blood via phlebotomy.

Haemochromatosis – iron overload
Haemochromatosis is a metabolic disorder caused by excessive intestinal iron absorption, resulting in deposition of iron in cells, leading to tissue and organ damage. The normal iron content of the body equals iron loss. If intestinal mucosal iron absorption is 3–4 g and this level is maintained for at least 12 months. Venesection implies the withdrawal of blood via phlebotomy.

The normal iron content of the body is 3–4 g and this level is maintained if intestinal mucosal iron absorption equals iron loss. Menstruating women lose approximately 1.5 mg of iron per day, and adult males 1 mg per day.

If the absorption of iron from the intestinal mucosa is greater than iron loss, then iron can accumulate in tissues and, with time, cause significant tissue damage. Iron overload can cause arthralgia, diabetes mellitus, hypogonadotropic hypogonadism, cardiomyopathy and cirrhosis of the liver. The liver is often the first organ affected. Cardiac failure, liver failure, hepatic carcinoma or portal hypertension are the principle causes of death in untreated patients with this condition. In advanced disease, the colour of the skin may change to appear metallic gray, or to having a slate blue hue.

Early in the disease, symptoms can be vague, making diagnosis difficult. These vague symptoms may include lethargy, fatigue, abdominal pain and polyarthropathy. In the past, haemochromatosis was called ‘bronze diabetes’ due to hyper-pigmentation, which is also an early symptom of iron overload. The arthropathy associated with haemochromatosis can occur in the second and third metacarpophalangeal (MCP), which makes it difficult for the patient to form a fist. This clinical sign is referred to as the ‘iron salute’.

Secondary causes of haemochromatosis
Acquired iron overload can result from thalassaemia (an iron overload anaemia) or sideroblastic anaemia. This acquired form of haemochromatosis presents with similar symptoms as the genetic form.

Diagnosis
In making a diagnosis, family history is considered and genetic testing may be recommended. Screening the family members of patients with confirmed haemochromatosis will often uncover asymptomatic relatives. In patients with haemochromatosis, iron studies will reveal elevated plasma iron, an increase in transferrin saturation and elevated ferritin levels. Liver function tests or liver biopsy will determine the extent (if any) of liver damage.

Managing haemochromatosis
The goal of management of this condition is to prevent organ damage as, if patients are treated in the pre-cirrhotic phase, life expectancy is normal. This is done by regular venesection so as to restore ferritin levels to the lower end of the normal reference range (see Table 1). This may require venesection of 500 mL of blood weekly, with maintenance venesection three times per year so as to keep serum ferritin concentration below 100 mcg/L.

Venesection can reverse hepatomegaly, improve liver function, decrease skin pigmentation and reverse cardiac failure. Diabetes improves in approximately 40% of patients. However, venesection does not improve hypogonadism or arthralgia. Chelating agents such as deferasirox are useful in chronic iron overload due to frequent blood transfusions, but it too is not indicated, or effective, in hereditary haemochromatosis.

Medication review issues
From the interview with Mr B, and from the concerns raised by the GP in the referral, the following issues were considered:
1. Pharmacological cause of morning dizziness
2. Cause of fatigue
3. Simplification of medication regimen
4. Management of insomnia
5. Lifestyle advice (nicotine use and alcohol consumption).

Table 1. Comparison of iron values in normal subjects and patients with haemochromatosis

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Symptomatic haemochromatosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma iron (m/L)</td>
<td>9–27</td>
<td>32–54</td>
</tr>
<tr>
<td>Total iron-binding capacity (micromole/L)</td>
<td>45–66</td>
<td>36–54</td>
</tr>
<tr>
<td>Transferrin saturation (%)</td>
<td>22–46</td>
<td>50–100</td>
</tr>
<tr>
<td>Serum ferritin (mcg/L)</td>
<td></td>
<td>900–6000</td>
</tr>
</tbody>
</table>

Men                  | 20–250   |
Women                | 15–150   |
**Actions and recommendations**

**Morning dizziness after taking tablets**

Mr B takes all of his medications in the morning. Atorvastatin, felodipine and metoprolol are all commonly associated with causing dizziness.a

**Recommendation:** Mr B may benefit from taking the atorvastatin/felodipine tablet at night, before retiring. A 24 hour blood pressure study may provide useful information as to whether hypotension may be the cause of his dizziness. Mr B, however, did not describe his dizziness as due to changes in position.

**Fatigue**

Fatigue is an early sign of iron overload, especially if ferritin levels are elevated.

**Recommendation:** As Mr B has haemochromatosis and has not had venesection for more than 12 months, it would be appropriate for the GP to undertake iron studies and to check Mr B’s liver function. Ideally Mr B would have had his hepatic function assessed at baseline before the introduction of valproate.

**Simplification of regimen**

Fasting blood glucose should be reviewed to exclude diabetes, another complication of haemochromatosis. Mr B takes ten tablets each morning. The indication for the thiamine, folic acid, magnesium and calcium was not clear from the referral, nor from Mr B.

**Recommendation:** The GP could review Mr B’s calcium and magnesium status and adjust doses as necessary. Assessing the patient’s folic acid, vitamin B12 and B13 levels may direct the need for continued supplementation and potentially reduce his tablet load.

**Management of insomnia**

Oxazepam was not effective in providing sedation for Mr B. If the source of Mr B’s daytime fatigue is determined and effectively managed, then his sleep may improve.

**Recommendation:** The reviewing pharmacist could discuss sleep hygiene. Temazepam could be used on the nights that sleep escapes Mr B, but the use of temazepam should be restricted to only three nights per week, to avoid physiological and psychological dependence.

**Lifestyle advice**

If liver function tests are performed and hepatic damage is revealed, Mr B should be advised to abstain from consuming alcohol. There is a 10-fold increase in the risk of cirrhosis in patients with hereditary haemochromatosis who consume alcohol.1 Cigarette smoking is a known risk factor for cardiovascular disease, and the accredited pharmacist could emphasise the implications of nicotine use and offer suggestions for cessation.

**Summary**

Haemochromatosis can be a life-threatening condition if it is not treated. Appropriate management with venesection prevents serious complications and minimises tissue damage. Haemochromatosis can be overlooked, as iron build-up in tissues can take many years to occur and the patient may only become symptomatic after substantial organ damage has already taken place.

Pharmacists working in community pharmacy are in a position to discuss symptoms and family history and refer patients to their GP for investigation, if symptoms and family history suggest haemochromatosis. Although medication is rarely used in the management of haemochromatosis, medication review pharmacists can ensure hepatic damage from other medications does not occur.

This HMR resulted in positive feedback from Mr B’s GP, with all recommendations implemented.

**References**


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**Questions**

1. **Males with hereditary haemochromatosis account for what percentage of all hereditary haemochromatosis cases?**
   a) 20%.
   b) 1 in 300.
   c) 60%.
   d) 10%.
   e) 1 in 2.

2. **Which of the following is not an early symptom of haemochromatosis?**
   a) Metallic grey skin colour on face and neck.
   b) Fatigue.
   c) Abdominal pain.
   d) Polyarthropathy.
   e) Lethargy.

3. **Venesction is undertaken in male patients with haemochromatosis to keep serum ferritin levels below:**
   a) 150 mcg/L.
   b) 130 mcg/L.
   c) 100 mg/L.
   d) 100 mcg/L.
   e) 300 mcg/L.

4. **Elevated ferritin levels can be caused by:**
   a) thalassaemia.
   b) hereditary haemochromatosis.
   c) repeated blood transfusions.
   d) sideroblastic anaemia.
   e) all of the above.

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A score of 3 out of 4 attracts three quarters of a credit point.