Haemochromatosis International

– Haemochromatosis International Taskforce.

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Introduction

Although guidelines are available for hereditary haemochromatosis (HH), a high percentage of the recommendations within them is not shared between the different guidelines [1]. Our main aim is to provide an objective, simple, brief and practical set of recommendations about therapeutic aspects of the *HFE* haemochromatosis, based on published scientific studies and guidelines.

We need to reach agreement, if possible, on the treatment parameters and relevant issues.

We need to have the best available reference material to support our recommendations.

In due course, we intend to present these recommendations in a form that is reasonably comprehensible to patients and people without medical training.

The following is a draft of the pre-final recommendations which, after this round of comment, will be presented at Haemochromatosis International meeting on 12th May 2017 in Los Angeles.

Haemochromatosis International

Therapeutic recommendations in *HFE* haemochromatosis

Draft of Pre-final document

Treatment

Venesection (phlebotomy therapy) is the standard treatment for patients with HH having been used for more than 60 years. It is effective in reducing morbidity and mortality of HH [2].

Who to treat and when to start

Patients with *HFE* p.Cys282Tyr (C282/C282Y) homozygous genotype and biochemical evidence of iron overload, i.e., increased serum ferritin (>300 µg/L in male and postmenopausal female and >200 µg/L in premenopausal female) and increased fasting transferrin saturation (≥ 45%) [3, 4].

Considerations:

- A judgment has to be made for each individual patient taking into account their ferritin level, age, gender, local reference value and co-morbidities.
- Recent studies observed a beneficial effect of early and sustained management of patients with iron excess, even when it is mild [5].
- High serum ferritin values are very common and the most frequent causes are not associated with HH, but with metabolic syndrome, dysmetabolic iron overload syndrome, inflammation (ferritin is an acute-phase protein), alcoholism, and liver damage. Thus, it is critical to investigate rigorously the cause of high serum ferritin values.
- Magnetic resonance imaging (MRI), when available, for investigating evidence of iron overload in the liver (or in other organs) can be valuable.

How to treat

Initial or induction phase

A venesection schedule of the order of 400-500 mL, considering body weight, weekly or every two weeks has been proposed [3, 6].

The objective in this phase is usually to reach serum ferritin ≤ 50 µg/L. Serum ferritin should be checked once a month until the values reach the upper normal limits, and every two weeks thereafter, until the final goal of SF is reached [3, 6].

Considerations:

-The volume and frequency of the venesections should be adapted to the clinical characteristics and tolerance of the patient.

- Venesections can be performed in a clinic, hospital, transfusion/blood donor centers or in certain circumstances at home (under the supervision of a nurse).

- Patients should be well hydrated and fed.

- Tolerance: clinical data (general tolerance, blood pressure); haemoglobin (Hb levels should not decrease below 11g/dL or by more than 2g/dL compared with baseline levels) [6].

-A growing number of patients with uncomplicated haemochromatosis donate blood or qualify as blood donors in certain countries. Once iron levels have been normalized, blood removed from therapeutic phlebotomy can be safely used for transfusion [7].

Maintenance phase

The maintenance phase follows the induction phase.

The patient with HH needs lifelong follow-up.

One venesection every 2 to 4 months, depending on the patient's iron status [3, 6].

Efficacy: the usual aim is to maintain ferritin levels between 50 and 100 µg/L [3, 4].

Considerations:

- The frequency of maintenance venesection varies among individuals, some patients require monthly venesections, whereas others may need only 1-2 venesections per year [4].

- Haemoglobin levels should not be < 11g/dL.

- It may be useful to assess the Hb value preceding the next venesection, especially in older patients, who are more susceptible to anaemia and chronic blood losses.

- Serum ferritin should be checked every other venesection (at the same time as haemoglobin).

- Fasting transferrin saturation should also be checked (twice a year, together with haemoglobin and serum ferritin).

When to stop

Patients who have had iron overload should never stop having their iron status monitored and their treatment planned in the light of their iron status.

Special attention for patients with complications

In some cases, patients with liver cirrhosis may need special care during treatment due to loss of blood pressure.

Patients with arthritis are often treated with nonsteroidal anti-inflammatory drugs, which may cause gastrointestinal bleeding and low hemoglobin levels. Where this occurs it may contraindicate venesections.

Complementary options

Diet

A healthy varied diet should be eaten, avoiding foods with iron fortification such as breakfast cereals. Iron and vitamin C supplementation and high alcohol consumption should also be avoided [4].

Dietary restriction should not replace phlebotomy therapy for haemochromatosis patients.

Proton pump inhibitors (PPI)

A recent study showed the effects of PPI drugs on reduction of the frequency of phlebotomy in patients with HH [8].

Chelation therapy

Iron chelation is usually indicated for iron overload related to chronic anaemias that need repeated transfusions. However, iron chelators are an alternative treatment (or adjuvant) used in rare and special cases of HH, when venesections are medically contraindicated, simply impossible owing to poor vein conditions, or the efficacy was not achieved with venesections.

Possible future of HH therapeutics

Hepcidin supplementation might, in future, become a potential adjunct treatment to venesection in the induction phase or a replacement for the venesection maintenance phase.

References

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