Haemochromatosis: evaluating the effectiveness of a novel patient self-management approach to venesection as blood donation

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ABSTRACT

AIM: We set out to evaluate the effectiveness of a new model of self management of haemochromatosis, whereby patients with stable ferritin control were discharged from the New Zealand Blood Service (NZBS) therapeutic venesection clinic and educated to manage their own venesection by regular blood donation and annual serum ferritin check by their general practitioner.

METHOD: Data regarding the frequency of blood donation and serum ferritin level were collected from the NZBS and Concerto records of haemochromatosis patients in the Wellington region who had been discharged back to the care of their general practitioner between January 2014 and June 2015.

RESULTS: Of the 107 patients, 93% continued to donate blood after discharge. A serum ferritin level was checked in 78% of patients by their general practitioner. The mean number of blood donations per year decreased after discharge, with a corresponding rise in the average ferritin level (difference 28 mcg/L; range 13–43 mcg/L; p<0.005).

CONCLUSION: The new model of self management was effective for the majority of patients who were discharged from the therapeutic venesection clinic. Longer follow up is required to assess the overall pattern of ferritin control in patients who self manage their haemochromatosis by regular blood donation.

Haemochromatosis is an autosomal recessive condition in which mutations in the HFE gene (Hereditary Fe [iron] gene) can lead to excessive and dysregulated intestinal iron absorption with progressive iron deposition and injury to multiple organs.1,2 Although the majority of patients are asymptomatic, left untreated, this disease can cause cirrhosis, endocrine problems such as diabetes, thyroid dysfunction, gonadal dysfunction, cardiac problems, arthritis and other complications.1,4 Early diagnosis and treatment is important to prevent development of complications.

Treatment of haemochromatosis aims to reduce body iron stores by regular venesection. Once iron stores have been reduced, the goal of maintenance venesection is to avoid iron re-accumulation. There are no controlled trials to support a specific target ferritin level.2 A target maintenance ferritin level of 50–100mcg/L is recommended by the Best Practice Advocacy Centre (BPAC) of New Zealand,2 as well as numerous international guideline groups and journals.2,4,6

The New Zealand Blood Service (NZBS) provides a therapeutic venesection service for people with haemochromatosis at a number of sites across the country. Patients are referred by their general practitioner or specialist to the NZBS for regular venesection and monitoring of their serum ferritin. The therapeutic venesection clinic is run by medical staff and specialist nurses.
Patients undergo regular venesection following a management guide developed by the NZBS. Initially, patients undergo an induction phase to achieve a target ferritin of 30–50mcg/L. Once this is achieved, patients enter the maintenance phase. This involves regular venesection tailored to ferritin levels. Normally, patients will require venesection every two to four months.

Prior to late 2013, patients would continue to attend the venesection clinic once their serum ferritin reached the target range. Provided they met usual blood donor criteria, patients became ‘therapeutic donors’ ie, their blood was managed in the same way as standard voluntary donations. They continued to attend the clinic for therapeutic venesection and monitoring of ferritin levels.

The number of patients referred for therapeutic venesection continues to increase. Long-term venesection is required in order to maintain ferritin levels within an acceptable range. In late 2013 the New Zealand Blood Service implemented a new model for the management of haemochromatosis whereby patients who met the eligibility criteria to become blood donors were discharged from the venesection clinic when their serum ferritin reached the target range, and educated to manage their own venesection by regular blood donation and an annual serum ferritin check by their general practitioner.

We set out to evaluate the effectiveness of the new model of patient self-management of haemochromatosis by regular blood donation in the Wellington region. Specifically, we examined patient compliance and control of serum ferritin levels.

Method

Data were collected from the NZBS records of haemochromatosis patients that had been discharged back to the care of their general practitioner between January 2014 and June 2015. These are patients that had received therapeutic venesection via the NZBS and whose iron levels were deemed stable by the discharging doctor or nurse. For the majority of patients, this meant a serum ferritin of less than 100mcg/L. These patients are no longer being actively managed via the therapeutic venesection clinic. They make appointments to donate in the same way as whole blood donors using either the NZBS call centre or online appointment system. They are considered to be ‘normal whole blood donors’ and can be bled at either mobile or static collection sites.

In order to become normal whole blood donors, patients met the following eligibility criteria:

- Normal liver function tests
  - At least the last two liver function tests were normal if the highest ferritin value was greater than 500mcg/L.
  - The last liver function test was normal if the highest ferritin value was less than 500mcg/L.
- No documented cirrhosis, cardiac disease or diabetes due to iron overload.
- Met the usual criteria for acceptance of blood donors in New Zealand.

For each eligible patient, a control period was identified in the 12–36 months prior to discharge from the clinic, to allow comparison of the frequency of venesection and ferritin level before and after discharge from the therapeutic clinic.

In order to allow comparison of maintenance venesection before and after discharge, the following inclusion criteria were used for the study:

- The patient was actively undergoing venesection prior to discharge.
- The patient had been referred to the therapeutic clinic at least 36 months prior to discharge (in order to ensure that the patient was in maintenance rather than induction phase in the control period prior to discharge).
- A ferritin result was available within 12 months prior to the discharge date (to allow comparison between pre- and post-discharge ferritin results).
- At least 12 months of follow up was possible following discharge from the therapeutic clinic.
- The patient was discharged to their general practitioner (not to a specialist haematology service).
- The patient’s NZBS medical file was available for review.
Data collection
For each patient, the number of blood donations (including all therapeutic venepunctures) during the control period and the post-discharge period was obtained using the New Zealand Blood Service “eProgesa” database. The average number of donations per year in each period was then calculated.

Serum ferritin results at the beginning and end of the control period were obtained from the patient files. The serum ferritin result after discharge was obtained via the electronic Concerto “Regional Lab Results”. If a result was not available on this electronic system, the patient’s GP practice was contacted. For patients who did not have a follow-up ferritin result, the GP practice was asked whether the patient was an enrolled patient and whether the patient was on a recall system to have an annual ferritin check.

The model was identified as “successful” for those patients who continued to donate after discharge and who also had their ferritin checked. The model was identified as “partially successful” for patients who either continued to donate but did not have their ferritin checked, or did not donate but had their ferritin checked. The model was identified as “failure” for patients who did not donate after discharge and did not have their ferritin checked.

One hundred and seventy patients were initially identified from the NZBS records, 63 patients did not meet the inclusion criteria, leaving a study group of 107 patients.

Statistical analysis
SPSS version 22 was used to compare ferritin levels, numbers of donations per year and follow-up period in the time intervals: from beginning of control period to end of control period, and from end of control period to the most recent evaluation. Mean values were compared using both paired t tests (which assume normally distributed data) and Wilcoxon rank sum tests (which do not). The results were the same, and so only the t test results are reported here. The level of ferritin control was also compared between time points by defining the subjects as being <100mcg/L, 100–200mcg/L, or 200–500mcg/L. To compare the subjects grouped ferritin results over time, the McNemar-Bowker extension of McNemar’s test was used. This statistic is a chi-squared statistic, which tests whether there is a consistent trend over time, with subjects moving either to a higher or a lower group.

Results
Of the 107 patients included in the study, 81 patients were male (76%) and 26 patients were female (24%). The average patient age was 54 years. The average duration of follow up was 25 months in the control period, and 28 months in the post-discharge period.

Of the 107 patients, 100 patients (93%) continued to donate blood after discharge. Seven patients (7%) did not donate blood after discharge. Twenty-two patients (21%) continued to donate at an increased frequency compared to donations in the control period. Twenty-two patients (21%) continued to donate at an increased frequency compared to donations in the control period. Forty-one patients (38%) continued to donate at a decreased frequency compared to the control period. Thirty-seven patients (35%) did not change their frequency of donations in the two periods (Figure 1).

Figure 1: Donations after discharge from therapeutic clinic.
Follow-up ferritin

Of the 107 patients, 83 patients (78%) had a follow-up serum ferritin level checked after discharge from the therapeutic venesection clinic. Twenty-four patients (22%) did not have a serum ferritin level checked. Of the 24 patients who did not have a follow-up ferritin checked, 20 patients (83%) were not on a recall system at their GP practice. Four patients were on a recall system (17%), however, they did not attend to have their blood test despite being sent reminders.

New model success or failure?

The new model was identified as “successful” for 76 patients (71%) as they continued to donate after discharge and had their ferritin checked. The model was identified as “partially successful” for 31 patients (29%). Twenty-four patients (22%) continued to donate and did not have their ferritin checked. Seven patients (7%) did not donate, however, they did have their ferritin checked.

No patient failed to both donate and have his or her ferritin checked; therefore, the model was not identified as a “failure” for any patient.

Comparison of serum ferritin level and frequency of blood donations during the therapeutic venesection programme versus after discharge

Figure 2 shows that at the beginning of the control period, 89 patients (83%) had a serum ferritin of <100mcg/L, 16 patients (15%) had a serum ferritin of 100–200mcg/L and two patients (2%) had a serum ferritin of 200–500mcg/L. No patient had a serum ferritin of >500mcg/L.

At the end of the control period, that is, at the time of discharge from the therapeutic venesection clinic, 77 patients (72%) had a serum ferritin of <100mcg/L, 27 patients (25%) had a serum ferritin of 100–200mcg/L and three patients (3%) had a serum ferritin of 200–500mcg/L (Figure 3). No patient had a serum ferritin of >500mcg/L.

At the follow-up point after discharge, 24 patients (22%) had not had their ferritin checked (Figure 3). Of the patients who did have their ferritin checked, 47 patients (57%) had a serum ferritin of <100mcg/L, 27 patients (33%) had a serum ferritin of 100–200mcg/L and nine patients (11%) had a serum ferritin of 200–500mcg/L. No patient had a serum ferritin of >500mcg/L.

Table 1 outlines the serum ferritin level and average number of donations per year during attendance at the therapeutic venesection clinic (control period) and after discharge from the clinic. The serum ferritin level measured after discharge was significantly higher on average than the serum ferritin level at the end of the clinic (mean difference 28mcg/L, 95% confidence interval 13–43mcg/L, p<0.0005). Additionally, the average number of donations per year was lower after discharge than before discharge (difference of 0.6 donations per year, 95% confidence interval 0.3–0.8, p<0.0005). The follow-up times were longer after discharge than pre-discharge (difference of three months, 95% confidence interval 2.0–3.9, p<0.0005). Equivalent results were found when using the Wilcoxon test (p<0.0005).

Figure 2: Serum ferritin value at the beginning and end of the control period, and post discharge.
Table 1: Comparison of serum ferritin level, number of donations and duration of follow up during the control period and the post-discharge period.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. Dev</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Comparison between control period and post-discharge period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferritin result at end of control period (mcg/L)</td>
<td>79</td>
<td>49</td>
<td>65</td>
<td>11</td>
<td>249</td>
<td>Mean difference: -28 95% CI: -43 to -13 P&lt;0.0005</td>
</tr>
<tr>
<td>Ferritin result after discharge (mcg/L)</td>
<td>106</td>
<td>76</td>
<td>91</td>
<td>15</td>
<td>337</td>
<td></td>
</tr>
<tr>
<td>Average number of donations per year during control period</td>
<td>3</td>
<td>1.3</td>
<td>3</td>
<td>.5</td>
<td>6.5</td>
<td>Mean difference: 0.6 95% CI: 0.3 to 0.8 P&lt;0.0005</td>
</tr>
<tr>
<td>Average number of donations per year: From discharge date to June 2016</td>
<td>2.5</td>
<td>1.2</td>
<td>2.6</td>
<td>.0</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>Duration of control period (months)</td>
<td>25</td>
<td>4.7</td>
<td>25</td>
<td>8</td>
<td>39</td>
<td>Mean difference: -3.0 95% CI: -3.9 to -2.0 P&lt;0.0005</td>
</tr>
<tr>
<td>Duration of follow-up period after discharge (months)</td>
<td>28</td>
<td>2.6</td>
<td>29</td>
<td>15</td>
<td>36</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 compares the serum ferritin level over time. The serum ferritin level after discharge was more likely to be in a higher group than the ferritin level at the end of the venesection clinic (p=0.005).

Table 2: Comparison of change in serum ferritin level over time.

<table>
<thead>
<tr>
<th>Ferritin result post discharge (mcg/L)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>200–499</td>
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<tr>
<td>Ferritin result at the end of control period (mcg/L)</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>% of Total</td>
</tr>
</tbody>
</table>

Figure 3 examines the relationship between changes in serum ferritin level and changes in the number of donations. The change in ferritin level was negatively correlated with the change in the number of donations (p<0.0005).
Discussion

This study showed that after discharge from the NZBS therapeutic venesection clinic, 93% of haemochromatosis patients continued to donate blood. Seventy-eight percent of patients had a follow up serum ferritin level checked. Of the patients that did not have a follow up serum ferritin level checked, 83% were not on a recall system by their general practice.

Based on our criteria of ongoing blood donation and monitoring of serum ferritin after discharge from the therapeutic venesection clinic, the new model of patient self management was successful for the majority (71%) of patients who were eligible for the scheme. Twenty nine percent of patients were partially successful, in that they either continued to donate or had their serum ferritin level checked. No patient failed to achieve at least one of the criteria.

The mean number of blood donations after discharge from the venesection clinic was lower than that during the maintenance phase when patients were attending the clinic.

Several factors are likely to affect donation frequency and serum ferritin control after discharge from the therapeutic venesection clinic. As the patient no longer receives appointment times for venesection after discharge, it becomes his or her responsibility to remember to attend to donate blood. Furthermore, as blood tests to monitor serum ferritin are no longer performed at the blood donor centre after discharge, it becomes the patient’s responsibility to attend the community laboratory for a blood test, and also to liaise with his or her general practitioner regarding serum ferritin control.

The period of monitoring of patients in the self-management phase was relatively short and it is probably too early to assess the overall effectiveness of the new model. In particular it will be important to evaluate the overall pattern of ferritin levels over a longer period to ensure that patients are able to modify donation frequency based on their ferritin results.
on the trend in ferritin level. Ferritin levels may have increased in many patients during the period of monitoring but it is reassuring to see that in no patient did this increase to more than 500 mcg/L.

The number of blood donations may also be influenced by factors that are outside of patient control. For example, patients may present to donate but be deferred due to various health reasons. A short-term deferral is unlikely to have significant consequences for overall control of ferritin levels. However, patients developing criteria that will lead to longer or permanent deferrals may need to be referred back to the clinic for ongoing venesection.

This study was limited by its retrospective design, and the control and follow-up period for each patient was variable. Additionally, not all patient files were available. Further, the follow-up time was short, as the new model was implemented two and a half years ago. Nonetheless it showed that many patients continued to donate after discharge from the therapeutic venesection clinic, albeit with decreased frequency.

When patients are discharged from the therapeutic venesection clinic they receive a letter outlining the ongoing need to donate and have their ferritin checked. Compliance might be improved if clearer written instructions are given to them outlining the transition of responsibility to the patient to donate blood as a method of self-management of their haemochromatosis.

For patients who do not donate blood in a 12-month period, reminder letters or phone calls via the New Zealand Blood Service may also improve compliance. Systems are now being developed to ensure that this occurs.

Twenty-two percent of patients in the study failed to have their serum ferritin level monitored after discharge. Further steps could be taken to increase follow-up rates, such as reminders from more general practices for patients to have a follow-up serum ferritin level checked annually. Furthermore, on discharge from the therapeutic clinic, clear recommendations for patients to have their own reminder system, for example, using a calendar on their phone may be useful.

This study also highlighted that some patients were discharged from the therapeutic clinic with serum ferritin levels exceeding 100mcg/L. This is not consistent with the clinical protocols developed for the new model. The therapeutic venesection clinic provides an opportunity for frequent venesection with close monitoring, and further attempt should be made to reduce iron stores in these patients prior to discharge.

Competing interests:
Nil.

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