Hemochromatosis patients as voluntary blood donors

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The present study was designed to investigate hemochromatosis patients' suitability as blood donors as well as their perceptions and experience with the current public donation system. Participants were gathered from a list of current hemochromatosis patients (n=120) and members of the Canadian Hemochromatosis Society (n=1000). Of the 1120 surveys mailed out to these groups, 801 surveys were returned completed. The sample respondents had a mean age of 57.44 years (SD=12.73; range 19 to 87 years), and 57% were men. It was found that 20% (160) of the respondents have donated blood since their diagnosis; however, only 12% of the respondents indicated that they use voluntary blood donation as a means of maintaining their iron levels. Forty per cent of the respondents indicated that they had been refused from voluntary donation. Despite the fact that in May 2001 the Canadian Blood Services, in collaboration with the Canadian Hemochromatosis Society, began a promotion campaign to encourage hemochromatosis patients to become voluntary blood donors, the present study found that 15% of the respondents reported having been refused from the voluntary blood donation service due to the diagnosis of hemochromatosis. With respect to quality of life, it was found that individuals who donate blood were generally healthier with respect to physical functioning and bodily pain, however, these findings may indicate that hemochromatosis patients who are healthier are better able to donate at public blood banks, rather than that voluntary blood donation has an effect on the donors' physical functioning over phlebotomy clinic users. These study findings suggest that although there may be other medical factors limiting individuals from donating, hemochromatosis patients are interested in being voluntary blood donors and this potential resource is currently underused.

Key Words: *Blood donors; Hemochromatosis; Phlebotomy*

Les patients atteints d'hémochromatose sont des donneurs volontaires de sang

La présente étude a été conçue pour explorer la recevabilité des patients atteints d'hémochromatose comme donneurs de sang ainsi que leurs perceptions et expériences à l'égard du système public actuel de don de sang. Les participants ont été colligés à partir d'une liste de patients atteints d'hémochromatose (n=102), ainsi que parmi les membres de la Société canadienne de l'hémochromatose (n=1 000). Sur le nombre à qui on a envoyé un sondage, 801 l'ont retourné rempli. L'échantillon était composé à 57 % d'hommes d'un âge moyen de 57,44 ans (ÉT=12,73; entre 19 et 87 ans). On a découvert que 20 % (160) des répondants avaient donné du sang depuis leur diagnostic, mais seulement 12 % des répondants indiquaient qu'ils utilisaient le don volontaire de sang pour maintenir leur taux de fer. Quarante pour cent des répondants ont précisé qu'ils avaient été rejetés comme candidats au don volontaire de sang. Même si, en mai 2001, la Société canadienne du sang, en collaboration avec la Société canadienne de l'hémochromatose, a entrepris une campagne de promotion pour inciter les patients atteints d'hémochromatose à devenir des donneurs volontaires de sang, notre étude révèle que 15 % des répondants ont été rejetés comme donneurs volontaires en raison de leur diagnostic d'hémochromatose. Pour ce qui est de la qualité de vie, il a été établi que les personnes qui donnaient du sang avaient généralement une meilleure fonction physique et moins de douleurs corporelles, mais ces observations indiquent peut-être que les patients atteints d'hémochromatose en meilleure santé sont plus aptes à faire des dons de sang aux banques publiques plutôt que de démontrer que le don volontaire de sang a un effet sur la fonction physique du donneur par rapport aux usagers des cliniques de phlébotomie. D'après ces résultats, même si d'autres facteurs médicaux empêchent peut-être les individus de donner du sang, les patients atteints d'hémochromatose sont intéressés à être des donneurs volontaires de sang, et cette ressource potentielle est sous-utilisée pour l'instant.

Hemochromatosis is one of the most common genetic diseases in Canada (1-3), with a prevalence of 1 in 200 in persons of northern European ancestry. The disorder involves a missense mutation in the *HFE* gene on chromosome 6 (the C282Y cytosine-to-tyrosine substitution) with a resulting excess of iron accumulating in the organs in many, but not all, C282Y homozygotes. However, unlike many genetic disorders, this disease is easily treated. At the time of diagnosis, a weekly regimen of removal of 500 mL of blood begins and continues until the serum ferritin decreases to the low normal range of approximately 50 ug/L. This process can take from several months to several years depending on the stage of the disease at diagnosis. Despite medical evidence that blood from such phlebotomies is safe for donation (4,5), these weekly donations are currently not used in Canada because all voluntary blood donors can donate no more frequently than every eight weeks. However, once their excess iron is depleted, many hemochromatosis patients begin a lifelong program of maintenance phlebotomy which occur three to four times per year to maintain normal iron stores. It is at this time that hemochromatosis patients may become long term voluntary blood donors in Canada. It has been found that regular blood donors who then find out they have hemochromatosis do not have lower iron stores than those individuals who are diagnosed without

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a history of blood donation (6). The screening of the general population with genetic testing could lead to the discovery of approximately 92,000 new C282Y homozygotes (1-3,7). If most of these cases are eligible to be voluntary blood donors this could greatly expand the blood donor pool in Canada.

Since 1991 in Canada, healthy hemochromatosis patients have been allowed to be voluntary blood donors and more recently, Canadian Blood Services (CBS) has formed a partnership with the Canadian Hemochromatosis Society to encourage healthy hemochromatosis patients to donate blood (8). However, despite their eligibility, few hemochromatosis patients have become voluntary blood donors and many patients have been rejected as donors on the basis of hemochromatosis. In fact, in 1998 Levstik and Adams (7) found that as many as 44% of their sample (largely based in London, Ontario) who had attempted to donate blood at a Canadian facility were excluded from doing so because of a diagnosis of hemochromatosis. Hence, one of the goals of the current study was to investigate hemochromatosis patients' interest in donating blood through the public donation system, as well as to investigate the current refusal rate. Additionally, because the current study is Canada-wide, it was intended that the sample would provide a more representative indicator as to the experiences of hemochromatosis patients as voluntary donors across the country.

A further goal of the current study was to investigate barriers that continue to be an issue for healthy hemochromatosis patients who wish to have their blood used after phlebotomy. Although it has been found that hemochromatosis patients may be more likely to be above the age range of acceptable donation or suffer from a comorbid exclusionary condition (such as diabetes, hypertensive medication, cirrhosis, skin discoloration, hepatitis B, hepatitis C or human immunodificiency virus [9,10]) there remain a large number of eligible individuals who have been unable to donate according to the Levstik and Adams study (7).

Finally, it has been suggested that the altruistic aspect of blood donation may positively affect one's mental health (11). However, there is also research to suggest that any regular procedure that maintains one's idea that they are 'sick' will negatively affect their mental, and possibly physical state (12). Thus, it was hypothesized that those individuals who have their blood drawn through phlebotomy may be less healthy, particularly mentally, than those hemochromatosis patients who gave regularly as voluntary blood donors.

METHODS

Participants

Participants were gathered from two sources. The questionnaire was mailed to 120 individuals with active hemochromatosis (all C282Y homozygotes) (all patients of Dr Paul Adams), 16 of whom had been identified in a previous population screening study of voluntary blood donors (1,2). Additionally, all members of the Canadian Hemochromatosis Society (n=1000) who self-identified as hemochromatosis patients were mailed questionnaire packages. Of those who were mailed a survey, 802 surveys (RR=73%) were returned completed. The authors received notification that eight individuals on the mailing list had passed away and that 32 individuals had moved without a forwarding address. Of the 802 respondents, 57% were male (456 men, 356 women) and the mean age was 57.44 years (SD=12.73; range 19 to 87 years).

Questionnaire

The questionnaire consisted of the Medical Outcomes Survey Short Form-36 (SF-36) (13) as well as a survey constructed for the purpose of this study. The survey included questions relating to sex and age, initial ferritin (iron) levels, genetic testing, regular blood draws for the treatment of hemochromatosis and the number of units of blood to iron depletion. History and experience with blood donations were also queried (ie, "Before diagnosis with hemochromatosis, had you ever donated blood as a volunteer?" "Have you donated blood since your diagnosis with hemochromatosis?" "Have you been refused as a voluntary blood donor?").

RESULTS

Knowledge of genetic testing results

Seventy-two per cent (578 of 802) of the respondents indicated that they had undergone genetic testing for hemochromatosis. Of those individuals, 46% (266 respondents) self-identified as C282Y homozygotes and 37% (214 respondents) indicated that they did not know their genetic test result. Thirteen per cent (75 respondents) identified themselves as compound heterozygote (C282Y/H63D), 1.4% (eight respondents) identified as H63D heterozygote and 0.7% (four respondents) indicated they were H63D homozygotes.

Hemochromatosis patients eligible to become donors after diagnosis

Of the 802 respondents, 160 (20%) have become voluntary blood donors since being diagnosed with hemochromatosis, but only 12% (96 of 802) of the respondents indicated that they use voluntary blood donation as a means of maintaining their iron levels. Additionally, only 8% of those who have donated since diagnosis (64 respondents) are new donors. A comparison of the exclusion criteria by the CBS and respondents self-identified health markers suggest that as many as 24% (192 of 802) of the individuals in the sample were eligible to donate blood.

Of the 266 respondents who indicated they were C282Y homozygote, 25% (66) have become voluntary blood donors since diagnosis and 14% (37) indicated that they use voluntary blood donation to maintain their iron level. Forty per cent of those who donated after their initial diagnosis were new donors. A review of the same CBS exclusion criteria indicated that 60% (159 of 266) of these individuals were eligible to donate blood (Figure 1).

Barriers to hemochromatosis patients as voluntary blood donors

Of the 802 respondents, 321 (40%) indicated that they had been refused from voluntary donation for any of the exclusionary reasons. Of the 266 C282Y homozogous patients, 142 (53.5%) indicated they had been refused. However, 15% of all of the respondents (120 of 802) and 28% of the homozygotic patients (74 of 266) had been refused from the voluntary blood donation service solely due to the diagnosis of hemochromatosis. Additionally, of the 433 participants who indicated they would be willing to donate their blood to a voluntary blood service, 190 (44%) indicated that the only limiting factor to donation was the fact that they believed that the blood agency would not accept a donation from a hemochromatosis patient. There were no other significant differences between homozygotic patients and other respondents on any of the other noted barriers to blood donation, hence, no distinction was made in the present analysis.

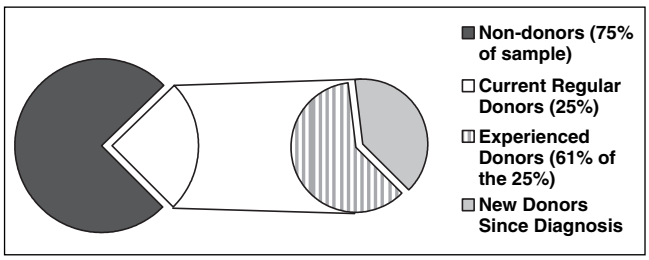

Figure 1) *Blood donations by C282Y homozygotic patients since diagnosis. Of the 66 patients who donated since their diagnosis, 26 (40%) were new donors*

Of the 433 individuals who responded positively to the question as to whether they would be willing to donate blood, 7% (30 respondents) indicated they would only do so with their physicians approval and 6% (26 respondents) indicated they prefer to have their own blood taken at the phlebotomy clinics and sent to the CBS.

Other barriers to donating blood identified by the respondents are provided in Table 1.

TABLE 1
Patients' perceived barriers to donating blood

Barrier	Respondents (n=433), n(%)
Donation services	
Clinic availability in community	22 (5.08)
Phlebotomies needed more often than allowed to donate at CBS	6 (1.39)
Need ferritin levels provided to physician	17 (3.93)
CBS staff not trained for regular phlebotomy donors (ie, handling small or collapsed veins, fainting)	39 (9.01)
Other exclusion criteria	
Age limit	25 (5.57)
Medical condition (ie, arthritis, blood pressure medication hepatitis, cirrhosis)	78 (18.01)

CBS Canadian Blood Services

Comparison of health status of hemochromatosis patients who are voluntary blood donors with hemochromatosis patients who undergo regular phlebotomy

Individuals who donated regularly through the CBS were found to be significantly different from those who opt for blood draw at phlebotomy clinics in regard to age, physical functioning and bodily pain. The 706 individuals who opted for phlebotomy treatment as a means of controlling their iron levels (mean [M]=58.44±12.72) were significantly older than were those who opt for donation (M=52.14±10.54; P=0.0001). Additionally, SF-36 subscale scores indicated that those who opted for phlebotomy treatment were significantly lower on physical functioning scores (M_{phleb}=68.93±27.67; $M_{donation}$=81.36±22.80; P=0.00001) and experienced more bodily pain (M_{phleb}=56.15±22.48; $M_{donation}$=65.60±23.44, P=0.004) than those who chose to donate their blood through a donation service (Figure 2).

Similar comparisons were also made between C282Y homozygotic patients and other hemochromatosis patients (non-C282Y or unknown genetic result). Only the general mental health subscale of the SF-36 was significantly different. C282Y homozygous patients scored significantly higher (M=64.87±7.94) on the general mental health scale than did other hemochromatosis patients (M=62.83±9.64, P=0.01). Upon separation of the C282Y homozygous patients from the other hemochromatosis patients it was found that C282Y homozygous blood donors did not significantly differ on the general mental health scores (M=63.11±7.07) from those C282Y homozygous patients who opted for phlebotomy (M=65.15±8.07, NS). However, non-C282Y homozygote hemochromatosis patients did have significantly higher general mental health scores in those who opted to donate blood (M=65.59±8.59) over phlebotomy treatment (M=62.42±9.74, P=0.03).

The iron burden on hemochromatosis patients who were blood donors before diagnosis

In all, 654 individuals (81.55%) knew their ferritin levels at the time of diagnosis. Of those individuals, 27% (219) said

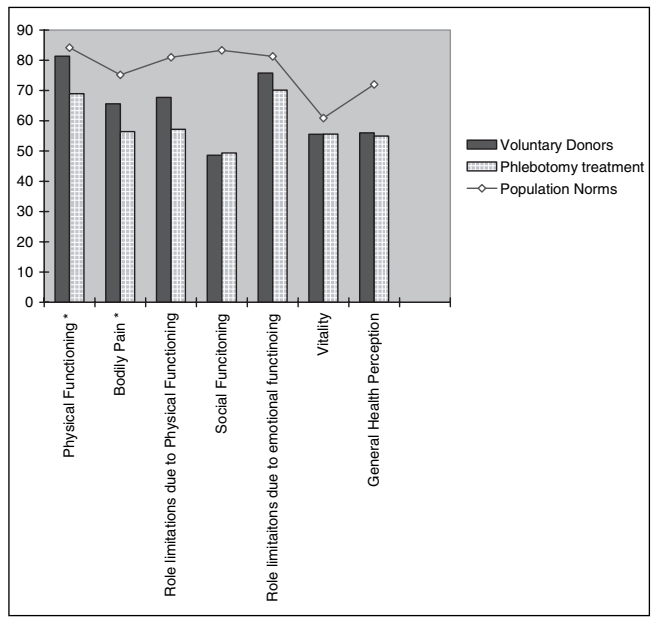

Figure 2) *Short Form-36 subscale score comparison between hemochromatosis patients who opt for voluntary blood donation and patients who opt for phlebotomy treatment. *Significant difference according to independent samples* t *tests, P<0.05*

that they were regular donors before diagnosis of hemochromatosis. No significant difference was found between self-reported initial ferritin levels of C282Y homozygous patients (M=1119.07±1219.10) and other hemochromatosis patients (M=1213.86±1513.72, P=NS). There was also no significant difference in self-reported initial ferritin levels between those who were donors before diagnosis (M=1073.07±1133.93) and those who were not (M=1260.28±1586.33, P=NS).

DISCUSSION

These findings suggest that there is a significant percentage of hemochromatosis patients who are willing and able to donate as voluntary blood donors, given the appropriate opportunity. If the number of donations by hemochromatosis patients increase, the blood supply in Canada could be expanded. Despite the fact that it has been over 10 years since

hemochromatosis patients became eligible as voluntary blood donors, there remain a number of perceived barriers preventing them from doing so in Canada.

Largely, the perceived barriers relate to the coordination of medical facilities with the voluntary blood donation clinics. These findings suggest that despite the fact that the delivery of therapeutic phlebotomy differs from voluntary blood donation and requires monitoring of ferritin and hemoglobin, many hemochromatosis patients would be willing to have their blood used by CBS should these levels be able to be monitored through donation clinics. Indeed, one recent study in the Unites States (14) which investigated a program in which blood donation facilities were adapted to also serve as a phlebotomy treatment centre suggested that it is safe and beneficial to the blood supply to combine blood donations centres with hemochromatosis treatment facilities. However, it remains to be seen what additional costs and administration would be required to adapt therapeutic phlebotomy facilities to allow for the use of hemochromatosis blood to enter the voluntary blood donation pool (many of these factors have hindered the use of hemochromatosis blood in the United States).

However, it should be borne in mind that some of the studied barriers need to be further investigated in order to draw conclusions as to whether these barriers are actual or simply perceived. For example, a number of participants indicated they had been refused donation for reasons that are actually no longer used to defer potential donors (eg, taking blood pressure medication). Hence, these barriers may actually be perceptions of potential donors based on an attempt to donate before the change in donation rules, or simply incorrect assumptions on the part of potential donors.

It is suggested that future research should collect corroborative objective data pertaining to reasons for refusal, as well as the date and specific diagnosis of hemochromatosis. With this information, more concrete conclusions could be drawn as to whether healthy hemochromatosis patients are indeed still being refused from blood donation or whether the barrier is one of perception.

Based on the limited scope of the current study, there is reason to suggest that the main problem with hemochromatosis patients acting as blood donors remains in public education, both with respect to hemochromatosis patients as well as physicians and staff in voluntary blood service clinic donation sites.

Although it was found that those hemochromatosis patients who donated blood at voluntary clinics rather than through phlebotomy treatment centres functioned better physically, had fewer physical role limitations and had less bodily pain, caution should be taken in interpreting these results to mean that these patients were healthier because of the positive effect of altruistic donation. Rather, the interpretation may lie in the fact that those hemochromatosis patients who are healthier, are more likely to be able to donate at voluntary clinics without medical supervision.

Thus, despite little evidence that voluntary donation improves the quality of life for the hemochromatosis patient, it does appear that there are a large number of patients who remain eligible and interested in having their blood used for public purposes but have been refused or feared to try at a CBS clinic due to the mistaken impression that it would not be allowed. These findings suggest that more public information campaigns need to target staff at voluntary blood banks, the medical profession as well as hemochromatosis patients themselves to educate the public as to the suitability and untapped resource of hemochromatosis patients as blood donors.

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