Iron Status and Novel Risk Factors for Iron Depletion in a Diverse Donor Population

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Abstract Text:

Background/Case Studies: Blood centers and regulators in the United States (US) are evaluating strategies for minimizing iron depletion in blood donors. The logistics of donor management might differ across blood centers, but the optimal approach may also vary according to biological or behavioral differences across sub-populations of donors. Studies in US donors have been conducted in predominantly Caucasian populations, which may differ from racial/ethnic minority donors in iron metabolism and capacity to undergo repeat phlebotomy.

Study Design/Method: Over 12,600 donors were enrolled from 4 US blood centers for ferritin testing. The study population was enriched for racial minorities [1600 African-American (AA), 1600 Asian (As), 1000 Hispanic (Hisp)] and for “Super Donors” (1600, who had completed 10+ donations in two years without low hemoglobin deferral). The minority donors and the remaining 6800 non-Hispanic White (NHW) donors were an unselected population with no specific eligibility criteria. Subjects completed questionnaires on risk factors for iron depletion. Logistic regression was used to identify demographic and behavioral predictors of Absent Iron Stores (AIS, ferritin <12 ng/ml) and Low Ferritin (LF, ferritin <26 ng/ml).

Results/Findings: Across all subjects, 19% had AIS and 42% had LF, with a high degree of variability based on demographic factors and donation behavior. In models stratified by race, expected patterns common to all 4 groups included a sharp increase in risk with increasing donation intensity, and a large decrement in risk for females > 50 years old. In models including all subjects, race was an independent predictor of both AIS and LF controlling for age, sex, body weight, donation frequency, and other factors (Table). AA and As donors showed ≈20% decreased risk for AIS compared to NHW, while Hisp donors had 25% higher risk. Daily use of exogenous iron reduced risk for LF and AIS by 30 to 40%, respectively, while the estimated benefit from less-than-daily use was lower (5 to 19% protection). Regular use of antacids was associated with a 20% or greater increment to risk. Reported use of hormone supplements showed opposing effects in males and females. Use of oral contraceptives or estrogen in females reduced risk by ≈15-20%, while males who reported current use of supplemental testosterone had twice the estimated risk for AIS.

Conclusion: This large study confirms the high prevalence of LF and AIS in US donors and the principal risk factors of age, sex, and donation frequency. The diverse population studied and the questionnaire data from donors identify additional demographic and behavioral risk factors of secondary importance. In developing iron mitigation strategies, practices based on age and gender could be further refined depending on a given blood center’s operational context and donor population.
Table: Selected risk factors for absent iron stores and low ferritin (ferritin < 12 and < 26 ng/mL)*

<table>
<thead>
<tr>
<th></th>
<th>Ferritin &lt; 12 ng/mL</th>
<th>Ferritin &lt; 26 ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (OR)</td>
<td>95% CI OR</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA vs NHW</td>
<td>0.81</td>
<td>(0.68, 0.95)</td>
</tr>
<tr>
<td>As vs NHW</td>
<td>0.76</td>
<td>(0.62, 0.91)</td>
</tr>
<tr>
<td>Hispanic vs NHW</td>
<td>1.25</td>
<td>(1.04, 1.52)</td>
</tr>
<tr>
<td>Iron supplementation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily vs none</td>
<td>0.59</td>
<td>(0.52, 0.66)</td>
</tr>
<tr>
<td>Less than daily vs none</td>
<td>0.81</td>
<td>(0.70, 0.94)</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antacid use any vs none</td>
<td>1.24</td>
<td>(1.08, 1.42)</td>
</tr>
<tr>
<td>Hormone use in females vs none</td>
<td>0.85</td>
<td>(0.72, 1.0)</td>
</tr>
<tr>
<td>Hormone use in males vs none</td>
<td>2.29</td>
<td>(1.35, 3.89)</td>
</tr>
</tbody>
</table>

*Results from logistic regression models also controlling for age, sex, an age by sex interaction, body weight, donation frequency, blood center, and smoking.

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