Donor vigilance: a global update

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Background Without blood donations and the availability of blood transfusion, many important therapeutic advances could not have been achieved. Donor haemovigilance is the systematic monitoring of adverse reactions and incidents in the whole chain of blood donor care, with a view to improving quality and safety for blood donors.

Method This 'global update' draws on work by the International Haemovigilance Network and International Society for Blood Transfusion haemovigilance working party, experience in the Netherlands, as well as a PubMed search using terms blood donor and adverse reaction. Results are discussed for vasovagal reactions, needle-related complications, long-term morbidity, donor iron status and frequent apheresis.

Results and Discussion The occurrence of vasovagal reactions is associated with young, female donors, smaller estimated blood volume, first-time donor status. A reduction in vasovagal reactions has been documented with use of a water drink before donation, muscle tensing, social distraction and lower collection volume for donors with small estimated blood volume. Needle injury is relatively frequent as a cause in cases of long-term morbidity; needle injury is associated with traumatic phlebotomy, and in some cases, nerve damage is documented. Repeated whole blood donations lead to reduction in body iron stores and in some cases anaemia. Some blood services adjust donation intervals to avoid or reduce this, while others have or are considering a policy of iron replacement therapy. Fewer studies on acute complications in plasma and other types of apheresis have been published. Preliminary studies of bone density and protein levels in non-commercial frequent plasma donors have not substantiated any specific hazard despite theoretical concerns of calcium or protein depletion. International collaboration in strengthening donor vigilance definitions and data analysis may in future increase potential for study of risk factors and measures to improve donor care worldwide.

Conclusion Donor vigilance is gaining international interest and has increased knowledge of risk factors for vasovagal reactions associated with blood donation. There remains a need of research and of developing preventive measures, including prevention and treatment of needle injury as well as possible long-term effects of frequent apheresis.

Key words: adverse reaction, apheresis, blood donor, iron deficiency, needle injury, vasovagal reaction, whole blood donation

Introduction

Without blood donors and their willingness to donate whole blood or blood components, the blood transfusions and many important therapeutic advances would not have been achieved. We owe all donors high standards of
medical care and all possible measures to prevent adverse consequences of donation and minimise their impact when they do occur. Donor haemovigilance is the systematic monitoring of adverse reactions and incidents in the whole chain of blood donor care, with a view to improving quality and safety for blood donors. Donor haemovigilance includes all activities which contribute to improving the health outcomes for blood donors as well as the safety and effectiveness of blood donation for purposes of medical treatment of patients [1].

Although the term ‘donor haemovigilance’ was not introduced till approximately 2009, publications reporting the occurrence and incidence of complications sporadically appeared well before 1980 [2]. Since 1980, there has been an exponential rise in the number of publications in this domain. Until about 2000, the great majority of articles came from North America but since then important contributions have been made in all continents.

Recording the occurrence of complications of blood donation – including complications of collection of blood components by apheresis – is relevant at different levels: (1) Care for the individual donor (medical dossier). Moreover, meticulous recording of problems at collection is essential to enable donors to justly receive (insurance) compensation for injury. (2) Information available next time to trigger extra care at the next donation in order to reduce likelihood of recurrence. (3) At the organisational level: know what the rate of reactions is. (4) Analyse risk factors, implement and evaluate preventive measures, compare between departments and organisations for purposes of learning and improving. This ‘global update’ draws on work by the International Haemovigilance Network and International Society for Blood Transfusion haemovigilance working party, experience in The Netherlands, as well as a PubMed search using terms blood donor and adverse reaction. Results are discussed for vasovagal reactions, needle-related complications, long-term morbidity, donor iron status and frequent apheresis.

Definitions and international data comparison

Capturing national data on complications of blood donation has lagged behind vigilance regarding adverse reactions and adverse events affecting the recipients of blood transfusions. The European Commission in its guidance on the mandatory reporting of aggregate data on serious transfusion reactions and serious adverse events in the transfusion chain has encouraged reporting of serious donor adverse reactions on a voluntary basis [3]. In the USA, deaths associated in time with blood donation (including plasmapheresis and other automated donations) as well as those in transfusion recipients are subject to mandatory reporting to the FDA, which publishes the findings annually [4].

For the purposes of comparing figures between countries and blood collection organisations, agreement is necessary on the types of complications of blood donation to be collected. To this end, from 2006, the International Haemovigilance Network (then still the European Haemovigilance Network) in collaboration with the International Society for Blood Transfusion (ISBT) working party on haemovigilance developed a standard list of definitions for the main types of donation complication [5]. In 2013, the ISBT HV working party launched a revision of the existent definitions (which date from 2008) to align with the new insights so that data capture will better support organisations in their efforts to adopt and monitor the effects of preventive measures as well as enabling organisations to compare their data. Donor reactions are included in the ‘ISTARE’ International Surveillance Database for Adverse Reactions and Events which is owned and hosted by the International Haemovigilance Network, into which haemovigilance systems can (anonymously) enter their aggregate data and compare their own with other countries’ data [5].

Vasovagal reactions

In recent years, studies from different countries have analysed the incidence and risk factors for donors feeling weak and dizzy or actually fainting during or following a whole blood donation or component donation by apheresis. The term ‘vasovagal reaction’ is used for this constellation of symptoms, although strict diagnostic criteria to confirm increased parasympathetic (vagal nerve) activity are generally not formally applied. Reported rates of vasovagal reactions vary considerably depending on the donor population, but lie in the range of 0.4–1% or higher if reporting includes mild to moderate reactions [6–10].

Knowledge of risk factors opens possibilities for targeting groups of higher-risk donors for preventive measures. Authors concur in finding higher incidences among female, younger and first-time as well as inexperienced donors. Rates are also higher among donors with smaller estimated blood volume (this estimation is based on donor gender, weight and height), anxious donors and those with a lower predonation blood pressure [8, 9, 11, 12]. Less investigated and not yet explained, a higher predonation haemoglobin level has been shown by two groups to be independently associated with vasovagal reactions [13, 14]. Associations have also been described
with increased predonation heart rate [8] and with increasing duration of phlebotomy [15, 16].

Several types of preventive measure have been evaluated and found successful in reducing the incidence of vasovagal reactions (Table 1): predonation hydration, deferral or reduced collection volume for smaller donors, muscle tension or leg crossing, social support and specific donor information. The first three measures effectively reduce the percentage of a donor’s blood volume which is donated. Using combined interventions in a large-scale study among younger donors, Tomasulo et al. [17] found an encouraging aggregate reduction of 24% of reactions. Nevertheless, much work remains to achieve clarity about the possible types of intervention and practical parameters and which donors to target in different settings.

### Needle injury

Needle-related complications include haematoma, arterial puncture and painful arm, which may result from nerve irritation through a haematoma or from direct injury to a nerve or other structure. It is recognised that arm symptoms from needle-related complications may take several weeks or longer to resolve, and these complications are over-represented among reported cases where there is long-term morbidity following a blood donation [24]. There is an association between traumatic venepuncture and the occurrence of nerve injury [25].

### Whole blood donations and donor iron status

Repeated blood donation (primarily whole blood donation, but repeated apheresis also carries this risk, [26]) tends to deplete donor iron reserves and may lead to haemoglobin levels below the donation threshold or frank iron deficiency anaemia [27, 28]. It is not known whether the state of iron-deficient erythropoiesis has any adverse consequences in an adult non-anaemic asymptomatic donor. There are different approaches to address the problem or iron depletion. The interdonation interval may be increased through deferrals or pre-emptively [29] – however, this leads to loss of donations and reduced donor retention. Blood service-based programmes of iron replacement have been found effective in reducing haemoglobin deferrals and retaining donors [30, 31]; in Canada, blood donors are informed of the risk of iron depletion and encouraged to discuss iron supplementation with their general practitioners [32]. It is clear that predonation Hb determination – or an alternative method such as the copper sulphate solution or haematocrit – does not detect donors with depleted iron stores. Further work is necessary to evaluate possible methods for monitoring donors for iron depletion – these include determination of serum ferritin and zinc protoporphyrin. A recent small randomised, placebo-controlled trial of iron supplementation in iron-depleted non-anaemic female donors increased ferritin and haemoglobin levels but failed to demonstrate clinical benefit [33]. So far, haemovigilance systems have not adopted definitions for reporting iron depletion or for monitoring and benchmarking between blood establishments.

### Effect of complications of blood donation on donor return

Studies are consistent in reporting reduced return following donor reactions although the methods of measuring donor return vary, as do the baseline return rates. For instance, France et al. reported return rates of 42% for first-time donors and 70% for repeat donors overall; return by the novice donors was halved in donors with higher scores on the Blood Donor Reactions Inventory [34]. Newman (in 2006) reported a reduced blood donor return following complications, rising to an 85% reduction among donors who suffered from vasovagal reactions combined with painful arm and fatigue [35]. In the Netherlands, with overall return rates (subsequent donation within a year) of 75–80% and 85–90% among

### Table 1 Measures to reduce vasovagal reactions (VVR)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Authors (selected)</th>
<th>Remarks</th>
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</thead>
<tbody>
<tr>
<td>Hydration</td>
<td>Newman [18]</td>
<td>500 ml water drink; 21% reduction in VVR (high school donors)</td>
</tr>
<tr>
<td>Muscle tensing</td>
<td>Ditto [19]</td>
<td>Less prefaint reactions (Blood Donor Reactions Inventory, BDRI)</td>
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<td></td>
<td>Kowalsky [20]</td>
<td>Female donors: attenuated decrease of cerebral oxygenation</td>
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<td></td>
<td>Ditto [21]</td>
<td>Possible support for increased return in subgroup of male donors</td>
</tr>
<tr>
<td>Social support</td>
<td>Hanson [22]</td>
<td>Inexperienced donors [0–2 previous donations]; lower scores on BDRI</td>
</tr>
<tr>
<td>Deferral (or reduced collection volume)</td>
<td>Eder [23]</td>
<td>VVR 20% reduced in 16–18 years donors after introducing requirement of ≥3.5 l EBV</td>
</tr>
<tr>
<td>for small body weight/EBV donors</td>
<td>Tomasulo [17]</td>
<td>Aggregate VVR reduction of 24% of WR (17- to 22-year-old donors)</td>
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</tbody>
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first-time donors and repeat donors, respectively, return was reduced more strongly following vasovagal reactions (first-time donor return rate approximately 55%) than venepuncture-related problems (no reduction if collection was completed [14]). A Dutch questionnaire study noted a greater stopping risk among male than among female donors following a (self-reported) vasovagal reaction [36].

Apheresis

Fewer studies have described the incidence of apheresis complications than those focusing on whole blood donation. Broadly, there are higher rates of needle-related complications and lower rates of vasovagal reactions. Besides procedure-related and physiological explanations, differences in donor demographics have an effect, and there is undoubtedly selective retention of donors, particularly in plasmapheresis programmes. Specific apheresis-related complications are citrate toxicity, as well as some extremely rare hazards such as the risk of air embolism. Theoretical long-term risks such as the possibility of protein depletion from frequent plasma donation [37] or osteoporosis from calcium depletion by the citrate [38] have only recently received attention and are not (yet) included in lists for reporting and surveillance. The monitoring of acute and longer-term safety of donors who have been treated with growth factors for the donation of peripheral blood stem cells or granulocytes constitutes a special area which lies beyond the scope of this article.

Discussion

Through donor vigilance and the increased attention to complications of blood donation, it is now possible for blood operators to provide evidence-based information describing the possible complications, stating the incidences which are low but not negligible and giving practical tips on how to reduce their occurrence. This enables potential blood donors to take informed decisions about donation and to adopt behaviours which will minimise inconvenience or harm from their donation. Practical measures to avoid adverse reactions to blood donation are not new – ever since blood drives started, staff and volunteers have followed procedures to minimise complications. However, the recent increases in knowledge offer new opportunities to reduce acute complications of donation as well as the rare longer-term harms.

Some donors claim that they feel fitter after donating blood. The question has been asked whether there might be a physical health benefit from donation. Despite reports of a reduction in cardiovascular disease in blood donors and the suggestion that this might be a favourable consequence of lower body iron stores, to date, the association has not been confirmed. A ‘healthy donor effect’ looks a more likely explanation. Meanwhile, the (mostly non-serious) complications of blood donation are at least as common as minor physiological adverse reactions in the recipients of blood transfusion. There is an ethical as well as professional and regulatory onus on those involved in blood collection to follow state-of-the-art recommendations and procedures for donor care and safety.

The results of donor haemovigilance have so far have come from single or collaborating blood operators within single countries. Use of common definitions will enable haemovigilance systems to examine differences between donor (and recipient) haemovigilance findings from different countries. International collaboration is indispensable for the study of extremely rare complications. Looking for explanations for differences in rates will require data on donor demographics and epidemiology, blood collection procedures (e.g. volume drawn), component production and specifications, laboratory methods etc. Such study will be challenging but has the potential to contribute to the objective of using haemovigilance data as a starting point for improving safety for donors and throughout the transfusion chain.

Conclusions

International surveillance definitions for complications of blood donation and for non-infectious hazards are available on the websites of the ISBT and IHN. It is important to be clear about which cases are to be counted in international comparisons or surveillance so that people can as far as possible map their cases to the international list. As systems do this progressively better, it will become possible to analyse the differences to gain further understanding and potentially discover new ways of improving safety.

Acknowledgements

The authors wish to acknowledge the important contribution of Jan Jørgensen to putting complications of blood donation and donor haemovigilance on the map internationally.

Author contributions

All the authors are involved with supervising and Dutch data collection on complications of blood donation and analysing the results. JCW-O drafted the manuscript; the coauthors reviewed and critically commented on the manuscript and agree to its submission.
Disclosure

None of the authors have any financial conflicts to disclose.

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