MSBT 25/4

HAEMOVIGILENCE AND THE vCJD RISK

Dr Mortimer has provided a paper for discussion about the possibility of vCJD being passed through blood transfusion by a donor incubating vCJD and has put forward some options for consideration.

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Dr Pat Troop
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Dear Dr Troop,

Haemovigilance and the vCJD risk

Over the last two years I have become increasingly sceptical of there soon being a vCJD agent screening test that can be applied to blood donors. Consequently, I think measures to limit blood use in UK must be strengthened. This is because we simply cannot quantify the vCJD risk and it may turn out to be a big one. Because of the likely long incubation period young recipients are especially at risk and young children born in 1990s, especially since 1996, might yet present the first cases of provable blood borne vCJD.

I enclose a paper for your consideration in which I have set out my concerns and the steps I would propose. I know DH has and is holding CMOs' symposia on the subject, which I welcome. However, I fear that they alone will not sufficiently invigorate local transfusion committees and so achieve more parsimonious use of blood. That is a desirable aim whether or not there is a vCJD risk, especially as blood procurement is getting harder and less cost-effective in UK. In fact it could be seen as 'win-win' no matter whether there is a transfusion-associated risk.

Yours sincerely,

GRO-C

Philip Mortimer
Director SBVL

cc Prof. Borriello
Dr Walford

Blood use and vCJD: thinking about the unthinkable

Executive summary

The potential threat of vCJD to public health is now well appreciated, including the possibility of secondary, iatrogenic, infection. One such route might be blood transfusion from donors incubating vCJD. In the absence of an adequate laboratory test of donor blood and without any means of donor selection, it is unacceptable that homologous blood should be transfused unnecessarily, and autologous transfusion ought to be encouraged. 'Haemovigilance', a principle applicable at all points of blood use and involving investment in training and audit at both local and national levels, could produce a sustained downward trend in the use of homologous blood.

Background

On two previous occasions the UK blood services have been thought by some to have done too little, too late, to limit recipient exposure to transfusion related infection. It happened in 1984-5 when (it has since been argued) more rigorous donor selection and more timely anti HIV testing might have been introduced, and in 1990 when the first generation of anti HCV assays might have been adopted sooner than they were. In truth, the arguments for the slower, more considered action taken at those times were legitimate. Nevertheless, the recent Burton judgement has found that anti HCV tests should have been used as soon as they were available, i.e. some 2 years before anti HCV screening began. In several other countries, too, the speed and ways in which HIV and HCV screening was introduced has attracted criticism, notably in France where senior officials were convicted of criminal negligence alleged to have been committed in delaying HIV testing in 1985. Subsequently, blood and blood product use in France has come under continued close scrutiny and the useful term 'haemovigilance', describing a process of case by case evaluation of the justification for blood use, has been coined. It is plain from these considerations that national transfusion services have to be fully accountable for the way that they deal with the infectious risks of blood transfusion, and that this now includes a responsibility not only for blood provision but also for influencing the way it is used.

The recognition in 1996 of vCJD as a consequence of the UK epidemic of BSE represents an unquantifiable challenge to our national blood services. Executive decisions on a number of aspects of transfusion are having to be taken in the face of

unknowns, even though past experience with HIV and HCV does offer some guidance.

Two questions are:

- Is the vCJD agent transmissible by blood from human to human?
- Can the potentially vCJD-transmitting blood donor be identified and transfusion of their blood prevented?

If, as looks like continuing to be the case for several years, the answer to the above questions is 'not sure' then a third question arises:

- Does any further action need to be taken now?

Proposal

This paper suggests that though UK Health Departments and Blood Services have over several years become increasingly aware of the possible threat of secondary spread of vCJD by blood transfusion they have not yet taken enough steps to contain it. It goes on to argue that a set of further precautionary measures should be adopted that will, if the threat is realised, minimise its impact.

To be able to evaluate this proposal the first two questions posed above need further consideration. A recent paper has helpfully summarised animal experiments in which blood of TSE affected animals have been inoculated intracerebrally or intravenously into other susceptible animals[1]. The results are so far inconclusive, but there are two warning signals. First, in cattle, sheep and man, BSE/vCJD related changes are disseminated in lymphoid tissues in the pre-disease phase, implying possible infectivity in blood. Second, although the UK Blood Services have diligently sought evidence of CJD and vCJD transmission by blood transfusion to known cases, and from known cases to recipients, and have not found firm evidence of transmission, it must be recognised that there are epidemiological and ethical obstacles to obtaining quick or firm answers from such studies. Neither approach is going to furnish convincing evidence in the short term for or against transmission from human to human by blood as currently transfused in UK.

The second question posed asks 'Can the risky donor/donation be removed?' Continued donor selection and donation screening has made UK blood transfusion safe with regard to HIV, HCV and other infections. However, prospects for imminently removing the vCJD threat by the same means are not very good. This is because no lifestyle, not even vegetarianism, will determine that UK residents in the 1980s and 1990s were not exposed to vCJD (a fact that has led FDA to exclude them

from blood donation in USA), and because present candidate tests for vCJD in blood lack both the sensitivity and the specificity that a feasible donation screening test must have. In this respect progress over the last few years has been disappointing. There is a possibility that signal amplification in some form might soon lead to a more sensitive (though not necessarily more specific) test, but it could still take 3 to 5 years, or even longer, to get from initial success in this respect to a test applicable to blood donors.

Given these major uncertainties UK Health Departments and Blood Services need to be examining their options, as follows:

The first is not to take extra measures at present. Scientifically this might be defensible, especially if current experimental research could soon exclude the possibility of vCJD transmission by blood, or quickly yield a workable test for blood donations. Unfortunately neither of these outcomes seems likely. Furthermore, public expectations and judicial attitudes regarding blood borne viruses suggest that in the absence of science-based interventions, other precautions must now be considered. These other options can be listed:

i. Exclude donors who have received blood transfusions in the past. This might bring a small benefit if blood does indeed transmit vCJD, but it implies that their exposure to vCJD might be of a different order to UK residents as a whole, almost all of whom must have been dietarily exposed. This is unconvincing.

ii. Set up widespread autologous transfusion (pre surgery blood deposit) facilities. Autologous transfusion has long been resisted in UK for reasons of cost and logistic complexity, and because of local inertia and the broad argument that UK homologous blood is safe. This is no longer valid and, far from tolerating the present weak autologous blood services, UK needs to promote them with universal elective 'packages' to go hand in hand with those common surgical procedures that often involve transfusion.

iii. Evaluate indications both for the use and quantity of blood needed in each candidate for transfusion, especially in infants and in obstetrics where recipient survival means a greater potential for vCJD to develop. There are now accepted means (evidence based guidelines, training, audit) by which changes in practice can be achieved. Blood is legitimately used to ensure survival eg. after

major haemorrhage and emergency surgery, and certain other blood use is so therapeutically valuable that benefit greatly exceeds potential risk. However, in other cases blood may still be being transfused outside present guidelines, to speed recovery or even quite arbitrarily. In the face of the unquantifiable risk of vCJD, transfusions given solely for these last reasons ought not to happen.

Picking options

If, as I hope, the first ('no action at present') option is rejected, choosing other options is an exercise in cost-benefit analysis. The advantage of autologous transfusion is that it removes the transfusion risk of vCJD as well as other infections and immunological hazards. However, it is limited in its potential applications, costly and demanding of staff resources. Nation-wide autologous services should therefore be a goal, but not seen as a quick or by any means a total solution.

The goal of transfusion limitation, by contrast, is more quickly realisable. It requires professional education, training and audit, drawing on the expertise of specialists in transfusion and haematological medicine, anaesthetics and surgery to make sure that best national practice becomes normal local practice. This translation of nationally agreed best practice into action on the ground everywhere is, I suggest, fully achievable if resources are put into local 'haemovigilance', and perverse incentives are removed. One of the latter may be the market provider status of UK blood services which may tend to encourage maximisation, not minimisation, of blood use.

Another unhelpful incentive is the pressure on surgeons to speed post operative recovery and on physicians to increase bed turnover by ordering 'pick-you-up' transfusions. Effective audit of blood use at district general hospital level either directed by Blood Services that have been relieved of the imperative to sell blood or, perhaps better, by an independent body staffed by Transfusion Medicine specialists and a cadre of 'haemovigilance' officers, could significantly cut transfusion rates. This, incidentally, would also relieve the present shortfalls in the blood supply.

d/w dept how Service can be relied on to do this

Comment

The measures proposed above would have a significant cost (though modest by comparison with two recent transfusion innovations of unproven utility, namely HCV RNA testing and leucodepletion). There is bound to be value in promoting better transfusion decision making (as was done during the 1990s in France and

elsewhere); how great it is will mainly depend on whether transmission of vCJD by transfusion turns out to be a real threat. On the other hand, the cost in morbidity and mortality, and to the blood services in litigation and reputation, of not taking action may turn out to be very high. The precautionary principle should therefore apply. I advocate action now to establish haemovigilance in UK. I suggest, as a first step, an urgent study of how this has been achieved in France, followed by appropriate action in UK.

Transfusion nurses

Reference:

1. Brown P, Cervenáková L, Diringer H. Review Article: Blood infectivity and the prospects for a diagnostic screening test in Creutzfeldt-Jakob disease. J Lab Clin Med 2001;137:5-13.