UNITED KINGDOM HAEMOPHILIA CENTRE DIRECTORS ORGANISATION

NEW VARIANT CJD AND THE TREATMENT OF HAEMOPHILIA

There is concern about the possibility that blood and blood products might transmit the agent responsible for new variant CJD (nvCJD). As a result of the recent directive from the Committee for Propriety Medicinal Products (CPMP) two batches of factor VIII concentrate have been withdrawn in the UK by the manufacturer because they were produced from plasma containing donations from individuals who subsequently developed nvCJD.

The United Kingdom Haemophilia Centre Directors Organisation (UKHCDO) Executive Committee has met with authorities on transmissible spongiform encephalopathies to review the recent medical and scientific evidence that blood and blood products might transmit the agent responsible for nvCJD.

From studies undertaken in the USA and the UK there is as yet no evidence of transmission to patients of the agent responsible for classical or sporadic CJD (spCJD) by blood or blood products. We are not aware of any cases of spCJD in persons with haemophilia.

In 1996, nvCJD was first identified by the CJD Surveillance Unit in Edinburgh[1]. Recently published data indicates that nvCJD and BSE are caused by the same infectious agent[2,3,4]. nvCJD is clinically distinct and should be considered an entirely separate condition from spCJD. nvCJD in humans has probably arisen from ingestion of bovine products containing the agent responsible for BSE in cattle.

The largest epidemic of BSE has occurred in the UK where nearly all the cases of nvCJD have arisen and it is likely that more cases, currently asymptomatic, will present clinically in the future. The finding of the abnormal prion related protein (PrP) in the tonsils and spleen of humans with nvCJD raises the possibility that circulating lymphocytes in the blood of asymptomatic individuals could transmit the agent responsible for nvCJD[5].

For this reason the Spongiform Encephalopathies Advisory Committee (SEAC) recommended that consideration be given to leukodepleting blood in the UK and a risk assessment by the

Department of Health and a feasibility study by the National Blood Authority (NBA) is currently being undertaken. If such a policy is accepted it will take a considerable time to implement and meanwhile further cases of nvCJD in blood donors may lead to further recalls of clotting factor concentrates manufactured from plasma donated in the UK.

In 1996 UKHCDO recommended that recombinant factor VIII (rVIII) concentrate was the treatment of choice for those with haemophilia A[6]. Further and new uncertainties about the safety of plasma products with respect to nvCJD requires that these recommendations are implemented with greater urgency. The use of rVIII concentrate as a way of reducing the theoretical risk of nvCJD is further supported by a recent briefing paper prepared by the NBA. The Executive Committee therefore recommends that patients should be treated, as soon as possible, with rVIII manufactured without the use of bovine proteins or human albumin. Meanwhile we continue to recommend strongly the use of the current licensed rVIII concentrates for all people with haemophilia A. When rIX concentrate becomes licensed this will be the treatment of choice for those with haemophilia B. Consideration should be given to the use of rVIIa concentrate for patients with congenital factor VII deficiency, although it is not licensed for this purpose.

Patients for whom recombinant concentrates are not available will need treatment with plasma derived products. The choice lies between concentrates manufactured from plasma collected in countries with cases of nvCJD and BSE, or in those geographical regions in which there are currently no recorded cases of either of these conditions. From our current understanding of the epidemiology that nvCJD occurs almost exclusively in the UK, it is likely that any risk of transmission would be reduced by using concentrates prepared from donor plasma collected in other countries, e.g. USA, where there are no recorded cases of nvCJD or BSE.

We should not underestimate the anxiety which nvCJD has created for those with haemophilia. The recent withdrawal of concentrates and other blood products in the UK means that patients will require counselling; not only recipients of these batches, but also others at risk from products derived from the same source plasma.

The medical and scientific issues are complex and we shall endeavour to ensure that our guidelines are kept under close review as new information becomes available.

Christopher A Ludlam
Chairman
On behalf of the Executive Committee of the
United Kingdom Haemophilia Centre Directors Organisation
Department of Haematology
Royal Infirmary
Edinburgh

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