STUDY OF THE EFFECT OF INTRAVENOUS INFUSIONS OF FACTOR VIII ON SERUM ENZYME LEVELS IN HAEMOPHILIACS

Introduction

Recent studies have shown that 20-30% of haemophiliacs on long-term freeze-dried factor VIII therapy have chronically elevated SGOT and SGPT levels for periods of up to 6 months or more. Most of the patients have no other signs or symptoms suggestive of chronic liver disease. Evidence from the U.S.A. suggests that the proportion of patients treated with freeze-dried factor VIII with similar changes is higher - 30-40%.

Apart from chronic viral hepatitis, other causes include a toxic chemical or protein in the factor VIII which causes damage to liver or other cells, and over a period, produces repeated damage to liver with leakage of cellular enzyme into the bloodstream. This process could lead to chronic persistent, or chronic active, hepatitis with eventual progession to cirrhosis.

One possibility which must be excluded is that the infusion of factor VIII itself is associated with the appearance in the peripheral blood of elevated serum enzyme levels. This study is an attempt to assess the likelihood of the latter possibility.

Procedure

Up to 20 Haemophilia A patients at the Oxford and Edinburgh Haemophilia Centres will be selected for the study. An attempt will be made to include patients on home treatment, those receiving only cryoprecipitate, and haemophiliacs with a mild coagulation defect. Only patients of 18 years of age or above will be studied. The object of the study will be explained to each patient before he is included in the study, and his informed consent obtained.

Subjects will be asked to attend out-patients early in the day of the test, on an occasion when they attend the Haemophilia Centre for routine assessment. They should not have received any treatment with blood products for 48 hours before. The date, type and batch number of the product used for the last treatment

before the present occasion should be noted.

The following regime will be adopted:-

At each time of sampling, 5ml. of heparinised blood will be taken for aminotransferase, bilirubin and alkaline phosphatase and LDH. The plasma will be separated immediately after the specimen has been taken.

3ml. of clotted blood will also be taken for HB_sAg, Anti-HB_s and Anti-HB_c antibodies. IgM antibodies to hepatitis B core antigen will be estimated if indicated. The liver function tests will be performed locally at Oxford and Edinburgh. The results of the enzyme tests will be expressed as a multiple of the upper limit of the normal range at Oxford and Edinburgh.

Hepatitis B serology at Edinburgh will be carried out by Dr. Christopher Burrell at the Hepatitis Reference Laboratory, University of Edinburgh. Tests for Oxford patients will be performed by Dr. Craske at the Public Health Laboratory, Withington Hospital, Manchester.

Samples detailed as above will be taken before the infusion of one bottle of the selected blood product and if possible at 6, 12, 24 48 hours and 7 days after infusion. The product infused should be the same as the patient is currently receiving. If possible patients will be chosen so that most of the products used are studied in the project, e.g. 5 Hemofil, 5 Elstree factor VIII, 5 cryoprecipitate etc.

If for any reason it is not practicable to take blood at one of the stated times, then this will be disregarded and the next sample taken according to the protocol. The type of product, date and time of infusion will be noted. The bag numbers of the cryoprecipitate used will also be recorded. If any patient requires further transfusions of factor VIII before 7 days after the infusion under study, this will nto exclude the patient from the study but the details of treatment should be recorded, and further samples of blood taken if possible 24 hours and 7 days after the second transfusion.

Samples of serum left over from this study will be stored for further studies.

Results

When 20 patients have been studied in each Centre, the results will be analysed to see if any observed rise in enzyme levels is related to any of the following factors:-

1. The time since transfusion of the product under study.
2. The time since previous transfusion of factor VIII.
3. A history of hepatitis.
4. The presence or absence of previous 'transaminites'.
5. The type of product used, and the time since the patient first received that type of product.
6. The severity of the patient's coagulation defect, expressed as the numb r of bleeds per 100 days or the number of factor VIII units received per year.

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