0091

SNBTS HEAT TREATED FACTOR VIII

PRELIMINARY CLINICAL EVALUATION STUDIES

June 1984

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INTRODUCTION

There has been worldwide interest in the development of techniques designed to reduce the infectivity of pooled blood products and the option currently seen as the most appropriate for the SNBTS is wet heat treatment.

Methods have been introduced in which sugars are added to protect factor VIII from the effects of heat. In vitro virological studies have demonstrated that in the sugar medium selected (sorbitol) the traditional pasteurisation process (60°C for 10 hours) is less than optimal and an additional period at 70°C has now been included.

Preliminary in vivo and in vitro studies (carried out in Edinburgh and Glasgow), using a 60°C for 10 hours heating procedure demonstrated that the sugar appeared to prevent heat denaturisation of factor VIII. The proposed new studies will be performed using product exposed to the optimal heat treatment (includes a period at 70°C) and are designed to assess biological acceptability, clinical efficacy and residual infectivity.

It is proposed that all heat treated product made available for patient use until further notice will be issued exclusively for these clinical evaluation studies.

BIOACCEPTABILITY STUDIES (In vivo recovery and ½ life)

It is proposed that detailed studies are performed on a maximum of 12 severe multi-transfused haemophilia A patients. The suggested protocol is included in the Appendix section.

CLINICAL EFFICACY STUDIES

It is proposed that as much data as is reasonably possible is

obtained when sufficient stocks of heat treated product are available to examine its clinical efficacy on any patients. These studies (and product released for use) should only be instituted in circumstances when the efficacy of the heat treated product can be reasonably assessed. Thus it is essential to avoid clinical episodes in which different factor VIII preparations are used and as a consequence the efficacy of the heat treated material would remain unproven.

A suggested protocol is included in the Appendix section. It is unclear , at the present time, as to the number of patients required to complete this study. Certainly it will be important to include patients undergoing both minor and major surgery.

RESIDUAL INFECTIVITY STUDIES

These difficult but vital studies require access to patients who, ideally, have not been previously exposed to blood and blood products. The model protocol (see Appendix section) is based upon the work at the Oxford Haemophilia Centre and it should be noted that a prolonged period of study is required. It is suggested that a total of 15 patients should be studied, that as many batches as possible should be used and that the previous Oxford study using BPL intermediate VIII will be used as controls.

PRODUCT RELEASE/STUDY CO-ORDINATES

Clinical colleagues who wish to contribute to these studies, which will consume all the available heat treated factor VIII for the foreseeable future, will obtain their supplies of this material through their local Regional Transfusion Centre. Release of product for clinical evaluation will be made on a named patient basis only.

It is recognised that because of the pressure of work in Hospital Haematology Departments it would be helpful if senior consultant staff of the SNBTS gave some assistance with regard to the co-ordination of

these studies. It is proposed that when product is released the RTC staff involved will inform Dr F E Boulton (SEBTS) when studies on in vivo recovery and ½ life and/or clinical efficacy are initiated. Dr R J Crawford (WBTS) will be informed when product is released for residual infectivity studies. Drs Boulton and Crawford will give every assistance possible.

In the event of initial excess pressure on supplies of the heat treated product some priority will be given to the in vivo recovery and ½ life and residual infectivity studies.

FUTURE STUDIES

1. Von Willebrand patients

   It would be of considerable interest and importance to examine the clinical efficacy of the heat treated product in these patients.

2. Long term repeat exposure

   Consideration will be given as soon as possible to the selection of specific patients that will be exposed exclusively to the heat treated product. The main purpose of this study will be to investigate the occurrence of immune complexes, inhibitors and allergic reactions.

3. Inhibitor Patients

   It is suggested that these patients should be a low priority for future study, not least because of the likely quantities required. However, it is of some importance that these studies are undertaken in due course.

APPENDIX

SNBTS HEAT TREATED FACTOR VIII: IN VIVO RECOVERY AND ½ LIFE STUDIES

PATIENT'S NAME.....AGE.....

HOSPITAL.....

CONSULTANT.....

DATE OF INFUSION.....

Body Weight .....Kg

Dose Given.....i.u.

Solubility Time.....(minutes)

Batch Nos.....No. Vials.....

	Before	10 min.	20 min.	30 min.	40 min.	50 min.	60 min.	180 min.	360 min.	24 hrs.	10 days
TEMPERATURE											
BLOOD PRESSURE											
PULSE											
Factor VIII C											
Factor VIII Cag											
Factor VIII Rag											
Anti-HB (titre)											
10 mls plasma stored at -30°C											

NOTES: (1) Dose (approx. 20 i.u. kg) should be infused in 20 minutes.

(2) 10 mls plasma should be aliquoted (1 ml) and stored for future studies.

(3) Patients selected for this study should be haemostatically stable (no clinical evidence of active bleeding).

(4) PLEASE RETURN COMPLETED FORM TO DR F BOULTON, EDINBURGH & SOUTH EAST BLOOD TRANSFUSION SERVICE, ROYAL INFIRMARY, EDINBURGH.

Clinical Comment (untoward reactions etc)

Signed.....

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SNBTS HEAT TREATED FACTOR VIII: CLINICAL EFFICACY STUDY

PATIENT'S NAME.....

HOSPITAL.....

CONSULTANT.....

CLINICAL CONDITION/SURGERY etc.....

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Body Weight.....

Dose Schedule: Day (1).....Day (2).....

Day (3).....Day (4).....Day (5).....

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Batch Nos.....

Date Treatement Initiated.....

CLINICAL NOTES

(1) Was Haemostasis satisfactorily controlled?

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(2) Was amount of Factor VIII used similar to anticipated use of non-heated VIII product?

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(3) Were there any untoward reactions? (If so, please specify)

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(4) Any other comments?

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(5) On how many occasions has this patient received heat treated factor VIII concentrate?
(include information on the use of other haemostatics)

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NOTE: Please return to Dr F Boulton, Edinburgh & South East Scotland Blood Transfusion Service, Royal Infirmary, Edinburgh, along with any laboratory assay values.

Signed.....

(Medical Practitioner)

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