Complete Summary

GUIDELINE TITLE

Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant.

BIBLIOGRAPHIC SOURCE(S)

O'Shaughnessy DF, Atterbury C, Bolton Maggs P, Murphy M, Thomas D, Yates S, Williamson LM, British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. Br J Haematol 2004 Jul;126(1):11-28. [92 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Conditions requiring infusion of fresh-frozen plasma, cryoprecipitate, and cryosupernatant, including:

- Single coagulation factor deficiencies (e.g., factor V deficiency)
- Multiple coagulation factor deficiencies
- Thrombotic thrombocytopenic purpura
- Over-anticoagulation with severe bleeding
- Liver disease
- Surgical bleeding requiring massive transfusion

- Hemorrhagic disease of the newborn
- Coagulopathy plus bleeding in neonates

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Anesthesiology
Cardiology
Critical Care
Emergency Medicine
Gastroenterology
Hematology
Nursing
Pediatrics
Surgery

INTENDED USERS

Advanced Practice Nurses
Clinical Laboratory Personnel
Nurses
Physicians

GUIDELINE OBJECTIVE(S)

To assist clinical decisions about the transfusion of fresh-frozen plasma

TARGET POPULATION

Patients of all ages in the United Kingdom with bleeding disorders that require transfusion of fresh-frozen plasma, cryoprecipitate, and cryosupernatant

INTERVENTIONS AND PRACTICES CONSIDERED

1. Choice of fresh frozen plasma (FFP)
    - FFP recovered from whole blood or from plasmaphaeresis
    - Plasma from male donors
    - Plasma from non-United Kingdom donors
2. Handling of FFP
    - Freezing
    - Electrolyte content
    - Physical handling of plastic packs
    - Thawing
    - Inspection of thawed product
    - Preparation of cryoprecipitate and cryosupernatant
3. Reduction of pathogens in FFP
    - Methylene blue-treated FFP

    - Solvent detergent-treated FFP
    - Quality control
    - Efficacy and safety
4. Selection by blood group
    - ABO blood group compatibility
    - Rh factor compatibility
5. Dosage
6. Thawing (dry ovens, microwave ovens, water baths)
7. Handling of thawed product
8. Control of issue and transfusion
9. Monitoring response to transfusion and adverse effects
10. Identification of transfusion eligible patients
11. Advance directives for FFP transfusion

MAJOR OUTCOMES CONSIDERED

- Incidence of inappropriate use of fresh-frozen plasma transfusions
- Incidence of transfusion-related infection and side effects
- Rate of haemostasis
- Incidence of handling problems
- Mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

These guidelines are based on MedLine literature searches using appropriate keywords (including: plasma, plasma + randomized, plasma + trial, plasma + therapy, plasma + liver, plasma + cardiac surgery, plasma + surgical bleeding, plasma + thawing and plasma + storage). All these searches were repeated substituting either cryoprecipitate or cryosupernatant for plasma. A draft of a systematic review was also consulted. Existing guidelines were also reviewed, including that by the College of American Pathologists and several published by the British Committee for Standards in Haematology (BCSH).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Statements of Evidence

Ia Evidence obtained from the meta-analysis of randomized controlled trials.

Ib Evidence obtained from at least one randomized controlled trial.

IIa Evidence obtained from at least one well-designed controlled study without randomization.

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendations

Grade A Required at least one randomized controlled trial as part of a body literature of overall good quality and consistency addressing the specific recommendations (evidence levels Ia, Ib).

Grade B Requires the available of well conducted clinical studies but no randomized clinical trials on the topic of recommendations (evidence levels IIa, IIb, III).

Grade C Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (evidence level IV).

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendation grades (**A-C**) and levels of evidence (**Ia-IV**) are defined at the end of the "Major Recommendations" field.

Specifications, Preparation, Storage and Handling of Fresh-Frozen Plasma (FFP) and Cryoprecipitate

Fresh-frozen plasma prepared from units of whole blood and from plasmaphaeresis are therapeutically equivalent in terms of haemostasis and side-effect profile (**grade A recommendation, level I evidence**).

Pathogen-Reduced Plasmas (PRP)

In any patient for whom PRP is being considered, the risks of hepatitis A virus (HAV) and parvovirus B19 transmission and their clinical sequelae should be weighed against the likely benefits (**grade B recommendation, level II/III evidence**).

Selection of FFP Packs by Blood Group

ABO Blood Group Compatibility

With regard to ABO blood groups, the first choice of FFP is that of the same ABO group as the patient. If this is not available, FFP of a different ABO group is acceptable so long as it has been shown not to possess anti-A or anti-B activity above a limit designed to detect 'high titres'. FFP of group O should only be given to O recipients (**grade B recommendation, level III evidence**).

Group O FFP should not be used in infants or neonates who are not group O because the relatively large volumes required can lead to passive immune haemolysis (**grade B recommendation, level III evidence**).

Rh Blood Group Compatibility

Fresh-frozen plasma, methylene blue and light-treated FFP (MBFFP) and solvent detergent treated FFP (SDFFP) of any Rh type may be given regardless of the Rh status of the recipient. No anti-D prophylaxis is required if Rh D-negative patients receive Rh D-positive FFP (**grade B recommendation, level IIa evidence**).

Thawing and Storage of Thawed Product

Storage after Thawing

After thawing, and when factor VIII replacement is not required, FFP and cryosupernatant may be stored at 4 degrees C in an approved blood storage refrigerator before administration to the patient so long as the infusion is completed within 24 hours of thawing. If delay in transfusing cryoprecipitate is unavoidable, the component should be stored at ambient temperature and used within 4 hours (**grade B recommendation, level III evidence**). (Recommendation was amended; see Addendum 2 in the "Companion Documents" field for information.)

Adverse Effects

Infection

Patients likely to receive multiple units of FFP, such as those with a congenital coagulopathy, should be considered for vaccination against hepatitis A and B (**grade C recommendation, level IV evidence**).

Clinical Indications for the Use of FFP, Cryoprecipitate and Cryosupernatant

Thrombotic Thrombocytopenic Purpura

Single volume daily plasma exchange should ideally be begun at presentation (**grade A recommendation, level Ib evidence**) and preferably within 24 hours of presentation (**grade C recommendation, level IV**). Daily plasma exchange should continue for a minimum of 2 days after remission is obtained (**grade C recommendation, level IV evidence**).

Reversal of Warfarin Effect

Fresh-frozen plasma should never be used for the reversal of warfarin anticoagulation when there is no evidence of severe bleeding (**grade B recommendation, level IIa evidence**).

Vitamin K Policies in Intensive Care Units (ICUs)

Intensive care unit patients should routinely receive vitamin K; 10 mg thrice weekly for adults and 0.3 mg per kg for children (**grade B recommendation, level IIa evidence**).

Liver Disease

Available evidence suggests that patients with liver disease and a prothrombin time (PT) more than 4 seconds longer than control are unlikely to benefit from FFP (**grade C recommendation, level IV evidence**).

Surgical Bleeding

Massive Transfusions

Whether and how much FFP should be used for treating a patient with major blood loss should be guided by timely tests of coagulation (including near-patient tests). 'Formulae' to guide replacement strategies should not be used (**grade B recommendation, level IIb evidence**).

Paediatric Use of FFP

Haemorrhagic Disease of the Newborn (HDN)

Management of Acute Haemorrhages, FFP

When haemorrhage due to HDN occurs, FFP (10 to 20 mL/kg) is indicated, as well as intravenous vitamin K (**grade C recommendation, level IV evidence**).

Prothrombin Complex Concentrate (PCC)

Although the coagulation defect in HDN may be reversed by PCC, there are no data to guide dosage in this situation (**grade C recommendation, level IV evidence**).

Neonates with Coagulopathy and Bleeding, or at Risk of Bleeding from an Invasive Procedure

Neonates with significant coagulopathy, and risk of bleeding or who are about to undergo an invasive procedure, should receive approximately 15 mL/kg of FFP as well as a dose of vitamin K (**grade C recommendation, level IV evidence**). Shortening of the prolonged clotting times is unpredictable and should be checked following administration.

Prevention of Intraventricular Haemorrhage in Preterm Infants

Routine administration of FFP to prevent periventricular haemorrhage (PVH) in preterm infants is not indicated (**grade A recommendation, level IIb evidence**).

Red Cell T Antigen Activation

In the absence of definitive data, each clinical unit should formulate its own policies and protocols for the investigation of any unexpected haemolysis associated with a transfusion of plasma to a baby with necrotizing enterocolitis (NEC) or a similar septic condition. A selective testing strategy and transfusion management protocol may be required (**grade C recommendation, level IV evidence**).

If there is a high suspicion of T-activated haemolysis, an exchange transfusion using low titre anti-T plasma and red cell products may be indicated. In this situation, administration of low anti-T titre (washed/resuspended) platelet concentrates may be indicated (**grade C recommendation, level IV evidence**).

Note, avoiding transfusion of plasma-containing blood components in infants with T-activated red cells may risk suboptimal treatment for patients requiring haemostasis support (**grade B recommendation, level II/III evidence**).

Definitions:

Statements of Evidence

Ia Evidence obtained from the meta-analysis of randomized controlled trials.

Ib Evidence obtained from at least one randomized controlled trial.

IIa Evidence obtained from at least one well-designed controlled study without randomization.

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Grades of Recommendations

Grade A Required at least one randomized controlled trial as part of a body literature of overall good quality and consistency addressing the specific recommendations (evidence levels Ia, Ib).

Grade B Requires the available of well conducted clinical studies but no randomized clinical trials on the topic of recommendations (evidence levels IIa, IIb, III).

Grade C Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (evidence level IV).

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate use of fresh-frozen plasma, cryoprecipitate and cryosupernatant
- Reduced morbidity and mortality

POTENTIAL HARMS

- Allergic reaction and anaphylaxis
- Transfusion-related acute lung injury
- Complications associated with leucocyte depletion
- Infection
- Graft versus host disease
- Venous thromboembolism

CONTRAINDICATIONS

CONTRAINDICATIONS

- Fresh-frozen plasma (FFP) is contraindicated for volume expansion.
- FFP is not indicated in disseminated intravascular coagulation without bleeding.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

While the advice and information in these guidelines is believed to be true and accurate at the time of going to press, neither the authors nor the publishers can accept any legal responsibility or liability for any omissions or errors that may be made.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

O'Shaughnessy DF, Atterbury C, Bolton Maggs P, Murphy M, Thomas D, Yates S, Williamson LM, British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. Br J Haematol 2004 Jul;126(1):11-28. [92 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Jul

GUIDELINE DEVELOPER(S)

British Committee for Standards in Haematology - Professional Association

SOURCE(S) OF FUNDING

British Committee for Standards in Haematology

GUIDELINE COMMITTEE

British Committee for Standards in Haematology, Blood Transfusion Task Force

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Task Force Members: J. Duguid (*Chairman*); D. F. O'Shaughnessy (Convenor, Task Force nominee), Southampton University Hospitals, Southampton; C. Atterbury (RCN nominee), Queen Elizabeth Hospital, Kings Lynn; P. Bolton Maggs (RCPCH nominee), Central Manchester and Manchester Children's University Hospitals, Manchester; M. Murphy (Task Force nominee), NBS Oxford, Oxford; D. Thomas (RCA nominee), Morriston Hospital, Swansea; S. Yates (representing Biomedical Scientists) Blood Transfusion Laboratories, Southampton University Hospitals, Southampton; L. M. Williamson (Task Force nominee) NBS Cambridge, Cambridge, UK

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the British Committee for Standards in Haematology Web site.

Print copies: Available from the British Committee for Standards in Haematology; Email: bcsh@b-s-h.org.uk.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Addendum 1 to guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. 2007. 1 p. Available from the British Committee for Standards in Haematology Web site.
- Addendum 2 to guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. 2007. 1 p. Available from the British Committee for Standards in Haematology Web site.

Print copies: Available from the British Committee for Standards in Haematology; Email: bcsh@b-s-h.org.uk.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on May 23, 2008. The information was verified by the guideline developer on June 30, 2008.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 11/3/2008