Superior Health Council

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Guidelines for the transfusion of fresh frozen plasma

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1. INTRODUCTION AND ISSUES

In Belgium, the number of 200 ml units of fresh frozen plasma that are distributed on a yearly basis amounts to around 100,000. In contrast to the other developed countries, there does not appear to have been any upward trend in the use of fresh frozen plasma in our country in the last decades. There are few indications for fresh frozen plasma and there are no chronic indications that require the transfusion of plasma over several years. Nowadays, the innate or acquired deficiencies of nearly all coagulation factors are treated with specific concentrates, which are often obtained through genetic manipulation. The extensive use made of human blood and of derived blood products for therapeutic purposes, as well as the wide discrepancies that can be observed amongst Belgian hospitals in their transfusion practice, have made it necessary to develop guidelines for the optimal use of these products. The recommendations made by these programmes aim at guaranteeing a safe, permanent supply in accordance with ethical rules, as well as ensuring an adequate and rational clinical use of the donated blood.

Transfusions are a necessary part of healthcare: not only are they needed when dealing with medical and surgical emergencies (road accidents, burn victims…), they are also required for surgical operations and therapies aiming at improving the health of the recipient (leukaemia patients, haemophiliacs…). Transfusion Committees have been set up in Belgian hospitals as a result of the Royal Decree of April 16th, 2002 and have been ordered to draw up transfusion guidelines for hospitals. In addition, these Committees closely monitor the use of every blood component in the hospital. This surveillance, as well as large-scale studies carried out in some European countries, reveals that hospitals exhibit a great lack of consistency with respect to the indications for transfusions. Finally, if strict rules are implemented in transfusion establishments, a particular effort will also be required to standardise and rationalise clinical indications.

In order to remedy these divergences and to provide a scientific basis to the Transfusion Committees, the Superior Health Council (SHC) has organised an expert meeting on fresh frozen plasma with the *Belgian Haematological Society*. This meeting was designed to collect the most recent knowledge on the subject of fresh frozen plasma transfusion as well as its alternatives in order to enhance the harmonisation of transfusion practice in Belgium. Thus, the Superior Health Council is required to draw up a code of good practice concerning the correct administration of blood or blood products, in keeping with article 3 of the law of July 5th, 1994 on blood and blood products of human origin, modified by the programme law of April 8th, 2003, Chap. X, Art 158.

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These issues were discussed during the meetings of the working group «blood and blood products» that took place on September 21st and November 23rd, 2006, as well as on January 18th, 2007. The provisional advisory report of the members of the working group was approved on January 23rd, 2007 and validated by the SHC Board on February 7th, 2007.

Assignment

1. The organisation of an expert meeting on the indications for transfusing fresh frozen plasma;

2. The assessment of the most recent knowledge on the subject of fresh frozen plasma transfusions;

3. The drawing up of guidelines for fresh frozen plasma transfusions.

2. CONCLUSIONS

Assignment 1. The Superior Health Council (SHC) set up a working group, which met on several occasions in 2006 in order to prepare an expert meeting «*Transfusion Guidelines: Pathogen reduction, products and indications for the transfusion of plasma*». This conference, which was held in collaboration with the *Belgian Haematological Society*, took place in Brussels on May 11th, 2006. Four speakers discussed the indications for transfusing fresh frozen plasma, the different methods available for pathogen-reduction and the alternatives to transfusing this blood component.

Assignment 2. Assessing the most recent knowledge on the subject of fresh frozen plasma transfusions was performed in numerous steps. On the one hand, there were papers and subsequent discussions, followed by the final discussion of the meeting, on the other, there were (a) the preparation of transfusion guidelines by the rapporteurs and (b) the validation of the recommendations proposed by the members of the working group "blood and blood products" of the SHC.

Assignment 3. The working group has been able to draw up a substantial series of recommendations aiming at standardising and rationalising clinical indications for fresh frozen plasma transfusions in Belgium. These recommendations are included in the report entitled "*Guidelines for the transfusion of fresh frozen plasma*", which is to be published in a scientific journal.

3. FURTHER DETAILS AND ARGUMENTATION

a) *The organisation of an expert meeting on the indications for transfusing fresh frozen plasma*

The expert meeting «*Transfusion Guidelines: Pathogen reduction, products and indications for the transfusion of plasma*» was held in Brussels on May 11th, 2006. Its aim was to rationalise the prescription of fresh frozen plasma by providing guidance for practitioners in their decision-forming processes, thus enhancing the quality of transfusions and providing help in homogenising the practice under discussion. In order to achieve this goal, the organising committee gleaned the most relevant contributions from the literature and asked that, in preparing their papers, four speakers pay particular attention to the available meta-analyses and the *evidence based medicine* approach. Moreover, the speakers were asked to clearly identify any opinions of their own. A printed version of the papers was given to the chairmen (K. Jochmans, Brussels and Ph. Baele, Brussels) and the rapporteurs (D. De Backer, Brussels, and B. Vandekerckhoven, Ghent) in order to enable them to prepare the discussions, for which a large amount of time had been programmed.

There were four papers, each on a highly specialised subject:

1. « *Indications and levels of evidence for clinical transfusion of fresh frozen plasma* » (S. Stanworth, Oxford);
2. « *Pathogen reduction for fresh frozen plasma* » (L. Williamson, Cambridge);
3. « *Plasma-derived concentrates: indications in 2006* » (C. Hermans, Brussels);
4. « *Alternatives to allogenic transfusion: indications for the transfusion of autologous products* » (Ph.Van der Linden, Brussels).

b) The assessment of the most recent knowledge on the subject of fresh frozen plasma transfusions

Each paper was immediately followed by an in-depth discussion of the analyses put forward. Next, during the discussion following the set of papers, each recommendation suggested was re-examined and assessed during an intense exchange involving both the experts and the doctors in charge of transfusions who attended the meeting.

Thanks to this meeting, it was possible to set up guidelines for the transfusion of fresh frozen plasma. These reflected the expertise of the members of the working group "blood and blood products" of the SHC, who based them both on the analyses outlined in the papers and on the arguments or opinions expressed during the discussions on the report, which goes into the details of the principles behind fresh frozen plasma transfusions. The members of the working group adapted this document and produced a final version, which was approved on January 23rd, 2007 (reference a).

c) The drawing up of guidelines for fresh frozen plasma transfusions.

These recommendations do not provide a description of user requirements, but can be used as a means of assessing minimum standards of good practice.

1. Coagulation tests often fail to predict the risk of bleeding.

2. Coagulation tests should be performed to assess the severity of dilutional coagulopathy and disseminated intravascular coagulation (DIC) and to monitor their evolution under the influence of therapeutic interventions.

3. Plasma administration slightly improves altered coagulation tests but usually fails to normalise them.

4. Despite the lack of randomised controlled trials, it is advisable to transfuse plasma in patients with a massive haemorrhage (life-threatening) caused by e.g. trauma or surgery. Plasma should be administered in adequate amounts to prevent further bleeding (10-15 mL/kg). This operation should be repeated if the bleeding persists.

5. Every effort should be made to correct other factors leading to coagulopathy as well. These include treating acid-base disorders, preventing and treating hypothermia, anaemia, and thrombocytopenia.

6. Priority should be given to controlling the source of bleeding in patients with massive haemorrhage due to trauma, obstetrical problems, medical problems, or surgery.

7. Plasma should not be administered prophylactically to patients with normal coagulation tests submitted to high-risk surgery or invasive diagnostic procedures.

8. It has not been proved that the administration of plasma prevents bleeding in patients with abnormal coagulation tests. This does not rule out that plasma can be useful for specific patient populations.

9. Plasma is not the first choice to neutralise anticoagulation with coumarinic agents in bleeding patients and prothrombin complex concentrates should be given instead. The administration of plasma can be taken into consideration when there are no prothrombin complex concentrates available.

10. Patients with DIC should not be given plasma in order to correct abnormal coagulation tests. The administration of plasma can be taken into consideration for patients with DIC who are actively bleeding.

11. Transfusing plasma can improve the fibrinogen deficiency associated with dilutional coagulopathy. Fibrinogen may be administered if severe hypofibrinogenemia persists.

12. Plasma must not be given to treat hypovolemia.

13. Plasma should not be used routinely for plasma exchange.

14. Plasma must be used in case of thrombotic thrombocytopenic purpura (TTP). The various plasma products may show slight differences in their effectiveness in treating TTP. However, there are insufficient data to support the claim that one product is superior to another.

15. Children suffering from the haemorrhagic disease of the newborn should be given plasma or a prothrombin complex concentrate (in conjunction with vitamin K). As regards the remaining indications, plasma should be administered in the same way as to adults.

16. All validated pathogen reduction techniques are acceptable and equally efficacious.

17. All validated pathogen reduction techniques induce an acceptable and comparable loss of factors that are important for blood clotting.

18. As regards the risk of vCJD transmission, plasma derived from individual donations is theoretically safer than plasma obtained from pools, which contain several donations. Hospital blood supplies should therefore standardise on single unit plasma products.

19. Neonates should be given blood group AB plasma in order to reduce the risk of blood group incompatible transfusions.

20. In order to reduce the risk of blood group incompatible transfusions, it is advisable to replace blood group O plasma by blood group A plasma for both plasma production and the supply of hospital blood banks.

The recommendations above constitute one of the appendixes to the «*Good transfusion practice for hospitals* » (SHC no 8167).

4. REFERENCES

Report « *Guidelines for the transfusion of fresh frozen plasma* », 18/01/07, 16 pages.

5. APPENDIXES

None.

6. COMPOSITION OF THE WORKING GROUP

The following experts were involved in issuing this advisory report:

- BAELE Philippe (anaesthesiology);
- BONTEZ Walter (blood, tissues and cells);
- DE BACKER Daniel (intensive care);
- DE PAEP Rudi (intensive care);
- FERRANT Augustinus (clinical haematology);
- LAMBERMONT Micheline (transfusion);
- LATINNE Dominique (haematological biology);
- MUYLLE Ludo (blood, tissues and cells);
- PEERLINCK Kathelijne (internal medicine, haematology);
- SCHOTS Rik (haematology);
- THOMAS Isabelle (TSE, virology);
- TOUNGOUZ Michel (immunology, haematology, transfusion);
- VANDEKERCKHOVE Bart (clinical biology, cell therapy);
- VOETS Ellen (blood and blood products, TSE, virology).

This working group was chaired by Mr. TOUNGOUZ Michel, the scientific secretary was Mr. HÜBNER Roland.