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SHORT COMMUNICATION

THE USE OF WHOLE BLOOD IN PATIENTS WITH MAJOR TRAUMA BLEEDING: SUMMARY AND CONSENSUS OF AN INTERDISCIPLINARY PANEL MEETING

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Introduction

The effectiveness and safety of the concept of "whole blood" (WB) administration has been a debated topic in many developed countries in recent years. Although the results of observational studies from military conflicts and civilian settings suggest a benefit of WB administration on survival of patients with polytrauma and massive bleeding (1, 2), the results of prospective studies do not provide clear evidence of the benefit of WB administration in civilian settings (3, 4). However, PK administration is considered safe and logistically advantageous (5). In the Czech Republic (CR), administration of WB in the form of a universal transfusion product with the official name "Whole blood deleukotized for universal administration" is possible from 2020. At present, the concept of WB administration is implemented in the University Hospital Hradec Králové, Medical rescue service of the Hradec Králové Region, Military University Hospital Prague, University Hospital Prague - Motol, University Hospital Ostrava, Medical rescue service of the Moravian-Silesian Region, University Hospital Olomouc, and the Medical rescue service of the Czech Armed Forces in Plzeň - Líně. According to unpublished data (Bohoněk M., Kutáč D., Řeháček V., Blahutová Š, Galuszková D.: Use of Low Titre Group O Whole Blood in the Czech Republic - abstract submitted to ISBTABS24-903), approximately 800 PKDUs were administered in 400 patients in the Czech Republic.

The aim of the interdisciplinary panel was to discuss the use of WB in patients with life-threatening shortening due to trauma and to formulate a common consensus position on the administration of WB in the conditions of the Czech health care system. The panel did not have the time or resources to prepare a comprehensive systematic review on the subject.

Methods

The Accurate Consensus Reporting Document (ACCORD) methodology (6) was used to develop the opinion of the interdisciplinary panel.

Project registration

The project was not registered prior to its initiation.

Procedure for selecting the members of the interdisciplinary panel

The interdisciplinary panel was initiated by the committee of the Czech Society of Anaesthesiology, Resuscitation and Intensive Care Medicine. The presidents of the selected professional societies (PS) were contacted by e-mail with a request to nominate experts to the interdisciplinary panel for their respective PS. OSs that are affected by the issue of PK administration were contacted.

Composition of the interdisciplinary panel (in alphabetical order)

- ass.prof. MUDr. Bláha Jan, Ph.D., MHA, LLM (BJ)
- COL (GS) MUDr. Bohoněk Miloš, Ph.D. (BM)
- prof. MUDr. Černý Vladimír, Ph.D., FCCM, FESAIC (CZ)
- ass,prof.. MUDr. Kočí Jaromír, Ph.D., FACS (KJ)
- MUDr. Loužil Jan (LJ)
- MUDr. Řeháček Vít, Ph.D. (RC)
- MUDr. Truhlář Anatolij, Ph.D., FERC (TA)
- MUDr. Zýková Ivana (ZI)

Panel Methodologist

- PhDr. Klugar Miloslav, Ph.D. (KM)

Participating OS (alphabetically, delegated representatives in brackets)

- Czech Society of Hematology (LJ)
- Czech Resuscitation Council (TA)
- Czech Society of Anaesthesiology, Resuscitation and Intensive Care Medicine (BJ, ČV, ZI)
- Czech Society for Thrombosis and Haemostasis (BJ)
- Czech Society of Trauma Surgery (KJ)
- Society for Transfusion Medicine (SV)
- Society of Emergency and Disaster Medicine (KJ, TA)
- Society of Military Medicine (BM)

Panel meeting

The panel meeting was held on 14th December 2023 in Prague. All nominated panel members were contacted by email in advance of the meeting date to prepare a discussion on the three issues on the panel agenda:

1 What is the opinion of the panel members on the administration of whole blood as part of the treatment of life-threatening bleeding in trauma?
2 Should whole blood administration become the preferred procedure in the treatment of life-threatening bleeding in trauma?
3 Should we systematically promote the administration of whole blood as part of the treatment of life-threatening bleeding in trauma?

Consensus process

Panel members were provided with draft position statements for comment after the panel meeting, and upon receipt, the panel chair prepared a version of each position statement for comment by panel members using a modified Delphi method. Expressions of agreement or disagreement were on a scale of 1-9 (7-9 = strong agreement, 5-6 = weak agreement, 1-4 = disagreement). Strong agreement was required from at least 2/3 of the panelists to adopt the position paper. If the results of the vote did not meet the definition of agreement, the text of the opinion was revised and another round of voting proceeded.

Statistical methods

The numerical values of the votes on each opinion were evaluated using descriptive statistical methods and are presented as median and interquartile range (IQR).

Results

The panel members' votes were taken in 4 rounds, and the panel members' vote values are presented for each individual opinion in summary as median and IQR.

Opinion 1

Whole blood in the Czech Republic an individually manufactured blood product, group 0, obtained from blood donors with a history of low risk of HLA alloimmunization as a prevention of TRALI, with low anti-A/B IgM antibody titers, and deleukotized with a platelet-sparing filter. The properties and composition of whole blood are not completely standardisable, i.e. whole blood shows variability in terms of haemoglobin content, platelet count and function, and coagulation factor activity.

Panel vote: 9 (0)

Summary of Panel position: position 1 adopted

Panel Comment: The amount of WB production is limited in terms of availability of suitable donors (e.g. for blood group 0 RhD neg (0-) about 1% of donors meet the requirements for PKDU collection, for blood group 0 RhD poz (0+) about 9% of donors meet the requirements, donors with low risk of TRALI are mainly male, low anti-A/B antibody titer about 80% of donors meet the requirements). The biological activity of whole blood is influenced by the length of storage (the longer the storage time, the lower the biological activity), which distinguishes WB from mass-produced and industrially produced drugs.

Opinion 2

The main biological benefit of early administration of whole blood in adult patients with life-threatening bleeding in severe trauma may lie in its complexity (volume replacement, oxygen transport, procoagulant and coagulant activity), in the ease of its use, especially in pre-hospital conditions or in hospital emergency departments.

Panel vote: 9 (0)

Summary of Panel position: position 2 adopted

Opinion 3

The current state of expertise and scientific evidence on the subject does not allow to designate whole blood administration as the preferred method in the management of massive blood loss or in the treatment of trauma-induced coagulopathy.

Panel vote: 9 (1.25)

Panel position summary: position 3 adopted

Opinion 4

Administration of whole blood is a possible alternative to current treatment modalities for patients with life-threatening bleeding in severe trauma, particularly in the prehospital care setting or in hospital emergency departments.

Panel vote: 7.5 (2)

Panel position summary: position 4 adopted

Opinion 5

The decision to implement a whole blood administration program in a given health care facility should be supported by a) an analysis of the patient population where whole blood administration is being considered, b) an assessment of the quality and organization of follow-up care, and c) consensus on the organizational and professional framework for whole blood administration among all disciplines involved in the issue in the health care facility.

Panel vote: 9 (0)

Summary of the Panel's position: position 5 adopted

Panel Comment: A prerequisite for the implementation of whole blood administration is the need to have an assured manufacturer and supplier partner - the transfusion service facility. This is due to the complexity of producing whole deleukotized universal blood and the limited number of donors where special testing is required.

Opinion 6

In the context of Opinion 3, the Panel notes the need for further scientific evidence on the benefits, risks and indicators of long-term clinical outcome for patients where whole blood has been administered. The Panel agrees on the appropriateness of conducting a national multicentre clinical trial to compare whole blood administration-based procedures with existing procedures.

Panel vote: 9 (1)

Summary of Panel position: position 6 adopted

Discussion

The formulated opinions of the interdisciplinary panel represent for the first time in the national literature the opinion of relevant professional societies on the subject matter. The course and content of the discussion among the panel members allow us to conclude that WB administration is a topical issue in the Czech Republic that deserves to be discussed in a responsible professional and methodologically transparent manner - in the context of the mentioned population of trauma patients, WB administration has a rational physiological basis and carries the potential for clinical benefit - recent evidence supports this thesis.

The concept of WB also carries a number of, to some extent problematic and not yet fully clarified, aspects that cannot be ignored or marginalised in an evidence-based debate. The conclusions of the panel on WB administration can be used as a starting point for follow-up expert discussions on a number of questions that arise in the context of WB use and to which we should seek a data-based answer if we want to promote a systemic implementation of WB administration based on the tools of evidence-based medicine. Conducting a clinical trial in a sufficient number of patients and with appropriate methodology is essential in this context, although the clinical experience of the proponents of the WB concept will play a significant role in this debate.

For all the differences of opinion on selected aspects of WB administration, the goal is common from the perspective of real-world practice - to exploit the unique properties of WB in the optimal time window and to place WB administration in a biologically rational manner in the context of all downstream coagulation support procedures.

Other information

As part of the panel members' ongoing review of the individual opinions, a proposal was made to add a comment on PK in terms of its role in the replacement of low fibrinogen levels to Opinion 4. After extensive discussion, there was no consensus among the panel members over the inclusion of the commentary (3 members opposed the inclusion of the commentary, 3 members were in favour of the inclusion of the commentary, 2 members were not in favour) and the commentary was removed from the relevant section of the text.

Conflict of interest of panel members

- Bláha Jan does not indicate a conflict of interest on the subject matter
- Bohoněk Miloš does not indicate a conflict of interest on the subject matter
- Černý Vladimír has no conflict of interest on the subject matter
- Kočí Jaromír does not declare a conflict of interest in the subject matter
- Loužil Jan does not declare any conflict of interest in the subject matter
- Řeháček Vít does not declare any conflict of interest in the subject matter
- Truhlář Anatolij has no conflict of interest in the subject matter
- Zýková Ivana does not declare any conflict of interest in the subject matter
- Klugar Miloslav has no conflict of interest in the subject matter

Financing of the project

The project was not financed by any commercial or other entity. The panel members were not remunerated for their participation or work in the panel. The panel meeting was held free of charge at the premises of the Institute of Medical Research in Prague. Refreshments during the panel meeting were provided by Military University Hospital Prague.

Contribution of individual authors to the text

Author contributions are reported in accordance with the CRediT (Contributor Roles Taxonomy) https://www.elsevier.com/researcher/author/policies-and-guidelines/credit-author-statement methodology (conceptualization, methodology, software, validation, formal analysis, research/experiment conduct, evidence analysis, sources, data management; writing (original draft), writing (review and editing), visualization, leadership and coordination, project administration, fundraising.

- Bláha Jan: writing (review and editing)
- Bohoněk Miloš: conceptualization, writing (reviews and editing)
- Černý Vladimír: conceptualization, methodology, writing (original design), writing (reviews and editing), project management and coordination, project administration
- Klugar Miloslav (methodology, reviews and editing)
- Kočí Jaromír: writing (reviews and editing)
- Loužil Jan: writing (reviews and editing)
- Řeháček Vít: writing (reviews and editing)
- Truhlář Anatolij: writing (reviews and editing)
- Zýková Ivana: writing (reviews and editing)

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