

Special article

Low-titer group O blood products (LTOWB) and freeze-dried plasma: a novel strategy for balanced hemorrhage resuscitation

Pimol Chiewsilp and Dootchai Chaiwanichsiri

National Blood Centre, Thai Red Cross Society

Introduction

Recent military conflicts have reinforced the critical importance of timely blood transfusion for the survival of combat casualties with life-threatening hemorrhage.¹ These operational challenges have driven continued refinement of transfusion strategies in both military and civilian trauma care. The concepts of Damage Control Resuscitation (DCR)^{2,3} and Remote Damage Control Resuscitation (RDCR)⁴ have evolved to emphasize the early administration of blood products, beginning in the prehospital setting whenever feasible, to reduce mortality associated with severe hemorrhage and hemorrhagic shock.

Among currently available blood products, Low-titer Group O Whole Blood (LTOWB) has emerged as the preferred first-line transfusion product for trauma resuscitation when available.⁵⁻⁸ LTOWB provides all three essential components required for balanced resuscitation within a single unit: red blood cells to restore oxygen-carrying capacity, platelets to support primary hemostasis, and plasma to replenish intravascular volume while supplying coagulation factors necessary for the correction of trauma-induced coagulopathy.^{6,7} In addition to its physiological advantages, LTOWB simplifies transfusion logistics by reducing the need to transport and administer multiple individual blood components.⁹

Current evidence indicates that LTOWB can be safely used as an emergency uncrossmatched blood product for most patients with unknown ABO blood type, particularly Rh-positive recipients, and in situations where compatibility testing is unavailable or would result in unacceptable treatment delays.^{10,11} The safety of this

approach depends on the use of group O whole blood containing low titers of anti-A and anti-B isoagglutinins, with acceptable titer thresholds defined according to national or institutional policies.¹²

Despite these clinical advantages, two important challenges limit the widespread implementation of LTOWB. First, the production capacity of LTOWB is inherently limited because only a relatively small proportion of blood donations meet the eligibility criteria for low-titer whole blood. Second, maintaining LTOWB inventories at multiple hospitals may result in substantial product wastage due to expiration, particularly in facilities with low transfusion demand, leading to unnecessary loss of valuable blood resources.

Consequently, there remains a need for an alternative transfusion strategy that preserves the principles of balanced resuscitation while improving product availability, inventory management, and logistical flexibility.

Concept of low-titer group O blood products (LTOWB)

To address the limitations associated with the implementation of LTOWB, we propose the concept of Low-titer Group O Blood Products (LTOWB) as an alternative blood product package for emergency hemorrhage resuscitation as well as product availability in emergency and resource-limited settings (Figure 1).

The LTOWB package consists of the following components:

1. Red blood cell-platelet component

A group O platelet-rich red blood cell (PR-RBCs) component suspended in an additive solution, providing both oxygen-carrying capacity and functional platelets.

Correspondence should be addressed to Assoc. Prof. Dootchai Chaiwanichsiri, M.D., National Blood Centre, Thai Red Cross Society, Henri Dunant Rd., Pathumwan, Bangkok 10330 E-mail: dootchai.c@redcross.or.th

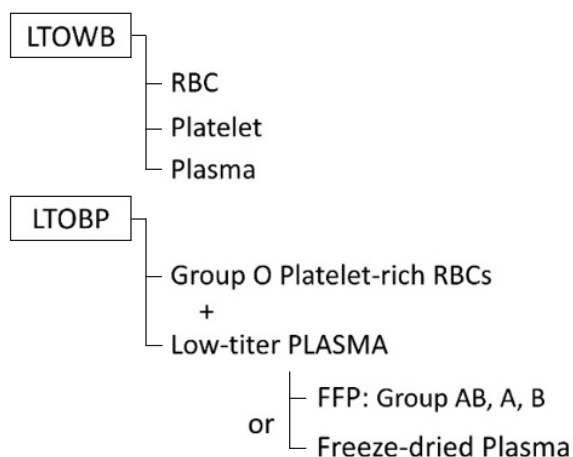


Figure 1 Concepts of LTOWB and LTOBP

2. Plasma component

Either of the following low-titer plasma products may be used:

Option 1 Fresh frozen plasma (FFP) selected according to ABO compatibility:

- Group AB FFP
- Low-titer group B FFP (low anti-A)
- Low-titer group A FFP (low anti-B)

Option 2 Freeze-dried plasma (FDP)¹³ manufactured from a single unit of fresh plasma meeting the same low-titer criteria described above.

By combining the cellular component with low-titer plasma products, the LTOBP package is intended to provide red blood cells, platelets, plasma volume, and coagulation factors in proportions comparable to those delivered by LTOWB, maintaining the fundamental principle of balanced resuscitation.

Preparation and operational characteristics of LTOBP

Preparation of group O platelet-rich red blood cells

Fresh group O whole blood is collected within 6 hours of donation, in accordance with the collection requirements for the preparation of conventional blood components. The whole blood is processed using a refrigerated centrifuge with a heavy-spin protocol, allowing the platelets to remain associated with the red blood cell component. This process produces one unit of group O platelet-rich red blood cells (PR-RBCs).

The storage duration of the PR-RBCs is determined by the type of anticoagulant and/or additive solution used for blood collection and storage. The resulting group O PR-RBCs may be used for transfusion in patients of any ABO blood group in emergency situations. The separated plasma is subsequently removed and may be used for other clinical or transfusion-related purposes.

Preparation of LTOBP

The cellular component (group O PR-RBCs suspended in additive solution) is combined with either low-titer FFP or low-titer FDP using a sterile closed system. Following preparation, LTOBP should ideally be transfused immediately to ensure platelet viability and clotting ability. If the unit is opened and spiked, it must be completely transfused within 4 hours. If the unit remains unopened after preparation, the PR-RBCs may continue to be stored at 1-6°C for the approved shelf life of the additive solution. Transportation must be maintained at 2-10°C in accordance with WHO blood cold chain guidelines (Figure 2).

Freeze-dried plasma (FDP)

Immediately before administration, FDP is reconstituted using sterile water for injection or the specified sterile diluent, according to the manufacturer's validated

Workflow for LTOBP Preparation

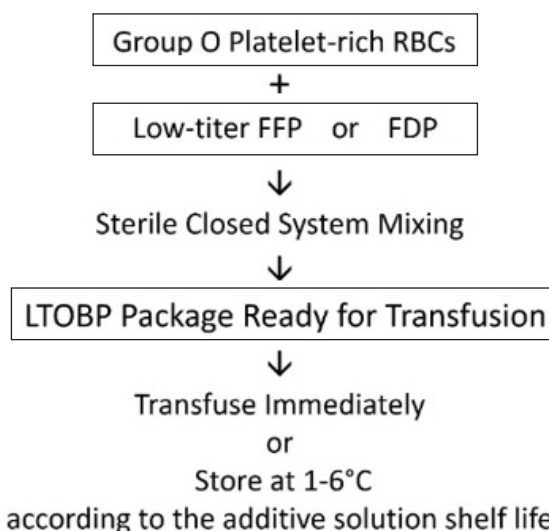


Figure 2 Workflow for preparation of Low-titer Group O Blood Products (LTOBP)

instructions. Reconstitution typically requires only a few minutes, allowing plasma therapy to be initiated substantially earlier than with conventional thawed FFP.¹⁴ Following reconstitution, FDP should preferably be transfused promptly and, where storage after reconstitution is permitted, used within the validated post-reconstitution storage period specified by the manufacturer's instructions. This period may vary among FDP products depending on validated stability data. Recent studies have demonstrated that modern FDP retains coagulation factor activity and overall hemostatic function comparable to conventional FFP following reconstitution.¹⁵⁻¹⁸

Recommendations for clinical practice

The LTOBP package is designed to facilitate emergency transfusion in patients of any ABO blood group including those whose blood type has not yet been determined (Figure 3).

Recommendation 1. Early plasma resuscitation

When packed red blood cells (PRCs) or whole blood are not immediately provided, FDP should be administered as early as possible to resuscitate and help preserve intravascular volume, supports coagulation factor replacement, and mitigates trauma-induced coagulopathy. It serves as an effective bridge therapy during the interval before whole blood or conventional blood components become available.^{18,19}

Clinical Practice for Massive Hemorrhage

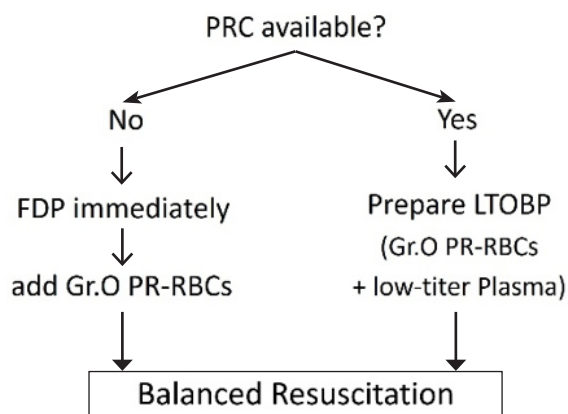


Figure 3 Clinical algorithm for emergency hemorrhage resuscitation using FDP and LTOBP

Recommendation 2. Balanced transfusion

Once red blood cells become available, balanced transfusion should continue according to current Massive Transfusion Protocols (MTPs), targeting an approximately balanced ratio of red blood cells, plasma, and platelets whenever clinically feasible.

Depending on clinical requirements, reconstituted plasma may either be combined with the group O PR-RBCs to create a complete LTOBP package or administered separately according to the patient's clinical condition and physician judgment.

Discussion

Unlike LTOWB, the proposed LTOBP strategy combines readily available blood components to replicate the physiological benefits of whole blood while providing greater flexibility in production and inventory management. This approach may enhance national blood preparedness by enabling existing blood component inventories to support balanced transfusion without requiring dedicated LTOWB programs at every institution.

Consequently, LTOBP may facilitate earlier hemostatic resuscitation during prolonged evacuation and in resource-limited settings, thereby supporting the principles of Remote Damage Control Resuscitation (RDCR) (Figure 4).

Current strategy

LTOWB

→ Balanced Resuscitation

Limitation

- Limited availability
- Inventory loss
- Short shelf utilization
- Cold chain transport

Proposed strategy

Group O Platelet-rich RBCs + Low-titer FFP or FDP

LTOBP Package → Balanced Resuscitation

- + Higher availability
- + Scalable production
- + Reduced wastage
- + Good inventory control
- + FDP 2–25°C, improved logistics

Figure 4 Comparison of balanced hemorrhage resuscitation strategies using LTOWB and LTOBP

From a transfusion safety perspective, this transfusion strategy also offers theoretical advantages. Whereas LTOWB contains both anti-A and anti-B isoagglutinins, the plasma component of LTOBP is selected as low-titer group A or low-titer group B plasma, exposing recipients to only one major ABO antibody specificity. Although clinical safety ultimately depends on validated low-titer thresholds, institutional policies, and appropriate patient selection, this strategy may theoretically reduce exposure to incompatible ABO isoagglutinins, although this hypothesis requires prospective clinical validation.

Another important consideration is preservation of coagulation function. In LTOWB, plasma coagulation factor activity gradually declines during refrigerated storage.²⁰ In contrast, the plasma component of LTOBP is supplied as either freshly thawed FFP or reconstituted freeze-dried plasma immediately before transfusion, preserving coagulation factor activity at the time of administration. This characteristic may contribute to more effective correction of trauma-induced coagulopathy during massive hemorrhage, although direct comparative clinical studies are still needed.

The incorporation of FDP into the LTOBP package extends the operational reach of balanced transfusion beyond hospitals by overcoming one of the principal logistical barriers associated with frozen plasma. These characteristics have made FDP an increasingly important component of military transfusion systems and prehospital trauma care in several countries, with growing evidence demonstrating coagulation performance comparable to conventional FFP after reconstitution.^{16,21,22}

Although the LTOBP concept is supported by current transfusion principles and available evidence regarding its individual components, prospective clinical validation is required before routine implementation. Future multicenter clinical studies should compare LTOBP with LTOWB and conventional component therapy with

respect to mortality, transfusion requirements, correction of trauma-induced coagulopathy, safety, and cost-effectiveness. Such studies will be essential to establish the role of LTOBP within modern trauma transfusion practice.

Conclusion

Low-titer Group O Blood Products (LTOBP) represent a readily implementable blood product package designed to support balanced transfusion during emergency hemorrhage resuscitation. By combining a group O PR-RBCs with either low-titer FFP or FDP, LTOBP is designed to provide the essential physiological functions of whole blood while offering important advantages in production, inventory management, distribution, and operational flexibility.

Among its components, FDP is particularly valuable because it combines hemostatic efficacy comparable to FFP with prolonged room-temperature storage, rapid bedside reconstitution, and simplified transportation. These characteristics make it especially suitable for combat casualty care, disaster medicine, aeromedical evacuation, prolonged field care, and remote healthcare environments.

This LTOBP strategy has the potential to expand access to balanced resuscitation in settings where LTOWB is unavailable or difficult to sustain, while having an advantage in health economics by reducing blood wastage. As freeze-dried plasma becomes increasingly available worldwide, integration of the LTOBP concept into national emergency blood preparedness programs may enhance resilience and responsiveness of modern transfusion services and strengthening emergency transfusion capability in Damage Control Resuscitation. However, further multicenter clinical studies should be performed to compare LTOBP with LTOWB and conventional component therapy.

References

1. Pons S, Frattini B, Daniel Y, Derkenne C, Chueca M, Cardinale M, et al. Revised French military transfusion doctrine for large-scale combat operations: a consensus framework. *Crit Care*. 2026;30:194.
2. Van PY, Holcomb JB, Schreiber MA. Novel concepts for damage control resuscitation in trauma. *Curr Opin Crit Care*. 2017;23:498-502.
3. April MD, Fisher AD, Hill R, Rizzo JA, Mdaki KS, Bynum JA, et al. Adherence to a balanced approach to massive transfusion in combat casualties. *Mil Med*. 2023;188:e524-30.
4. Jenkins DH, Rappold JF, Badloe JF, Berséus O, Blackbourne L, Brohi KH, et al. Trauma hemostasis and oxygenation research position paper on remote damage control resuscitation: definitions, current practice, and knowledge gaps. *Shock*. 2014;41(Suppl 1):3-12.
5. Joint Trauma System. Clinical practice guideline: whole blood transfusion. Fort Sam Houston (TX): Joint Trauma System; 2025.
6. Meizoso JP, Cotton BA, Lawless RA, Kodadek LM, Lynde JM, Russell N, et al. Whole blood resuscitation for injured patients requiring transfusion: a systematic review, meta-analysis, and practice management guideline. *J Trauma Acute Care Surg*. 2024; 97:460-70.
7. Rossaint R, Afshari A, Bouillon B, Cerny V, Cimpoesu D, Curry N, et al. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. *Crit Care*. 2023;27:80.
8. Joint Trauma System. Clinical practice guideline: transfusion of type a specific whole blood for the role 3. Fort Sam Houston (TX): Joint Trauma System; 2025.
9. Taylor AL, Corley JB, Cap AP, Swingholm MT, Nance ET, Gonzales R, et al. The U.S. Armed Services Blood Program support to U.S. Central Command 2014-2021: transformation of combat trauma resuscitation through blood product innovation and expansion of blood availability far forward. *Transfusion*. 2022;62(Suppl 1):S167-76.
10. Shackelford SA, Gurney JM, Taylor AL, Keenan S, Corley JB, Cunningham CW, et al. Joint Trauma System, Defense Committee on Trauma, and Armed Services Blood Program consensus statement on whole blood. *Transfusion*. 2021;61(Suppl 1):S333-5.
11. Almog O, Benov A, Beer Z, Sirotkin T, Shental O, Glassberg E. Deploying whole blood to the battlefield—The Israel Defense Forces Medical Corps initial experience during the 2023 war. *Transfusion*. 2024;64 (Suppl 2):S14-8.
12. Dorken-Gallastegi A, Spinella PC, Neal MD, Leeper C, Sperry J, Peitzman AB, et al. Whole blood and blood component resuscitation in trauma: interaction and association with mortality. *Ann Surg*. 2024;280:1014-20.
13. Sailliol A, Martinaud C, Cap AP, Civadier C, Clavier B, Deshayes AV, et al. The evolving role of lyophilized plasma in remote damage control resuscitation in the French Armed Forces Health Service. *Transfusion*. 2013;53(Suppl 1):S65S-71.
14. Joint Trauma System. The use of dried plasma in the deployed trauma system and contingency operations. Clinical practice guideline. Fort Sam Houston (TX): Joint Trauma System; 2026.
15. Garrigue D, Godier A, Glacet A, Labreuche J, Kipnis E, Paris C, et al. French lyophilized plasma versus fresh frozen plasma for the initial management of trauma-induced coagulopathy: a randomized open-label trial. *J Thromb Haemost*. 2018;16:481-9.
16. Shoara AA, Singh K, Peng HT, Moes K, Yoo JA, Sohrabipour S, et al. Freeze-dried plasma: hemostasis and biophysical analyses for damage control resuscitation. *Transfusion*. 2025;65(Suppl 1):S250-64.
17. Singh K, Shoara AA, Peng HT, Prifti V, Moes K, McGuinness C, et al. Dried plasma retains hemostatic function and thermal stability during Arctic military operations. *Transfusion*. 2026;66 (Suppl 1):S159-71.
18. Peddle M, Trojanowski J, Nolan B. The role of freeze-dried plasma in a world of whole blood: a Canadian prehospital and transport perspective. *Scand J Trauma Resusc Emerg Med*. 2026;34:90.
19. Pusateri AE, Kishman AJ, Ariffin MAB, Watts S, Kirkman E, Weiskopf RB, et al. Potential military applications for a new freeze-dried plasma. *Transfusion*. 2025;65(Suppl 1):S240-9.
20. Bhartia R, Kaur P, Mittal K, Tahlan A, Gupta V, Kaur R, et al. Coagulation factor stability and sterility of thawed fresh frozen plasma stored at 2-6 °C for five days: towards optimizing utilization. *Hematol Transfus Cell Ther*. 2025;47:103988. doi: 10.1016/j.htct.2025.103988.
21. Sheffield WP, Singh K, Beckett A, Devine DV. Prehospital freeze-dried plasma in trauma: a critical review. *Transfus Med Rev*. 2024;38:150807. doi: 10.1016/j.tmr.2023.150807.
22. Prifti V, Dion PM, Beckett A, Singh K. Dried plasma for trauma resuscitation: from Canadian Armed Forces to civilian prehospital and rural settings. *CMAJ*. 2025;197:E953-6.



สมาคมโลหิตวิทยาแห่งประเทศไทย
มีทุนสนับสนุนการทำวิจัย การเข้าร่วมประชุมวิชาการ
และทุนส่งเสริมการเรียนรู้ต่างๆ แก่สมาชิกของสมาคมฯ
ทั้งนี้สมาชิกสามารถดูรายละเอียดได้ที่เว็บไซต์
ของสมาคมโลหิตวิทยา: www.tsh.or.th