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IMMUNOADSORPTION-BASED PLASMA PREPARATION: *IN VITRO* EVALUATION OF ANTI-A AND ANTI-B ANTIBODY DEPLETION AND FACTOR VIII ACTIVITY PRESERVATION

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Introduction. Plasma transfusion remains an integral component of intensive care for massive hemorrhage, coagulopathies, and disseminated intravascular coagulation, particularly in emergencies where the recipient's blood group is unknown or cannot be determined immediately. In such cases, administering group-specific plasma is impossible, while the supply of group AB plasma is limited to 4–5% of the total donor pool. In this study, “ABO-universal plasma” is defined as a donor blood component suitable for use in recipients of any ABO blood group without prior determination of their blood type. This product is designed to expand intravascular volume and restore hemostasis. One promising approach to creating such a product is the immunoadsorption of anti-A/anti-B antibodies; however, domestic data regarding its effect on labile hemostatic factors—primarily Factor VIII (FVIII)—are scarce.

Objective. To evaluate the feasibility of using immunoadsorption to prepare a fresh frozen plasma (FFP) component that is free of anti-A/anti-B antibodies or characterized by ultra-low titres ($\leq 1:8$), with preserved activity of labile hemostatic factors. This product is intended for use in patients regardless of their ABO blood group, including for hemostasis restoration.

Materials and methods. This *in vitro* study utilized a paired pre-post design to evaluate 90 FFP samples (30 samples from each blood group: O, A, and B). Anti-A/anti-B antibodies were depleted using immunoadsorbents (POKARD, Russia) in a closed system at 22–25 °C (100-mL plasma volume; 30-min contact time). IgM antibody titers were determined by direct agglutination in gel cards, while IgG antibodies were assessed via the indirect antiglobulin test; Factor VIII activity (FVIII:C) was measured by activated partial thromboplastin time (aPTT) using a coagulometer. Statistical analysis was performed using the Mann-Whitney *U* test; differences were considered significant at $p < 0.05$.

Results. For initial anti-A and anti-B antibody titers of $\leq 1:32$, adsorption completely removed the antibodies; for initial titers ranging from $> 1:32$ to $1:512$, levels decreased to $1:2$ – $1:8$, which meets the international criteria for ultra-low titres plasma. FVIII activity decreased in all groups following adsorption, with technological losses amounting to 18–20%. Baseline FVIII activity in group O plasma was significantly lower than in groups A and B. Following adsorption, all samples from groups A and B retained compliance with the regulatory criterion ($FVIII \geq 0.7$ IU/mL), whereas up to 50% of group O samples failed to meet the required minimum and could not be labeled as FFP.

Conclusions. Immunoadsorption ensured effective removal of anti-A/anti-B antibodies from FFP; however, it was associated with an 18–20% loss of FVIII activity, which is critical primarily for group O plasma. The development of an “ABO-universal plasma” production technology using this method is feasible for special-purpose products — intended for use in emergency prehospital care, military medicine, and strategic reserve formation — provided that donors with baseline FVIII activity $\geq 95\%$ are prescreened (group O) and/or the product is reformulated into lyophilized “ABO-universal plasma”.

Keywords: ABO-universal plasma; immunoadsorption; fresh frozen plasma (FFP); isoagglutinins; anti-A and anti-B antibodies; Factor VIII (FVIII); ABO blood group system; plasma transfusion

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РАЗРАБОТКА ТЕХНОЛОГИИ ПОЛУЧЕНИЯ ПЛАЗМЫ МЕТОДОМ ИММУНОСОРБЦИИ: *IN VITRO* ОЦЕНКА ЭФФЕКТИВНОСТИ УДАЛЕНИЯ АНТИ-А/АНТИ-В АНТИТЕЛ И СОХРАННОСТИ АКТИВНОСТИ ФАКТОРА VIII

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Введение. Трансфузия плазмы остается неотъемлемым компонентом интенсивной терапии массивной кровопотери, коагулопатий и синдрома диссеминированного внутрисосудистого свертывания, особенно в экстренных ситуациях, когда группа крови реципиента неизвестна или время на ее определение отсутствует, использование группоспецифической плазмы невозможно, а ресурс плазмы группы АВ(IV) ограничен и составляет около 4–5% донорского ресурса. Под «универсальной плазмой» в настоящей работе понимается компонент донорской крови, пригодный для применения у реципиента любой группы по системе АВ0 без предварительного определения его групповой принадлежности как для восполнения объема циркулирующей крови, так и для коррекции гемостаза. Одно из перспективных направлений создания такого продукта — иммуносорбция анти-А/анти-В антител, однако отечественные данные о ее влиянии на лабильные факторы гемостаза, прежде всего фактор VIII (Ф.VIII), единичны.

Цель. Оценка возможности использования иммуносорбента для получения из свежзамороженной плазмы (СЗП) компонента, свободного от анти-А/анти-В антител или содержащего их на ультранизком уровне ($\leq 1:8$), с сохраненной активностью лабильных факторов гемостаза, пригодного для применения у пациентов независимо от их групповой принадлежности по системе АВ0, в том числе для коррекции гемостаза.

Материалы и методы. Исследование выполнено на образцах СЗП *in vitro* с парным сравнением показателей «до/после» обработки. Исследовано 90 образцов СЗП (по 30 образцов в группах 0, А и В). Сорбцию анти-А/анти-В антител проводили иммуносорбентами (НПФ «ПОКАРД», Россия) в закрытой системе при +22...+25 °С в объеме плазмы 100 мл и времени контакта 30 мин. Титры антител класса IgM определяли в реакции прямой агглютинации в гелевых картах, антител IgG — в непрямом антиглобулиновом тесте; активность фактора VIII (Ф.VIII:C) — по АЧТВ (активированное частичное тромбопластиновое время) на коагулометре. Статистический анализ произведен с помощью U-критерия Манна — Уитни; различия считали значимыми при $p < 0,05$.

Результаты. При исходных титрах анти-А и анти-В антител $\leq 1:32$ после сорбции антитела элиминировались полностью; при титрах $> 1:32$ – $1:512$ их уровень снижался до $1:2$ – $1:8$, что соответствует международным критериям «ultra-low titres» плазмы. Активность Ф.VIII после сорбции снижалась во всех группах, технологические потери составили 18–20%. Исходная активность Ф.VIII в плазме группы 0 была достоверно ниже, чем в группах А и В. После сорбции все образцы плазмы групп А и В сохраняли соответствие регуляторному критерию (Ф.VIII $\geq 0,7$ МЕ/мл), тогда как до 50% образцов группы 0 не достигали требуемого минимума и не могли маркироваться как СЗП.

Выводы. Иммуносорбция обеспечила эффективное удаление анти-А/анти-В антител из СЗП, однако была сопряжена с потерей Ф.VIII на 18–20%, критичной преимущественно для плазмы группы 0. Разработка технологии производства «универсальной плазмы» данным методом целесообразна для продукта специального (целевого) назначения — для экстренной догоспитальной помощи, военной медицины и формирования стратегических запасов — при условии прескрининга доноров группы 0 с исходной активностью Ф.VIII $\geq 95\%$ и/или переформатирования продукта в лиофилизированную «универсальную плазму».

Ключевые слова: универсальная плазма; иммуносорбция; свежзамороженная плазма; изоагглютинины; анти-А и анти-В антитела; фактор VIII; система групп крови АВ0; трансфузия плазмы

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Финансирование. Работа выполнена без спонсорской поддержки.

Соответствие принципам этики. Авторы заявляют, что одобрение комитетом по этике не требовалось, поскольку исследование осуществлено *in vitro* на образцах компонентов донорской крови. Всеми донорами подписано добровольное информированное согласие на донацию крови и ее компонентов.

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INTRODUCTION

Plasma transfusion remains an integral component of intensive care for massive hemorrhage, coagulopathies, and disseminated intravascular coagulation¹. In plasma transfusion, clinical significance is determined not by ABO system antigens, but by antibodies — specifically anti-A and anti-B — which are present in the donor's plasma and can cause hemolysis of the recipient's erythrocytes [1]. Consequently, the presence of anti-A and anti-B antibodies in donor plasma poses a key logistical problem in transfusion medicine: the inability to use group-specific plasma in emergency situations where the recipient's blood group is unknown or cannot be determined immediately. Compounding this issue, the availability of group AB plasma, which lacks isoagglutinins, is limited to approximately 4–5% of the total donor pool [2, 3].

In this study, “ABO-universal plasma” is defined as a donor blood component suitable for use in recipients of any ABO blood group without prior determination of their blood type. This product is designed to expand intravascular volume and restore hemostasis. Efforts to develop ABO-universal plasma currently focus on several approaches:

1. Pooling technology: This approach pools plasma from different blood groups to achieve mutual neutralization of anti-A and anti-B antibodies by soluble A and B antigens. This strategy has been implemented in commercial solvent/detergent-treated products such as Octaplas and Uniplas [4, 5].

2. Donor preselection: This involves the preliminary screening of group O donors to identify individuals with naturally low agglutinin titers (so-called low-titer group O plasma). This method is widely used in military medicine and prehospital care systems worldwide [3, 6].

3. Lyophilization: While this process does not remove antibodies, it ensures the long-term storage and transportation of already prepared ABO-universal plasma at room temperature, providing immediate availability under field conditions [7].

4. Direct removal via immunoaffinity: This approach focuses on the direct removal of anti-A and anti-B antibodies using immunoabsorption techniques. These include adsorption onto group A and B red blood cells, as well as the use of specialized adsorption devices, such as HemoDefend [3, 8, 9].

Russian transfusion medicine has established a solid foundation for the adoption of alternative plasma products. Specifically, blood product quality control, plasma transfusion protocols, and new plasma products — including virus-inactivated plasma — have been consistently developed² [10, 11]. Additionally, a domestic

initiative for the development and industrial production of lyophilized plasma (Lioplasma) has been successfully implemented, demonstrating preserved coagulation factor activity, clinical efficacy, and cost-effectiveness in the treatment of massive hemorrhage [12–14].

At the same time, labile hemostatic factors remain a vulnerability shared by all plasma processing technologies. This primarily concerns Factor VIII (FVIII), with reported losses under various treatments ranging from 12% to 21% [12, 15]. For the immunoabsorption of anti-A/anti-B antibodies, FVIII preservation becomes particularly critical due to a specific mechanism: FVIII circulates in plasma as a non-covalent complex with von Willebrand Factor (vWF), which carries ABO antigenic determinants on its surface [16, 17]. Consequently, it may be co-eliminated by the adsorbent targeted at anti-A/anti-B antibodies. Importantly, individuals with blood group O — the primary potential donors for ABO-universal plasma production — exhibit vWF and FVIII levels that are physiologically 20–30% lower than the levels in individuals with other blood groups [16, 17]. Despite this, virtually no systematic domestic data are available regarding FVIII during adsorptive removal of isoagglutinins from fresh frozen plasma (FFP). Furthermore, regulatory requirements for FFP — specifically ABO compatibility and a minimum FVIII activity of 0.7 IU/mL at expiration, as established by Government Decree of the Russian Federation No. 641 dated May 14, 2025³ — make this a critical factor for the technology's applicability.

This study aimed to evaluate the feasibility of using immunoabsorption to produce an FFP component that is either free of anti-A/anti-B antibodies or characterized by ultra-low titres ($\leq 1:8$) while preserving the activity of labile hemostatic factors. The resulting product is intended for use in patients regardless of their ABO blood group, including for hemostasis restoration.

MATERIALS AND METHODS

This *in vitro* study used a paired pre-post comparison design to evaluate FFP samples. The research was conducted at the Russian Research Institute of Hematology and Transfusiology of the Federal Medical and Biological Agency (RRIHT FMBA). The FFP samples were collected in accordance with current regulatory requirements⁴. The time from blood collection to plasma freezing complied with established protocols. A total of 90 FFP units were analyzed: group O ($n = 30$), group A ($n = 30$), and group B ($n = 30$). Group AB plasma was excluded from the study, as it lacks anti-A/anti-B antibodies by definition [1]. Following standard thawing at 37 °C, a pre-adsorption aliquot was collected from each sample. Antibody depletion was performed using anti-A

¹ Zhiburt EB. Rules for plasma transfusion: A guide for physicians. Moscow: Meditsina; 2008.

² Ibid.

³ Government Decree of the Russian Federation No. 641 dated 14 May 2025 “On Approval of the Rules for the Collection, Storage, Transportation, and Clinical Use of Donor Blood and its Components”. GOST R 53470-2009 “Donor Blood and its Components: Guidelines for the Use of Donor Blood Components”. Moscow: Standartinform; 2010.

⁴ Ibid.

and anti-B immunoadsorbents (POKARD, Russia) at the manufacturer-recommended ratio, within a closed system at 22–25 °C. The protocol utilized a plasma volume of 100 mL and a 30-min contact time under constant agitation with an ELMi RM-1L medical rotary mixer (Latvia) [3, 9]. This 22–25 °C temperature range was selected because anti-A and anti-B antibodies are classified as cold agglutinins with an optimal reaction temperature of 18–20 °C; their adsorption efficiency decreases at higher temperatures (37 °C). Maintaining a temperature of 22–25 °C within a closed system during this phase is technologically feasible and provides a compromise between adsorption efficiency and the preservation of labile coagulation factors. Following centrifugation, a post-adsorption aliquot was collected. As a control, plasma without added adsorbent was used; it was subjected to constant agitation for 30 min.

The titers of anti-A and anti-B antibodies (IgM) were determined via direct agglutination in neutral gel cards (Dia Pro, Turkey) using reagent erythrocytes of groups A and B (RRIHT FMBA, Russia). The assay utilized serial twofold plasma dilutions (1:2–1:512) following standard protocols [1]. Anti-A and anti-B antibodies of the IgG class were detected using an indirect antiglobulin test (IAT) with gel cards containing monospecific anti-IgG reagents (BIO-RAD, Switzerland). This approach ensured specific detection of IgG-class antibodies without prior removal of IgM. IgG antibodies were assessed qualitatively (detected/not detected).

Factor VIII (FVIII:C) activity was determined via the activated partial thromboplastin time (aPTT) assay on an ACL Top 300 CTS coagulometer (Instrumentation Laboratory, USA). The testing system utilized FVIII-deficient plasma and specific reagents (Instrumentation Laboratory, USA). The results were expressed as a percentage of the normalized value of 1 IU/mL (100%). Product compliance was assessed against the regulatory criterion: FVIII ≥ 0.7 IU/mL (70%), which represents the lower limit of the established standards for FFP. Baseline and post-adsorption samples were analyzed under

identical conditions to exclude the influence of time and temperature on labile factors.

Statistical analysis was performed using Microsoft Excel and Statistica 12.0 software. The nonparametric Mann–Whitney *U* test was applied to compare independent groups. Data are presented as $M_e [Q_1; Q_3]$; paired pre- and post-adsorption samples were compared using the Wilcoxon signed-rank test. Process-related losses of FVIII were calculated as follows: $[(FVIII_{pre} - FVIII_{post}) / FVIII_{pre}] \times 100\%$. Differences were considered significant at $p < 0.05$.

RESULTS

Anti-A/anti-B antibody titers post-adsorption

Following immunoadsorption, anti-A and anti-B antibodies fell below the limit of detection in all samples with baseline titres ≤ 1:32. In samples with higher initial titres (ranging from > 1:32 to 1:512), a significant reduction was observed. Specifically, antibody levels decreased to a range of 1:2–1:8 in plasma from blood groups O and B and to undetectable levels (“no agglutination”) or up to 1:2 in group A plasma. Following adsorption, IgG anti-A/anti-B antibodies were undetectable in group A and B samples with low baseline titers; however, they persisted in a subset of samples with high initial titers (see Table). Across all 90 plasma samples, regardless of baseline antibody titers, the residual anti-A/B agglutinin levels (≤ 1:8) met the criteria for ultra-low titres plasma, as defined in international emergency transfusion practice [3].

The titers of anti-A and anti-B antibodies before and after immunoadsorption are presented in the table.

Changes in Factor VIII activity

FVIII activity before and after adsorption is presented in the figure. Following adsorption, FVIII activity decreased across all plasma groups, with mean process-related losses amounting to 18–20%. Notably, baseline FVIII

Table. Anti-A/Anti-B antibody titers in plasma before and after adsorption

ABO blood group	Baseline titer			Post-adsorption		
	anti-A IgM	anti-B IgM	IgG	anti-A IgM	anti-B IgM	IgG
O	≤ 1:32	≤ 1:32	0	0	0	0
	> 1:32–1:512	> 1:32–1:512	+	1:2–1:8	1:2–1:8	+
A	–	≤ 1:32	0	–	0	0
	–	> 1:32–1:512	+	–	no reaction — 1:2	0
B	≤ 1:32	–	0	no reaction — 1:2	–	0
	> 1:32–1:512	–	+	1:2–1:8	–	+

Table prepared by the authors using their own data

Note. +, IgG-class antibodies were detected; –, antibodies of this specificity were initially absent from the plasma of the corresponding blood group.

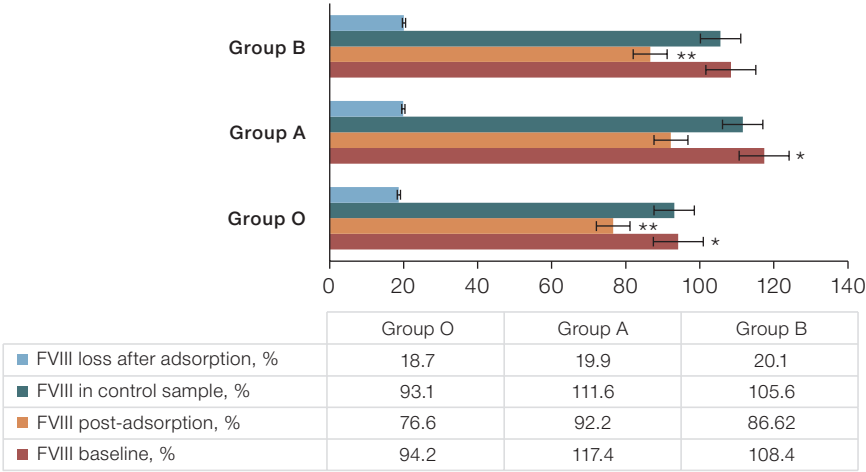


Figure prepared by the authors using their own data

Fig. Factor VIII activity before and after adsorption. FVIII, Factor VIII; * baseline differences in FVIII activity between groups O and A are statistically significant ($p = 0.042108$); ** differences in FVIII activity between groups O and B after adsorption are statistically significant ($p = 0.02843$)

activity in group O plasma was significantly lower [64.6; 95.2] than in groups A [100.9; 126.5] and B [108.4; 130.7], which is consistent with data on physiologically reduced vWF/FVIII levels in individuals with blood group O [16].

When assessing the compliance of adsorbed plasma with the regulatory criterion $FVIII \geq 0.7$ IU/mL (i.e., $\geq 70\%$) [18], it was established that in group A, final FVIII activity ranged from 82.5% to 99.9%, and in group B, it reached 80.3–114.3%. In both groups, all samples remained compliant with the standard. In group O, final FVIII activity ranged from 54.3% to 78.6%; however, a significant proportion of samples (up to 50%) failed to reach the required minimum of 70%, which precluded their labeling and use as FFP.

Thus, FVIII losses of 18–20% were non-critical for group A and B plasma but significant for group O units. This is attributable to the fact that these losses are superimposed on the physiologically lower baseline levels in the donors of this blood group [17]. Notably, the observed losses are comparable to reported FVIII activity reductions in other plasma processing technologies: 12.8–21.4% for lyophilization [14].

DISCUSSION

The conducted study demonstrated that immunoaffinity adsorption is a technologically feasible and effective method for removing anti-A and anti-B antibodies from FFP: at initial titers of $\leq 1:32$, the antibodies were completely eliminated; for initial titers ranging from $> 1:32$ to $1:512$, their levels decreased to $1:2$ – $1:8$ (Table). These results align with those of other authors who achieved titer reductions to $\leq 1:4$ in the majority of group O plasma samples during adsorption of anti-A and anti-B antibodies on group A and B erythrocytes [3], as well as with

domestic experience in processing plasma for the removal of immune anti-A/anti-B antibodies [9]. Residual titers of $\leq 1:8$ met the criteria for ultra-low titres plasma, which is approved for emergency use in several countries [3, 6]. However, the persistence of IgG anti-A/anti-B antibodies in some units with initially high titers warrants attention. While low residual titers present minimal clinical risk, this phenomenon should be taken into account when developing a product release standard [1, 3].

A key adverse finding of this work was an 18–20% decrease in FVIII activity across all plasma groups (Figure). Notably, comparable loss magnitudes (12.8–21.4%) have been described for other plasma processing technologies, specifically lyophilization, which indicates the particular vulnerability of this labile factor to any technological impact; meanwhile, the mechanism of losses during immunoaffinity adsorption appears to be two-component (specific and non-specific). The specific component is attributable to the fact that FVIII circulates in plasma as a strong non-covalent complex with vWF, which protects it from proteolysis [12, 16]; vWF carries ABO antigenic determinants on its surface, and the adsorbent targeted at binding anti-A/anti-B antibodies partially co-captures vWF together with bound FVIII. The non-specific component is associated with hydrophobic and electrostatic interactions between proteins and the polymer matrix: under these conditions, the largest complexes — fibrinogen and vWF/FVIII — are lost first. Prolonged contact of plasma with the matrix at room temperature also plays an additional role through the contact inactivation of labile FVIII [18].

A fundamentally important finding was the differentiated significance of FVIII losses across ABO groups. For plasma from blood groups A and B, an 18–20% decrease in activity did not cause the product to fall outside the regulatory standard⁵: final values were

⁵ Government Decree of the Russian Federation No. 641 dated 14 May 2025 “On Approval of the Rules for the Collection, Storage, Transportation, and Clinical Use of Donor Blood and its Components”. GOST R 53470-2009 Donor Blood and its Components: Guidelines for the Use of Donor Blood Components. Moscow: Standartinform; 2010.

80–115% against a requirement of $\geq 70\%$. Conversely, group O individuals exhibited 20–30% lower vWF and FVIII levels [16, 17], which was confirmed by the baseline values of 64–95% observed in this study. Due to the superimposition of process-related losses, adsorbed group O plasma failed to meet the FFP requirements (FVIII ≥ 0.7 IU/mL at expiration) in the majority of cases, which precluded its labeling as FFP⁶. A paradox emerged: the technology caused the greatest damage to precisely the donor group that is the primary source candidate for ABO-universal plasma [3].

The clinical significance of the identified decrease in hemostatic potential is determined by the specific clinical scenario. In a patient with massive hemorrhage, plasma with reduced FVIII content fails to effectively manage coagulopathy, thereby increasing the risks of dilutional coagulopathy and transfusion-associated circulatory overload⁷. This demonstrates that the clinical utility of these plasma products depends primarily on the preservation of their hemostatic activity, meaning that the adoption of new products must not compromise clinical efficacy [10, 11].

Three strategies can be employed to overcome the identified limitation:

1. Regulatory reclassification: registering adsorbed group O plasma as an independent component, specifically “universal plasma for emergency prehospital care.” This component is primarily designed for intravascular volume resuscitation and support of primary hemostasis in situations where recipient blood typing is impossible [7, 14].

2. Lyophilization: Prior domestic experience with Lioplasma demonstrates that optimizing stabilization conditions can maintain coagulation factor activity at levels comparable to those in FFP [12, 15]. Furthermore, process-related losses can be compensated for by adding a FVIII/vWF concentrate before sealing, which is particularly essential for strategic stockpiles and military medicine [7, 14].

3. Strict donor prescreening: selecting group O samples with baseline FVIII activity of at least 95%. This strategy guarantees regulatory compliance after 18–20% losses, although at the expense of narrowing the donor pool.

The feasibility assessment of this technology yields controversial conclusions. In military and emergency settings, the arguments in its favor are compelling: a universal product that eliminates the necessity of blood typing is critically needed during mass casualty incidents and for building strategic stockpiles [7, 14]. In the civilian sector, the high cost of the adsorbent increases the product price, while the loss of labile coagulation factors reduces clinical efficacy [11]. To address these limitations, several alternatives to adsorption are currently under consideration:

- selection of group O donors with naturally low agglutinin titers ($\leq 1:8$) [3, 6];
- pooling technology involving mutual antibody neutralization — the Uniplas model [4];
- red blood cell collection without plasma preparation.

The study was performed *in vitro* on a limited number of samples; the clinical efficacy and safety of adsorbed plasma were not evaluated. Residual anti-A/anti-B antibodies of the IgG class require further investigation using sensitive methods. A comparative evaluation of adsorbents and adsorption regimens (temperature, contact time, flow rate) appears promising for the purpose of minimizing FVIII losses. The assessment of other labile coagulation factors (V, XI, proteins C and S) and integral parameters (aPTT) was not an objective of the current stage of research and is planned for future studies.

While immunoaffinity adsorption effectively removed anti-A/anti-B antibodies, this process was associated with an 18–20% reduction in FVIII activity — a loss that is critically significant primarily for group O plasma. Further development of this technology is feasible through the optimization of adsorption regimens, donor prescreening, and/or reformatting the product into lyophilized universal emergency-use plasma.

CONCLUSION

Immunoadsorption ensured effective removal of anti-A and anti-B antibodies from FFP (groups O, A, and B). At initial titers of $\leq 1:32$, the antibodies were completely eliminated; for initial titers ranging from $> 1:32$ to $1:512$, levels decreased to $1:2$ – $1:8$, meeting the international criteria for ultra-low titres plasma. Adsorption was accompanied by process-related losses of Factor VIII at a level of 18–20%, values comparable to losses associated with other plasma processing methods. The FVIII losses are regulatorily and clinically non-critical for plasma from groups A and B (final activity: 80–115%); however, they are critical for group O units (final activity: 54.3–78.6%), which in most cases did not meet the FFP requirements (FVIII ≥ 0.7 IU/mL). The development of an ABO-universal plasma production technology using immunoaffinity adsorption is feasible as a special-purpose product for emergency prehospital care (including burn injuries), military medicine, and strategic stockpiling. This is conditional upon the prescreening of group O donors with baseline FVIII activity $\geq 95\%$ and/or the reformatting of the product into lyophilized “ABO-universal plasma” supplemented with FVIII. In routine civilian practice, alternative approaches are preferable: the selection of donors with low anti-A/anti-B antibody titers and the application of plasma pooling technology.

⁶ Government Decree of the Russian Federation No. 641 dated 14 May 2025 “On Approval of the Rules for the Collection, Storage, Transportation, and Clinical Use of Donor Blood and its Components”. GOST R 53470-2009 Donor Blood and its Components: Guidelines for the Use of Donor Blood Components. Moscow: Standartinform; 2010.

⁷ Zhiburt EB. Rules for plasma transfusion: A guide for physicians. Moscow: Meditsina; 2008.

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