Journal of Veterinary Emergency and Critical Care

BRIEF COMMUNICATION OPEN ACCESS

Serum Electrolyte Changes in Foals Receiving *Rhodococcus equi*–Specific Hyperimmune Plasma

Diego S. Larriva[1] | Luis G. Arroyo[2] | Brandon N. Lillie[3] | Macarena G. Sanz[1]

[1]Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Washington State University, Pullman, Washington, USA | [2]Department of Clinical Studies, Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada | [3]Department of Pathobiology, Ontario Veterinary College, University of Guelph, Guelph, Ontario, Canada

Correspondence: Macarena G. Sanz (msanz@iastate.edu)

Received: 24 March 2025 | **Revised:** 8 September 2025 | **Accepted:** 15 September 2025

Keywords: electrolytes | equine | plasma

ABSTRACT

Background: *Rhodococcus equi*–specific hyperimmune plasma (Re-HIP) is routinely administered to neonatal foals to help prevent rhodococcal pneumonia. In addition to pathogen-specific immunoglobulins, frozen plasma products (FPPs) contain electrolytes that may exceed concentrations found in neonatal foal plasma. Because FPPs are also used to treat failure of passive transfer and sepsis, understanding their effects on neonate homeostasis is crucial. This study evaluated the effects of administration of Re-HIP on the serum concentrations of Na^+, Cl^-, K^+, albumin, and globulin of healthy neonatal foals.

Key Findings: The concentration of Na^+ was high in Re-HIP when compared with normal plasma values. Administration of Re-HIP resulted in an increase in serum Na^+, Cl^-, albumin, and globulin concentrations in neonatal foals.

Significance: The serum electrolyte changes seen after Re-HIP administration were likely of no clinical significance in healthy foals. However, the administration of hypernatremic plasma to septic or dehydrated foals could exacerbate electrolyte imbalances. These results suggest that caution and close monitoring are warranted when administering FPPs to critically ill foals.

1 | Introduction

In equine medicine, frozen plasma products (FPPs) are commonly administered intravenously to treat failure of passive transfer, a condition that arises when foals do not receive adequate immunoglobulin G (IgG) from colostrum [1]. A plasma dose of 20 mL/kg increases IgG concentrations by 200–300 mg/dL in an average 45-kg foal, providing essential immune support and enhancing disease resistance [2]. Plasma transfusion also contributes to oncotic pressure maintenance, coagulation factor replacement, and immune modulation. Fresh frozen plasma (FFP) provides approximately 38 g/L of albumin, which transiently restores oncotic pressure, supports adequate tissue perfusion, and prevents the development of edema [3]. Although FFP has significantly lower coagulation factor concentrations than whole blood or fresh plasma products [4], its administration to horses with severe uncontrolled hemorrhage increases coagulation factors and offers advantages over crystalloids or synthetic colloids [1].

Rhodococcus equi–specific hyperimmune plasma (Re-HIP), a pathogen-specific FPP, is commonly administered to neonatal foals to decrease the severity of clinical rhodococcal pneumonia [2]. Its administration increases the concentration of *R. equi*–specific IgG and complement proteins, such as C1q, which are important for bacterial opsonization [5].

Abbreviations: FFP, fresh frozen plasma; FPP, frozen plasma product; Re-HIP, *Rhodococcus equi*–specific hyperimmune plasma.

Transfusion of hyperimmune plasma to young foals is not without risks. Hypersensitivity reactions and problems associated with intravenous catheterization and foal handling can occur but are uncommon [4]. While most research related to FPPs has focused on IgG concentrations and immune responses, little is known about the effects of FPPs on electrolyte balance. Commercial equine FF6P was shown to have greater [Na^+] variability than fresh equine plasma, with values ranging from 104 to 305 mEq/L [6]. Electrolytes are critical for maintaining homeostasis in neonatal foals, yet the effects of plasma transfusion on these parameters are unclear. In human neonates, FFP administration decreased calcium and increased potassium concentrations systemically, leading to potentially life-threatening hyperkalemia [7]. In equine neonates, electrolytes are regularly monitored to guide treatment decisions, modify fluid therapy, and serve as prognostic indicators [8]. Given the routine use of plasma transfusions for the treatment of failure of passive transfer, sepsis management, and the reduction of the severity of clinical rhodococcal pneumonia, understanding their effects on electrolyte and protein concentrations in foals is essential. The current study aims to characterize changes in electrolyte and protein concentrations after RE-HIP administration in healthy foals. Gaining insight into these physiologic effects will help refine plasma transfusion protocols and improve clinical decision-making in neonatal equine medicine.

2 | Materials and Methods

The study protocol was approved by the Ontario Animal Use Protocol #3575.

2.1 | Samples

Samples were collected after owner consent was obtained. Convenience sampling was used based on the availability of mares and foals for repeated blood sampling at the farm where the study was conducted. This farm was selected due to its willingness to participate and its suitability for longitudinal sample collection. With a sample size of 28 paired measurements for foals, 70 Re-HIP plasma bags, and 16 mares, our study had an estimated statistical power of 90% to detect a 4 mmol/L difference in serum Na^+ concentration at an alpha level of 0.05.

2.2 | Hyperimmune Plasma

Per the farm's protocol, all foals born on the farm receive 950 mL of *R. equi* hyperimmune plasma[1] intravenously. Plasma was thawed in warm water following the manufacturer's recommendations. A 2-mL sample was collected from the administration line after transfusion and used for chemistry analysis.

2.3 | Blood Samples

Blood was collected by jugular venipuncture from healthy foals within 24 h of birth (before routine intravenous administration of Re-HIP) and 24 h after Re-HIP administration. Blood was also collected by jugular venipuncture from the foals' mares 1–3 weeks before foaling. The mares' serum was used to establish normal horse electrolyte values. For blood collection, foals were manually restrained, and mares were restrained using a halter and lead rope.

2.4 | Plasma and Serum Chemistry Analysis

Serum from foals and mares and plasma from Re-HIP bags were analyzed for biochemical parameters using routine techniques within 4 h of collection at the Clinical Pathology Laboratory of the Ontario Veterinary College. Samples were analyzed at the same time with an automated analyzer[2].

2.5 | Statistical Analysis

Data were analyzed with commercial software[3]. Normality was assessed using the Shapiro–Wilk test, and the Brown–Forsythe test was used to assess variances. A Wilcoxon signed-rank test was used to compare values from foal serum before and after Re-HIP transfusion. Comparisons among Re-HIP, mare serum, and foal serum were performed using the Kruskal–Wallis test, followed by post hoc evaluation with the Tukey–Kramer test. Significance was set at $p < 0.05$.

3 | Results

Samples from 70 Re-HIP bags, 28 healthy foals that received Re-HIP plasma, and 16 mares (from the transfused foals) were included in this study. There was notable variation in the electrolyte and protein concentrations of Re-HIP bags (Table 1). When compared with adult horse serum (mares), Re-HIP had higher concentrations of Na^+ and globulin, and lower concentrations of K^+, Cl^-, total protein, and albumin (Table 1). With the exception of [K^+], all other measured components increased in foals after the administration of Re-HIP (Table 1). A comparison of the Na^+ concentration in all the samples collected is shown in Figure 1.

4 | Discussion

Much like adult horses, which experience a transient increase in colloid osmotic pressure, total protein, and albumin [6], changes in foals' electrolytes and proteins after administration of Re-HIP were seen in this study.

Hyperimmune plasma bags of the same lot showed variation in the concentration of electrolytes, particularly Na^+ and Cl^-, as well as proteins. This was not unexpected, as it has been previously reported [6, 9], and it is likely the result of variability in donor horse physiology and processing techniques. Each lot of the commercial Re-HIP product used in this study was derived from a single donor horse. Although this allows for precise traceability, it also decreases the uniformity of the products. When compared with mares' serum, Re-HIP had higher concentrations of Na^+ and globulin and lower concentrations of K^+, Cl^-, and albumin. The high Na^+ concentration in these products likely reflects the use of sodium citrate as an anticoag-

TABLE 1 | Plasma element medians (25%–75%) from Re-HIP bags ($n = 70$). Serum element medians (25%–75%) from foals ($n = 28$) before (Foals Pre) and 24 h after (Foals Post) Re-HIP administration, and from mares ($n = 16$).

Measured	Re-HIP bags Median (25%–75%)	Foals Pre Re-HIP Median (25%–75%)	Foals Post Re-HIP Median (25%–75%)	Mares Median (25%–75%)
Na^+ (mmol/L)	165 (160–171)[a]	131 (129.2–134.7)[b]	136 (132.2–138.7)[b] #	140 (135.7–142.7)[b]
K^+ (mmol/L)	3.1 (3–3.3)[a]	4.35 (4.0–4.5)[b]	4.15 (4–4.3)[b]	3.55 (3.2–4)[c]
Cl^- (mmol/L)	87 (86–90.2)[a]	96 (94–97)[b]	97 (94–99)[b] #	101 (98.5–103)[c]
Total protein [g/dL]	5.6 (5.3–5.9)[a]	4.3 (3.9–4.6)[b]	4.8 (4.5–5.2)[c] #	6.2 (5.9–6.4)[d]
Albumin [g/dL]	2.4 (2.3–2.6)[a]	2.6 (2.4–2.7)[a]	2.8 (2.6–2.9)[b] #	3.2 (3.1–3.4)[c]
Globulins [g/dL]	3.2 (2.8–3.4)[a]	1.7 (1.2–2.1)[b]	2.1 (1.7–2.6)[c] #	3.0 (2.7–3.1)[a]

Note: Different superscript letters indicate differences among Re-HIP, mare serum, and foal serum ($p < 0.05$). The # symbol denotes differences in foal serum before versus after Re-HIP administration ($p < 0.001$).
Abbreviation: Re-HIP, *Rhodococcus equi*–specific hyperimmune plasma.

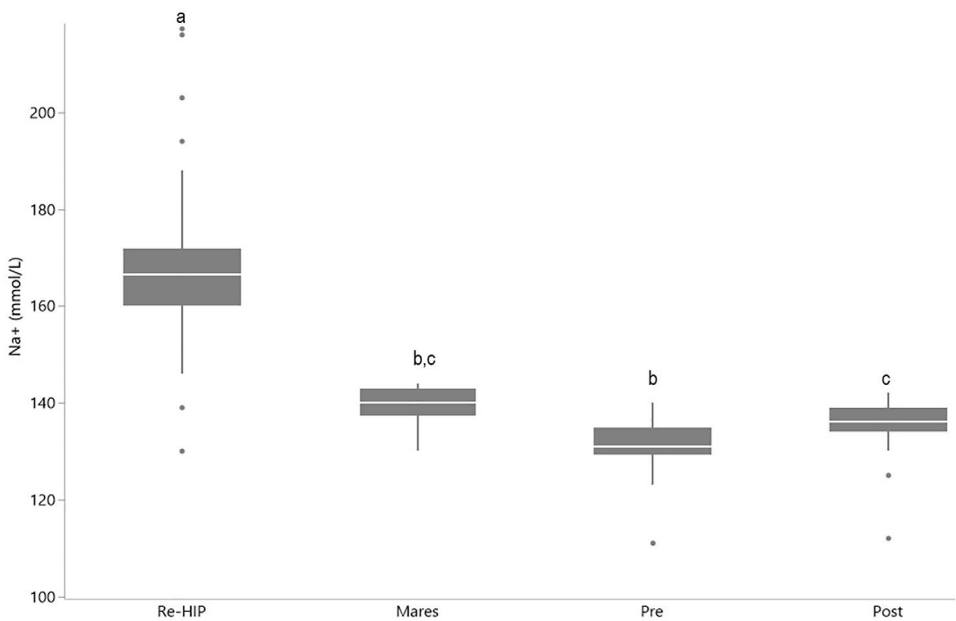

FIGURE 1 | Boxplot representing Na+ concentration (mmol/L) in *Rhodococcus equi*–specific hyperimmune plasma (Re-HIP, $n = 70$) and serum of mares ($n = 16$) and foals ($n = 28$) before (Pre) and after (Post) Re-HIP transfusion. The line in the middle of the boxplot represents the median, and the limits of the box represent the first and third quartiles; the upper and lower fences represent the maximum and minimum of the data. Individual data points that fall beyond the fences represent outliers. Different superscript letters indicate differences among Re-HIP, mare serum, and foal serum before and after Re-HIP administration ($p < 0.001$).

ulant [10]. For hyperimmune plasma production, donor horses are vaccinated to enhance pathogen-specific immunoglobulin synthesis. Therefore, the increased globulin concentrations in Re-HIP were expected and are a hallmark of these products. The decrease in K^+ and Cl^- remains unexplained, although it is likely linked to processing and donor variability. The lower albumin concentration may reflect losses caused by freezing or filtration during plasma processing. Additionally, late-term pregnant mares show physiologic increases in albumin and total solids due to altered metabolism and fluid dynamics [11]. As expected, Re-HIP administration increased foals' albumin and globulin concentrations [2]. In addition, an increase in serum Na^+ and Cl^- concentrations was observed. Although there were changes, these posttransfusion values remained within normal reference ranges for neonatal foals [12] and are likely clinically insignificant in healthy foals. An increase in Na^+ was also reported in human neonates after FFP transfusion [4] and in adult horses after frozen plasma transfusion [5]. Foal osmolality is tightly regulated, largely due to frequent milk consumption, which supports self-dilution of plasma solutes [6]. In the neonatal period, a foal that nurses 20% of its body weight in milk receives approximately 1.9 mEq/kg/day of Na^+, and its growth requirements are approximately 1 mEq/kg/day. This high intake, along with the Na^+ conserving mechanism of the neonatal kidney, creates a risk for Na^+ overload [12]. Administering hypernatremic plasma to septic or dehydrated foals could exacerbate electrolyte

imbalances, potentially leading to adverse outcomes; therefore, administration of FPPs should be closely monitored in these cases.

This study has limitations. Although the use of convenience sampling at a single farm limits generalizability, it allowed for efficient acquisition of relevant data from a population representative of the study setting. The relatively small sample size may reduce the statistical power to detect subtle effects or associations, a constraint resulting from the limited number of eligible animals available during the study period and logistical challenges related to repeated sampling. As such, findings should be interpreted with caution and validated in larger, more diverse populations in future research. A control group of foals that did not receive Re-HIP was not available, as administration of Re-HIP to all foals is the standard protocol on the farm for *R. equi* prevention. Although the inclusion of a control group would have strengthened the study, our primary objective was to evaluate changes associated with plasma administration rather than age-related changes. Nonetheless, the potential influence of age-related factors cannot be completely excluded and should be considered when interpreting the results. Despite these limitations, our findings provide valuable preliminary insights and can inform future research.

In conclusion, the administration of Re-HIP may lead to an increase in plasma Na^+ concentration in foals. Although this change may not be clinically significant in healthy foals, caution should be exercised when administering these products to foals with sodium imbalances.

Author Contributions

Diego S. Larriva: conceptualization, data curation, writing – original draft, writing – review and editing, formal analysis. **Luis G. Arroyo**: conceptualization, writing – review and editing, methodology. **Brandon N. Lillie**: methodology, data curation, writing – review and editing. **Macarena G. Sanz**: conceptualization, investigation, funding acquisition, writing – original draft, writing – review and editing, visualization, validation, methodology, formal analysis, project administration, supervision, resources, data curation.

Funding

Funding was provided by Equine Guelph and the McEachern Endowment Funds from WSU.

Ethics Statement

The study protocol was approved by the Ontario Animal Use Protocol (AUP) #3575.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Endnotes

[1] EquiPlasR, Plasvacc USA Inc., Templeton, CA.

[2] Cobas c 501 module, Roche Diagnostics, Scandinavia AB, Solna, Sweden.

[3] JMP Pro 17, JMP Statistical Discovery LLC, Cary, NC.

References

1. T. J. Divers, R. M. Radcliffe, V. L. Cook, L. C. Bookbinder, and S. D. A. Hurcombe, "Calculating and Selecting Fluid Therapy and Blood Product Replacements for Horses With Acute Hemorrhage," *Journal of Veterinary Emergency and Critical Care* 32, no. S1 (2022): 97–107, https://doi.org/10.1111/vec.13127.

2. M. G. Sanz, A. F. Oliveira, A. Page, and D. W. Horohov, "Administration of Commercial *Rhodococcus equi*-Specific Hyperimmune Plasma Results in Variable Amounts of IgG Against Pathogenic Bacteria in Foals," *The Veterinary Record* 175, no. 19 (2014): 485, https://doi.org/10.1136/vr.102594.

3. L. G. Arroyo, W. Sears, and D. E. Gomez, "Plasma Transfusions in Horses With Typhlocolitis/Colitis," *Canadian Veterinary Journal* 60, no. 2 (2019): 193–196.

4. E. M. Wilson, S. J. Holcombe, A. Lamar, J. G. Hauptman, and M. B. Brooks, "Incidence of Transfusion Reactions and Retention of Procoagulant and Anticoagulant Factor Activities in Equine Plasma," *Journal of Veterinary Internal Medicine* 23, no. 2 (2009): 323–328, https://doi.org/10.1111/j.1939-1676.2008.0254.x.

5. A. B. Bettencourt, D. Reiskind, P. Flores-Ahlschwede, et al., "Serum Activities of Complement 1q and Antibodies to the Virulence-Associated Protein A Are Lower in Foals That Develop Rhodococcal Pneumonia," *American Journal of Veterinary Research* 85, no. 3 (2024): 1–10, https://doi.org/10.2460/ajvr.23.08.0180.

6. E. C. McKenzie, J. Johns, C. Baumbach, and M. Busby, "Biochemical Characteristics of a Commercial Plasma Product and Response to Transfusion of Clinically Diseased Horses [Abstract]," *Journal of Veterinary Internal Medicine* 33 (2019): 2375–2547, https://doi.org/10.1111/jvim.15597.

7. S. Abdelghaffar, Y. Mansi, R. Ibrahim, and D. Mohamed, "Red Blood Transfusion in Preterm Infants: Changes in Glucose, Electrolytes and Acid-Base Balance," *Asian Journal of Transfusion Science* 6, no. 1 (2012): 36–40, https://doi.org/10.4103/0973-6247.95049.

8. N. M. Collins, J. B. Carrick, C. M. Russell, and J. E. Axon, "Hypernatraemia in 39 Hospitalised Foals: Clinical Findings, Primary Diagnosis and Outcome," *Australian Veterinary Journal* 96, no. 10 (2018): 385–389, https://doi.org/10.1111/avj.12749.

9. M. G. Sanz, A. Loynachan, and D. W. Horohov, "*Rhodococcus equi* Hyperimmune Plasma Decreases Pneumonia Severity After a Randomised Experimental Challenge of Neonatal Foals," *The Veterinary Record* 178, no. 11 (2016): 261, https://doi.org/10.1136/vr.103095.

10. T. Liu, J. Jiao, S. Tang, et al., "The Safety and Efficacy of Regional Citrate Anticoagulation for Multiple Consecutive Therapeutic Plasma Exchanges With Fresh Frozen Plasma as a Replacement Solution," *International Urology and Nephrology* 57, no. 4 (2024): 1319–1327, https://doi.org/10.1007/s11255-024-04305-0.

11. T. Aoki and M. Ishii, "Hematological and Biochemical Profiles in Peripartum Mares and Neonatal Foals (Heavy Draft Horse)," *Journal of Equine Veterinary Science* 32, no. 3 (2012): 170–176, https://doi.org/10.1016/j.jevs.2011.08.015.

12. D. M. Wong and P. A. Wilkins, "Clinical Neonatal Renal Physiology," in *Equine Neonatal Medicine*, ed. P. A. Wilkins (Wiley, 2024), 638–643, https://doi.org/10.1002/9781119617228.ch23.