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Prediction of Packed Cell Volume after Whole Blood Transfusion in Small Ruminants and South American Camelids: 80 Cases (2006–2016)

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Background: Calculation of desired whole blood transfusion volume relies on an estimate of an animal's circulating blood volume, generally accepted to be 0.08 L/kg or 8% of the animal's body weight in kilograms.

Objective: To use packed cell volume before and after whole blood transfusion to evaluate the accuracy of a commonly used equation to predict packed cell volume after transfusion in small ruminants and South American camelids; to determine the nature and frequency of adverse transfusion reactions in small ruminants and camelids after whole blood transfusion.

Animals: Fifty-eight small ruminants and 22 alpacas that received whole blood transfusions for anemia.

Methods: Retrospective case series; medical record review for small ruminants and camelids that received whole blood transfusions during hospitalization.

Results: Mean volume of distribution of blood as a fraction of body weight in sheep (0.075 L/kg, 7.5% BW) and goats (0.076 L/kg, 7.6% BW) differed significantly ($P < 0.01$) from alpacas (0.103 L/kg, 10.3% BW). Mild transfusion reactions were noted in 16% of transfusions.

Conclusions and Clinical Relevance: The generally accepted value of 8% for circulating blood volume (volume of distribution of blood) is adequate for calculation of transfusion volumes; however, use of the species-specific circulating blood volume can improve calculation of transfusion volume to predict and achieve desired packed cell volume. The incidence of transfusion reactions in small ruminants and camelids is low.

Key words: Alpaca; Anemia; Goat; Hematology; Sheep.

Transfusion of whole blood is necessary to treat anemia in a number of conditions in small ruminant and camelid species, including acute trauma, parasitism, toxicosis, or immune-mediated anemia.[1] Clinical triggers for whole blood transfusion often rely on packed cell volume (PCV) as a predictor of red blood cell mass, along with other clinical variables. General guidelines for whole blood transfusions recommend administration of blood when the PCV decreases below 15–20% in acute blood loss, or decreases below 10–15% in chronic anemia.[1] Additional clinical variables to evaluate necessity of whole blood transfusion include plasma protein, hemoglobin concentration, plasma lactate concentration, and clinical signs. Tissue hypoxia is at an increased risk secondary to compromised myocardial oxygenation at a hemoglobin level less than 5 g/dL or PCV less than 15%.[2]

The amount of blood to be transfused is variable and dependent on numerous factors, including the underlying condition.[3,4] Calculations to estimate transfusion requirements are based on the PCV of the donor and recipient, body weight of the recipient (in kilograms), estimated circulating blood volume of the animal (volume of distribution of blood, VDB), and desired target PCV.[2]

Abbreviations:

BV	blood volume (L/kg)
BW	body weight (kg)
CCC	Lin's concordance correlation coefficient
PCV	packed cell volume
RBCs	red blood cells
TV	transfusion volume (L)
VDB	volume of distribution of blood (L/kg)

$$\text{TV(L)} = \text{VDB} \times \text{BW(kg)} \times \frac{\text{Desired PCV (\%)} - \text{Recipient PCV (\%)}}{\text{Donor PCV (\%)}}$$

where TV is the transfusion volume (in liters) to achieve the desired PCV, recipient PCV is the PCV of the recipient-patient before transfusion, BW is the recipient's body weight (in kilograms), and VDB is the fraction of BW accounted for by circulating blood volume. Most published versions of the above equation employ a VDB equal to 0.08 (L/kg) or 8% BW.[2] These equations do not account for the transient increase in blood volume achieved when a blood transfusion is administered to an animal without active hemorrhage, potential ongoing blood loss during the transfusion, and potential variability in circulating blood volume between species.

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Whereas 8% is accepted as the standard value for VDB, to the authors' knowledge, no study has evaluated the accuracy of the above formula to predict final PCV after whole blood transfusion in small ruminants and camelids. The purpose of this study was to use PCV measurements before and after transfusion to evaluate the accuracy of a commonly used equation to predict PCV after transfusion in small ruminants and camelids. A secondary objective was to determine the nature and frequency of adverse transfusion reactions in small ruminants and camelids after whole blood transfusion.

Materials and Methods

Electronic and hard copy medical records from the New Bolton Center Large Animal Hospital at the University of Pennsylvania were searched for ovine, caprine, and camelid patients who received whole blood transfusions from January 1, 2006, to December 1, 2016. Information was recorded for signalment, history, presenting complaint, physical examination findings, and clinicopathologic data for each animal. Packed cell volume (PCV) and total solids were recorded for all blood donor animals. All medical records were included in descriptive data for animals which received a whole blood transfusion and survived to have at least 1 PCV after transfusion recorded. PCV after transfusion was defined as the PCV obtained 1–2 hours after transfusion. For some cases, a PCV was not recorded at that time, and the earliest PCV up to 12 hours after transfusion was used. Animals were included as separate transfusions in analysis if the blood transfusion occurred >24 hours after the initial transfusion, and the PCV before transfusion was that which prompted administration of additional transfusions. Transfusion reactions were defined as tachycardia, tachypnea, shivering, sweating, urticaria, dyspnea, or hyperthermia (>104°F or an increase of >2°F) occurring during or shortly after whole blood transfusion. Fluid overload was defined as a separate transfusion reaction and was identified by evidence of pulmonary edema as noted by dyspnea, foaming at the mouth, and/or onset of harsh bronchovesicular sounds on thoracic auscultation.

For calculation of VDB, animals were only included in final analysis when information was available for PCV before transfusion, PCV after transfusion, blood donor PCV, and measured recipient body weight (kg). Animals with estimated body weight were excluded. The VDB for use in the prediction equation was calculated by algebraic manipulation of the TV equation using recorded values before and after transfusion.

The generally accepted formula for blood transfusion volume,

$$\text{Transfusion volume (L)} = \text{VDB} \times \text{Recipient BW (kg)} \times \frac{\text{Desired PCV (\%)} - \text{Recipient PCV (\%)}}{\text{Donor PCV (\%)}}$$

was manipulated to solve for VDB:

$$\text{VDB} = \frac{\text{Transfusion volume (L)} \times \text{ Donor PCV (\%)}}{\text{Recipient BW (kg)} \times [\text{Final PCV (\%)} - \text{Initial PCV (\%)}]}$$

where Final PCV equates to the Desired PCV and Initial PCV equates to the Recipient PCV before transfusion.

To evaluate the utility of the TV equation, the mean VDB values for each species were used in the TV equation to calculate for each animal what would have been predicted for the posttransfusion PCV ("desired PCV") and compare to the actual outcome in those animals. This comparison was also performed using the VDB universal value of 0.08 L/kG in the TV equation for each animal.

Statistical Analysis

Descriptive statistics were used to report clinical and clinicopathologic findings. Numerical values are reported as medians and ranges unless otherwise specified. Statistical analyses were performed using standard statistical software.[a] Mean ± SEM was calculated for BV determined algebraically from the animal's data before and after transfusion. Analysis of variance was used to compare differences in the mean VDB based on species (sheep, goat, alpaca).

Lin's concordance correlation coefficient (CCC) analysis and the method of Bland-Altman were used to assess the agreement between actual final PCV, and the value predicted using the TV equation, using both the literature value of 0.08 L/kg for VDB for each animal and using VDB determined for each species.

Results

Animals

Fifty-eight small ruminants (goat and sheep) and 22 alpacas received 64 and 26 blood transfusions, respectively, during the study period. Of the 58 ruminants, 45 were goats receiving 50 transfusions and 13 were sheep receiving 14 transfusions.

Of the 45 goats, median age was 7 months (range, 2–120 months). There were 20 does, 15 bucks, and 10 wethers. Breeds included Pygmy (10), Nubian (8), Boer (7), crossbred (5), Fainting (2), Angora (1), LaMancha (1), Saanen (1), and 10 of unknown breed. Primary presenting complaints for goats included inappetence (8), recumbency (7), suspicion of anemia/parasites (7), diarrhea (7), unknown reasons (7), and one each of the following: trauma (vehicular), trauma (dog attack), ruminal bloat, hypothermia, submandibular edema, dystocia, mammary gland enlargement, vulvar bleeding, and routine vaccination. Diagnosis obtained during workup included endoparasitism (35), copper toxicity (2), trauma (2), unknown (2), and one each of the following: hemolytic anemia, uterine artery aneurysm, mammary gland adenocarcinoma, and dystocia.

Of the 13 sheep, median age was 5 months (range, 3–132 months). There were 8 ewes, 4 rams, and 1 wether. There were 4 Finnish Landrace, 3 crossbred, 1 Icelandic, 1 Shropshire, and 4 of unknown breed. Presenting complaints for sheep included suspicion of anemia/parasites (4), inappetence (4), recumbency (2), diarrhea (2), and submandibular edema (1). Diagnosis obtained during workup included endoparasitism (10), copper toxicity (1), uterine bleeding (1), and ruminal artery hemorrhage (1).

Median age for the 22 alpacas was 24 months (range, 7–156 months). There were 13 females, 4 intact males, and 5 castrated males. Alpaca breed was not recorded. Presenting complaints for alpacas included suspicion of anemia (10), recumbency (4), lethargy (4), weight loss (2), respiratory distress (1), and femoral fracture (1). Diagnosis obtained during workup included

endoparasitism (12), *Mycoplasma haemolamae* infection (3), lymphosarcoma (2), and femoral fracture with surgical blood loss (1). A definitive diagnosis was not obtained in 4 alpacas.

Transfusions

Mean (±SEM) length of hospitalization was 9.44 ± 10.19 days for small ruminants and 5.64 ± 4.02 days for alpacas. Of the 13 sheep, 9 survived to discharge, with 3 being euthanized and 1 dying during hospitalization. Of the 45 goats, 36 survived to discharge, 7 were euthanized, and 2 died. Of the 22 alpacas, 12 survived to discharge, 7 died, and 3 were euthanized.

Median PCV, TS, lactate, and transfusion volumes for small ruminants and alpacas are summarized in Table 1. Transfusion rate was not captured in the medical record review.

Adverse effects were noted in 10 of 64 ruminant transfusions and 4 of 26 alpaca transfusions. Six goats and 2 sheep developed hyperthermia, all of which were responsive to administration of a corticosteroid. One goat that developed hyperthermia also developed pigmenturia that was not pursued as to origin (i.e. RBCs vs. hemoglobin), upon which time the transfusion was stopped. One goat received blood from a herd mate donor that was seropositive for CAE virus, and developed bilateral carpal arthritis at later hospital admissions. Two alpacas developed evidence of pulmonary edema which improved with administration of furosemide. One alpaca developed hyperthermia, and another alpaca developed an irregular cardiac rhythm that resolved when the transfusion was stopped. Crossmatching was not performed before any of the transfusions and no pretreatments were administered.

Calculation of Volume of Distribution of Blood (VDB)

Forty-six animals were available for complete analysis of VDB for use in the TV equation. The mean VDB based on algebraic calculation using the PCV before and after transfusion in the TV equation varied significantly by species ($P < 0.01$). The alpaca VDB (0.103 ± 0.007 L/kg) was significantly different ($P < 0.01$) than that for goats (0.076 ± 0.004 L/kg) and sheep (0.075 ± 0.009 L/kg).

Lin's concordance correlation analysis was performed on observed final PCV vs. predicted final PCV, using the "universal" value of 0.08 L/kg for VDB, and also using predicted final PCV calculated using the species-specific VDB obtained algebraically from our data (goats 0.076, sheep 0.075, alpacas 0.103). This analysis revealed a CCC of 0.802, indicating good agreement, when the "universal" value of BV=0.08 for all species was used to calculate predicted PCV and a CCC of 0.908, excellent agreement, using the species-specific values. Bland-Altman plots displaying agreement between final PCV and predicted final PCV based on predictions using these VDB values are shown in Figures 1 and 2. Using the universal VDB for all animals of 0.08 yielded a bias of −0.06% PCV and 95% limits of agreement of

Table 1. Clinicopathologic data before and after whole blood transfusion in goats (n = 45), sheep (n = 13), and alpacas (n = 22).

	Median pretransfusion PCV (%) [range]	Median pretransfusion TS (g/dL) [range]	Median pretransfusion lactate (mmol/L) [range]	Median donor PCV (%) [range]	Median donor TS (g/dL) [range]	Median transfusion volume (mL/kg)	Median posttransfusion PCV (%) [range]	Median posttransfusion TS (g/dL) [range]
Small ruminant (n = 58)	9 [4–22]	4.4 [0.8–8.0]	4.0 [0.8–15.8][a]	32 [22–45]	7.2 [5.6–8.4]	28.5 ± 12.6	17 [9–32]	5.2 [2.7–7.8]
Alpaca (n = 22)	8 [5–19]	4.5 [3.0–7.0]	2.9 [0.9–20][b]	30 [25–41]	5.9 [4.9–6.5]	28.1 ± 12.5	16 [9–24]	4.7 [3.6–5.6]

[a]Lactate available for 43 small ruminants.
[b]Lactate available for 13 alpacas. TS, total solids (g/dL); PCV, packed cell volume (%).

−6.6 to 6.5%. Using the species-specific VDB values to predict final PCV yielded a bias of −0.6 PCV and 95% limits of agreement of −6.0 to 4.8%.

Discussion

This study evaluated the variable VDB (volume of distribution of blood) in small ruminants and South American camelids for use in the transfusion volume equation, as well as reporting the incidence of transfusion reactions in camelids.

Anemia due to severe endoparasitism was the most common indication for blood transfusion in this study, and is the most common reason for whole blood transfusions in small ruminants and camelids at our institution. It is notable that for many of these animals, the presenting complaint was recumbency, not anemia or suspicion of parasitism.

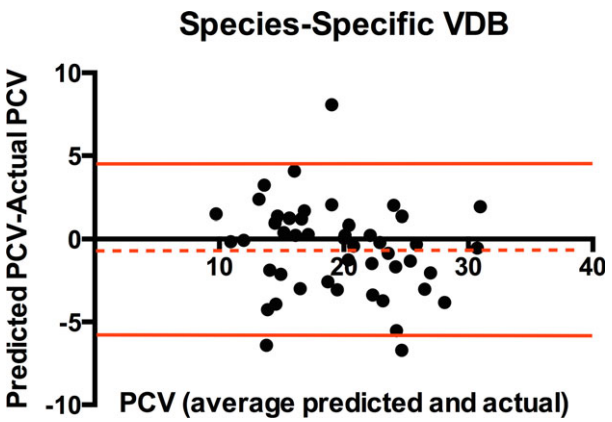

Fig 1. Bland-Altman plot exhibiting agreement between final packed cell volume (PCV) and predicted final PCV after whole blood transfusion in small ruminants and alpacas (n = 46) based on species-specific volume of distribution of blood (VDB) (goat: 0.076 L/kg; sheep: 0.075 L/kg; alpaca: 0.103 L/kg). The dashed line represents the average difference between predicted and final PCV, and the solid lines represent the 95% limits of agreement.

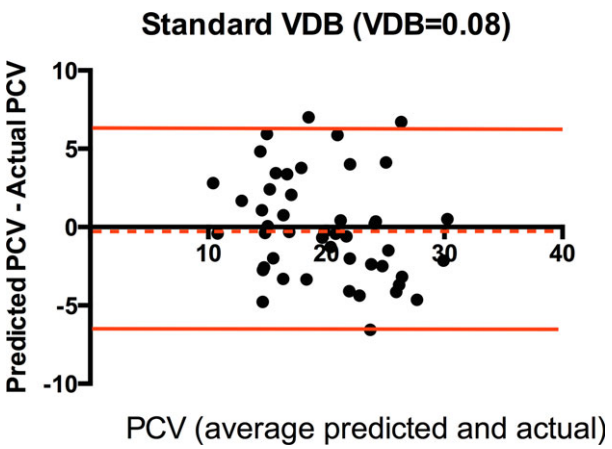

Fig 2. Bland-Altman plot exhibiting agreement between final packed cell volume (PCV) and predicted final PCV after whole blood transfusion in small ruminants and alpacas (n = 46) based on "universal" volume of distribution of blood (VDB) value of 0.08 L/kg. The dashed line represents the average difference between predicted and final PCV, and the solid lines represent the 95% limits of agreement.

Adverse reactions were seen in 16% of transfusions in this study. This is similar to what was noted in a recent equine study.[5] Agglutination cross-matching in ruminants is likely unnecessary in first-time whole blood transfusions to determine suitable donors and can be both time- and cost-prohibitive in an emergency situation.[1] Therefore, cross-matching is rarely performed before whole blood transfusion in small ruminants and camelids, yet the adverse reaction rate in this study was similar to that seen in horses,[5] where cross-matching is frequently performed. A recent study found 17% of ovine cross-matches to be incompatible.[13] There is a high degree of variation in goat and sheep blood group factors. Goats exhibit at least 6 blood group systems (A, B, C, E, F, and R), whereas sheep exhibit 7 blood group systems (A, B, C, D, M, R, X) with over 22 factors.[6,7] Six blood group factors have been reported in South American camelids, although very little is known about blood group variation in camelids.[8] Based on the results of this study, administration of non-cross-matched blood to small ruminants and alpacas represents minimal risk to the animal.

Data from this study were used to determine the optimum value to use for VDB, the volume of distribution of blood, in the transfusion volume equation. Published versions of this equation typically employ a universal value of 0.08 (or 8% BW) for all species, which is generally recognized as the circulating blood volume. Results from this study indicated that slightly improved accuracy of the equation can be achieved using species-specific values of 0.076, 0.075, and 0.103 L/kg for VDB for goats, sheep, and alpacas, respectively. However, the improved accuracy is only on the order of 1–2% PCV and is most likely clinically irrelevant. For example, if the equation were employed to calculate the volume of blood required to increase the PCV from 10 to 20% in a 30-kg alpaca, with a donor PCV of 33%, using VDB = 0.103 L/kg would yield a transfusion volume of 900 mL, vs. 725 mL for VDB = 0.08 L/kg. Or conversely, the predicted increase in PCV resulting from a transfusion of 725 mL to a 30-kg alpaca would be 9.9% using VDB = 0.08 L/kg, and 8% using VDB = 0.103 L/kg. This difference is unlikely to be clinically relevant given the arbitrary choice of target PCV, and also the availability of blood collection bags in certain volumes. The differences are even smaller for small ruminants.

For the purposes of this study, VDB is a mathematical proportionality constant representing the relationship between transfusion volume and change in the recipients' PCV. It hypothetically represents the animals' blood volume, but as mentioned above can also be influenced by other factors such as ongoing blood loss during the transfusion and fluid volume status of the animal. Actual blood volume has been determined in normal animals using dye or radioactive tracer dilution techniques, and these studies have yielded results similar to the VDB obtained in this study.[9–11] In those studies, normal sheep were found to have a blood

volume ranging from 0.056 to 0.071, 0.0635, and 0.056 L/kg, respectively. A similar study in goats yielded blood volume of 0.0750 and 0.0614 L/kg for dye and tracer dilution methods, respectively.[12] These are similar to the value of 0.075 and 0.076 L/kg for sheep and goats, respectively, in the current study, despite a major difference in the method of determining blood volume.

The limitations of this study are those inherent to any retrospective study. Retrospective studies rely on information extracted from medical records after the fact and are therefore limited by lack of complete medical records. Information bias is possible as cases were selected based on availability of medical records. With a small number of animals in each species, the significance of the variance in circulating blood volume cannot be fully assessed. In addition, the testing of circulating blood volume for prediction of PCV after transfusion was performed using the same set of animals used to initially predict the circulating blood volume, which can result in bias. Therefore, a second set of cases for testing the predictions based on different BV would have been ideal.

In summary, the results of this study suggest transfusion of non-cross-matched whole blood in small ruminants and alpacas represents minimal risk to the recipient. Furthermore, our results indicate that a VDB of 0.075 L/kg for sheep, 0.076 L/kg for goats, and 0.103 L/kg for alpacas might be more appropriate for use in the transfusion volume equation. However, given the individual variation in VDB, the variable effect of ongoing blood losses and changes in fluid balance, and the arbitrary nature of the target PCV chosen by the clinician to use in the equation, the impact of these small differences in BV is clinically negligible. Therefore, it seems a universal value for BV of 0.08 L/kg provides an acceptable estimate of blood volume to be used in the transfusion equation.

Footnote

[a] STATA 14, College Station, TX

Acknowledgments

Conflict of Interest Declaration: The authors declare no conflict of interest.

Off-label Antimicrobial Declaration: The authors declare no off-label use of antimicrobials.

References

1. Balcomb C, Foster D. Update on the use of blood and blood products in ruminants. Vet Clin North Am Food Anim Pract 2014;30:455–474.

2. Divers TJ. Blood component transfusions. Vet Clin North Am Food Anim Pract 2005;21:615–622.

3. van de Watering L. Red cell storage and prognosis. Vox Sang 2011;100:36–45.

4. Besier RB, Kahn LP, Sargison ND, Van Wyk JA. Diagnosis, treatment and management of Haemonchus contortus in small ruminants. Adv Parasitol 2016;93:181–238.

5. Hurcombe SD, Mudge MC, Hinchcliff KW. Clinical and clinicopathologic variables in adult horses receiving blood transfusions: 31 cases (1999–2005). J Am Vet Med Assoc 2007;231:267–274.

6. Penedo MC. Red blood cell antigens and blood groups in the cow, pig, sheep, goat, and llama. In: Bernard FF, Joseph GZ, Jain NC, eds. Schalm's Veterinary Hematology, 5th ed. Ames, IA: Lippincott, Williams, and Wilkins; 2000:777–782.

7. Rasmusen BA. Blood groups in sheep. Ann N Y Acad Sci 1962;97:306–319.

8. Penedo MC, Fowler ME, Bowling AT, et al. Genetic variation in the blood of llamas, Llama glama, and alpacas, Llama pacos. Anim Genet 1988;19:267–276.

9. Durotoye LA, Oyewale JO. Blood and plasma volumes in normal West African dwarf sheep. Afr J Biomed Res 2000;3:135–137.

10. Gillett DJ, Halmagyi FJ. Results and limitations of blood volume measurements in sheep. J Surgical Res 1966;6:211–214.

11. Coghlan JP, Fan JSK, Scoggins BA, Shulkes AA. Measurement of extracellular fluid volume and blood volume in sheep. Aust J Biol Sci 1977;30:71–84.

12. Klement AW, Ayer DE, Rogers EB. Simultaneous use of Cr51 and T-1824 dye in blood volume studies in the goat. Am J Physiol 1955;181:15–18.

13. Simonova G, Tung JP, Fraser JF, et al. A comprehensive ovine model of blood transfusion. Vox Sang 2014;106:153–160.