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The effects of lactated Ringer's solution (LRS) or LRS and 6% hetastarch on the colloid osmotic pressure, total protein and osmolality in healthy horses under general anesthesia

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Abstract

Objective—To investigate changes in colloid osmotic pressure (COP), total protein (TP) and osmolality (OSM) during anesthesia in horses given intravenous lactated Ringer's solution (LRS) or LRS and hetastarch (HES).

Study design—Prospective, clinical trial.

Animals—Fourteen horses presented for surgery. Mean age 8.3 ± 1.9 years; mean weight 452 ± 25 kg.

Methods—Horses were premedicated with xylazine intravenously (IV); anesthesia was induced with ketamine and diazepam IV, and maintained with sevoflurane. Butorphanol was administered IV with pre-medications or immediately after induction. Xylazine was administered IV for recovery if necessary. LRS was administered IV to all horses with a target rate of $5\text{--}10 \text{ mL kg}^{-1} \text{ hour}^{-1}$. Half of the horses also received 6% HES, 2.5 mL kg^{-1} over 1 hour in addition to LRS. Horses that received LRS only were considered the LRS group. Horses that received both LRS and HES were considered the LRS/HES group. Blood was drawn pre- and post-anesthesia, immediately following induction, and every 30 minutes throughout anesthesia. COP, TP and OSM were measured.

Results—COP and TP significantly decreased at similar rates for both treatment groups from pre-anesthetic values. Pre-anesthetic COP was significantly greater in the LRS group when compared to the LRS/HES group pre-, post- and throughout anesthesia. In the LRS group post-anesthetic OSM was significantly different than the pre-anesthesia value and that for the LRS/HES group.

Conclusions and clinical relevance—Administration of IV HES (2.5 mL kg^{-1} , over 1 hour) in combination with LRS does not attenuate the decrease in COP typically seen during anesthesia with crystalloid administration alone. Based on these results, administration of HES at this rate and total volume would not be expected to prevent fluid shifts into the interstitium through its effects on COP.

Keywords

colloid osmotic pressure; equine anesthesia; hetastarch; lactated Ringer's solution

Introduction

General anesthesia of horses is not without complications. Morbidity and mortality rates are higher than those for many other species (0.12–0.9%; Wagner 2008). Even in horses that are systemically healthy, anesthesia is associated with several complications including, but not limited to, hypotension and subsequent neuropathies and myopathies, and post-operative tissue and pulmonary edema. Although there are many treatment options aimed at reducing anesthetic-related hypotension, one widespread therapy is to administer IV fluids in an attempt to maintain or even increase intravascular volume (Wagner 2008). However, the type and manner in which IV fluids are administered affects fluid shifts between the vasculature and tissues, and may possibly contribute to the development of pulmonary and tissue edema. Though infrequent, post-anesthetic pulmonary edema in horses has been reported in several cases and is associated with increased morbidity (Kaartinen et al. 2010). The Starling-Landis equation describes the net filtration of fluids out of capillaries as determined by the balance of capillary and interstitial hydrostatic pressure, and capillary and interstitial oncotic pressure (Starling 1896; Landis & Pappenheimer 1963). Colloid osmotic pressure (COP) is a measured indication of the intravascular portion of this balance, and therefore knowledge of COP may aid in identifying fluid shifts.

Synthetic colloids are commonly administered IV to patients with hypoproteinemia to prevent extravasation of fluids. They are also frequently administered to hypovolemic patients as a component of resuscitation efforts. One of the most common synthetic colloids is 6% hetastarch (HES), a synthetic polymer of glucose (amylopectin) (Bateman & DiBartola 2006). Many commercial formulations of hydroxyethyl starch are available in veterinary medicine. For example, HES 450/0.7 has an average molecular weight of 450 kDa and has a molar substitution ratio of 7 hydroxyethyl groups per 10 molecules of glucose (Bateman & DiBartola 2006). HES's COP ranges from 29 to 32 mmHg (Posner et al. 2003; Pascoe 2006) and can increase the plasma volume in human and canine patients by the volume administered (Smiley 1992; Silverstein et al. 2005).

There have been numerous studies investigating the effects of fluid administration on COP. For example, in healthy horses administered IV crystalloids alone, COP and TP decrease in a linear fashion when given at a rate of 40 mL kg⁻¹ hour⁻¹ (Jones et al. 1997) while awake, and at 11 mL kg⁻¹ hour⁻¹ while anesthetized (Boscan et al. 2007). This is also true of horses given aggressive administration of IV crystalloids at a rate of 15–25 mL kg⁻¹ hour⁻¹ during colic surgery (Boscan & Steffey 2007). In addition, healthy, anesthetized dogs given crystalloids at a rate of 9.4 ± 4.6 mL kg⁻¹ hour⁻¹ have an average decrease in COP of 5 mmHg (Dismukes et al. 2010). Interestingly, anesthetized dogs that are not administered intravenous fluids have a similar decrease in COP (Wright & Hopkins 2008). The decrease in COP cannot be reliably predicted by the volume of crystalloids administered (Dismukes et al. 2010) or by the concurrent TP (Wright & Hopkins 2008; Dismukes et al. 2010). In contrast, COP increases in hypoproteinemic, un-anesthetized horses with the administration of HES at a rate of 8–10 mL kg⁻¹ over 4 hours (Jones et al. 2001) as well as in clinically normal, un-anesthetized ponies at a rate of 10 or 20 mL kg⁻¹ over 2 hours (Jones et al. 1997).

Although HES has been shown to increase COP in healthy, as well as hypoproteinemic, un-anesthetized horses, the ability of HES to increase COP in anesthetized healthy horses has not been evaluated. We tested the hypothesis that IV HES at 2.5 mL kg⁻¹ over 1 hour would attenuate the decrease in COP seen with the administration of crystalloids during general anesthesia in horses. Because TP and OSM are also factors that influence transvascular and transcellular fluid shifts, they were also evaluated.

Materials and methods

The experimental protocol was approved by the University of Wisconsin's Institutional Animal Care and Use Committee, protocol number V1372.

Experimental groups

Fourteen adult, healthy horses (ASA status I/II) presented for surgeries not involving the gastrointestinal tract at the Veterinary Medical Teaching Hospital were enrolled. Horses were fasted overnight but were allowed access to water until being walked from their stalls. Catheters (14-gauge, over-the-needle) were aseptically placed in a jugular vein per standard of care for the hospital. Xylazine ($0.5\text{--}1.0\text{ mg kg}^{-1}\text{ IV}$; Akorn, Inc., IL, USA) was administered to effect. Once sedation was achieved, anesthesia was induced with ketamine ($2.2\text{ mg kg}^{-1}\text{ IV}$; Fort Dodge Animal Health, IA, USA) and diazepam ($0.11\text{ mg kg}^{-1}\text{ IV}$; Hospira, Inc., IL, USA) and maintained with sevoflurane (Abbott Laboratories, IL, USA) in oxygen using a North American Drager Vapor 19.1 vaporizer and a North American Drager Anesthesia Machine (North American Drager, Telford, PA) with a large animal rebreathing circuit. Butorphanol ($0.025\text{--}0.05\text{ mg kg}^{-1}\text{ IV}$; Fort Dodge Animal Health, IA, USA) was administered with the pre-medications or soon after induction, if the procedure warranted additional analgesia. Routine monitoring was performed using a multiparameter monitor (Datascope Passport 2 and a Datascope Gas Module II; Mindray Medical USA Corp, Redmond, WA, USA). Monitoring included heart rate, base apex ECG, pulse oximetry, respiratory rate and end-tidal CO_2 . Direct arterial blood pressure was monitored with an aseptically placed 20-gauge catheter in the submandibular branch of the facial artery. The transducer was placed at the level of the patient's heart and zeroed to atmospheric pressure. Dobutamine was administered ($1\text{--}5\text{ }\mu\text{g kg}^{-1}\text{ minute}^{-1}\text{ IV}$; Hospira, Inc., IL, USA) to effect to maintain mean arterial pressures at or above 70 mmHg. All horses were mechanically ventilated to maintain end-tidal CO_2 within 35–45 mmHg (4.7–6 kPa). Xylazine ($0.05\text{--}0.1\text{ mg kg}^{-1}\text{ IV}$) was given immediately before recovery if deemed necessary by the anesthetist.

The 14 horses were divided into two groups. Upon inclusion in the study, the investigator was responsible for group assignment. Horses were assigned to treatment groups to maintain equal numbers within groups and on the basis of funding availability at the time of inclusion. Horses were assigned in the following order; four control horses, four treatment horses, two control horses, two treatment horses, one control horse and one treatment horse. Seven horses served as controls, receiving only LRS during anesthesia (LRS group). The remaining seven horses received LRS for the duration of anesthesia plus $2.5\text{ mL kg}^{-1}\text{ HES}$ in 0.9% saline, IV over the first hour of anesthesia (LRS/HES group). LRS was administered into the jugular catheter via gravity driven delivery from a 5 L bag hung 3 feet above the catheterized, nondependent jugular vein with a target rate of $10\text{ mL kg}^{-1}\text{ hour}^{-1}$. A fluid pump (FLO-GARD 6301; Volumetric Infusion Pump, Baxter, Deerfield, IL, USA) was used to deliver the accurate volume of HES. Researchers were not blinded to treatments.

Blood analysis

For analysis of COP, TP and OSM, blood samples were taken from the jugular venous catheter 1–2 hours prior to anesthesia, 2 hours post-anesthesia (defined as discontinuation of inhalant), as well as immediately post-induction, prior to administration of any fluids. Blood samples during anesthesia were taken every 30 minutes, beginning 30 minutes after the post-induction sample, from the facial arterial catheter. Six to 8 mL of blood was obtained at each time point. The samples were equally divided with half placed in blood collection tubes with no additive and half placed in heparinized blood collection tubes. The blood for serum collection was allowed to clot for 30–60 minutes and then centrifuged for 10 minutes (2500 g). Plasma was used to analyze COP with a Wescor 4420 Colloid Osmometer (Wescor Inc.,

Logan, UT, USA) calibrated minimally every 30 days with the Osmocell COP calibrator. The Osmometer filters used in the study had a 30 kDa molecular weight cutoff membrane. Serum was used to measure OSM using an Advanced Micro Osmometer Model 3300 (Advanced Instruments, Inc., Norwood, MA, USA) via freezing-point thermodynamics, and TP using a Hitachi 912 Chemistry Analyzer (Roche Diagnostics, Indianapolis, IN, USA) via the biuret reaction. Individual tests are calibrated every 6 months or when a new lot is started, whichever comes first.

Statistical analysis

For comparisons within and between treatment groups, a one-way ANOVA and Student-Newman-Keuls multiple comparison test was performed on time points with sufficient sample sizes (e.g., pre-anesthesia, post-induction, post-anesthesia, and 30–180 minutes for the LRS group, 30–150 minutes for the LRS/HES group). Missing data points were a result of variations in total anesthesia time among patients. Results are reported as mean $\pm$ SD except where there are only one or two data points within the time point. Then the data are simply reported as the mean with no error bars. In addition, the intra-anesthesia, arterial sample data were subsequently analyzed by fitting a mixed effect model aimed at examining the relationship between our measured variables (COP, TP, and OSM), time following induction until the conclusion of surgery, and the treatment (LRS alone *versus* LRS/HES). As such, the fixed effects were time and treatment with each subject (horse) as a random effect. We also considered fluid volume as a covariate in our initial model, because the volumes administered in each group were not exactly the same. Results were fitted into two mixed effect models, one with fluid volume included and one without. The contribution of the volume of LRS administered was tested to the likelihood of significance. It was found to be insignificant in both groups because it did not affect the parameters measured ($p > 0.05$); consequently, the volume of LRS administered was removed from the model. Statistics were performed using SigmaStat or the lme4 package in R (R Development Core Team, electronic edition, 2008). A p -value < 0.05 was considered significant.

Results

Fourteen horses: five Quarter Horses, two Paints, two Standardbreds and one each of Andalusian, Clydesdale, Thoroughbred, Morgan, and Welsh Pony breeds were enrolled in the study. The mean age was 8.3 ± 1.9 years. Surgeries consisted of three arthroscopies, two ocular enucleations, two mass removals, and one each of arthrodesis, nephrectomy, desmotomy, laceration repair, lateral splint bone removal, phallectomy, cryptorchid castration and neurectomy. Total anesthesia time was not statistically different between the groups; 158 ± 8 and 150 ± 7 minutes for the LRS and LRS/HES groups, respectively ($p > 0.05$). LRS volumes for the LRS and LRS/HES groups were 7.5 ± 1.1 and 7.8 ± 1.0 mL $\text{kg}^{-1} \text{hour}^{-1}$, respectively, and were not found to be statistically different between groups ($p > 0.05$).

Pre-anesthesia

There was a significant difference between the LRS and LRS/HES groups in the pre-anesthesia COP values (23.8 ± 0.7 mmHg *versus* 19.9 ± 0.7 mmHg, respectively; $p < 0.05$). However, there were no significant differences in pre-anesthesia values between groups in TP and OSM (both $p > 0.05$; Figs 1–3).

During anesthesia

After induction, COP, TP and OSM in the LRS group were 23.0 ± 0.7 mmHg, 6.4 ± 0.2 g dL^{-1} , 286 ± 1 mOsm kg^{-1} , respectively and were not significantly different than pre-anesthetic values (all $p > 0.05$; Figs 1–3). After induction, COP, TP and OSM in the LRS/

HES group were 18.8 ± 0.5 mmHg, 6.0 ± 0.22 g dL⁻¹ and 286 ± 2 mOsm kg⁻¹, respectively, and were not significantly different than pre-anesthetic values (all $p > 0.05$; Figs 1–3). However, COP and TP significantly decreased from pre-anesthesia values between 30 and 180 minutes in the LRS group and 30–150 minutes in the LRS/HES group (all $p < 0.05$; Figs 1 & 2).

For both treatment groups, there was a significant relationship between COP and time, with the COP values decreasing linearly over the measured time points ($p < 0.05$; LRS group $R^2 = 0.83$; LRS/HES group $R^2 = 0.88$; Fig. 1). There was a significant overall treatment effect with the LRS group having significantly higher COP values throughout the experiment ($p < 0.05$). However, the slope of the regression lines in the LRS and LRS/HES groups was not statistically different and therefore there was no difference in the rate of COP decrease between the treatment groups ($p > 0.05$; Fig. 1).

Similar to COP, there was a significant relationship between TP and time, with the TP decreasing throughout anesthesia ($p < 0.05$; LRS group $R^2 = 0.88$; Fig. 2; LRS/HES group $R^2 = 0.85$; Fig. 2). However, in contrast to COP, there were no significant treatment effects and no significant interaction terms (all $p > 0.05$). As suggested by Fig. 3, there were no significant changes in OSM throughout anesthesia resulting in no significant time, treatment or interaction effects (all $p > 0.05$; Fig. 3).

Post anesthesia

There were no clinically evident post-operative complications in any of the study horses. The post anesthesia COP, TP, and OSM in the LRS group were 23.5 ± 1.2 mmHg, 6.2 ± 0.2 g dL⁻¹, 290 ± 2 mOsm kg⁻¹, respectively whereas the post anesthesia COP, TP and OSM in the LRS/HES group were 19.6 ± 1.2 mmHg, 5.8 ± 0.3 g dL⁻¹, 286 ± 2 mOsm kg⁻¹, respectively. The post-anesthesia COP and TP in each group were similar to the pre-anesthetic values before induction for that group (both $p > 0.05$; Figs 1 & 2). The COP in the LRS group remained significantly higher than that in the LRS/HES group. In the LRS group, the post-anesthetic OSM was significantly greater when compared to pre-anesthetic levels in the same group, and the post-anesthetic OSM in the LRS/HES group ($p < 0.05$; Fig. 3).

Discussion

Our data indicate that similar to previously published reports, the administration of LRS results in a linear, significant decrease in COP and TP over the duration of the anesthetic period. However, the addition of 6% HES to the fluid administration for a total volume of 2.5 mL kg⁻¹ given over 1 hour did not attenuate this decrease. Our data also indicated that OSM did not change over time, although it was greater in the LRS *versus* the LRS/HES group post-anesthesia. The blood drawn for analysis was from two different sources, arterial and venous, based on a previous study showing no statistical or clinical difference between arterial and venous COP and TP (Boscan et al. 2007).

Endogenous colloids are large molecular weight particles that are present in plasma. The component of the total oncotic pressure in plasma contributed by colloids is the COP. In normal plasma, the major contributors to COP are proteins, more specifically, albumin, globulins (Thomas & Brown 1992) and fibrinogen (DiBartola et al. 2006). In one study on anesthetized horses, it was found that the sum of these proteins (TP) makes up 70.5% of COP and is therefore important in determining the fluid distribution between the vascular and interstitial spaces (Boscan et al. 2007).

In addition to the intravascular COP, there are three other main forces present at the level of the capillary that influence fluid distribution: interstitial and intravascular hydrostatic pressure and interstitial oncotic pressure (DiBartola et al. 2006). These forces dictate whether fluid will stay in the capillary or be filtered into the interstitial space. The Starling-Landis equation describes the relationship between oncotic pressure and the opposing hydrostatic pressure present in the capillaries (Starling 1896; Landis & Pappenheimer 1963):

$$Q = \kappa S [(P_c - P_i) - \sigma(\pi_c - \pi_i)],$$

where Q is the net transcapillary fluid exchange, κ is the net permeability of the capillary wall, S is capillary surface area, P_c is capillary hydrostatic pressure, P_i is interstitial hydrostatic pressure, σ is the capillary reflection coefficient, π_c is the capillary COP, and π_i refers to the interstitial COP.

According to this relationship, factors that cause oncotic pressure within the capillaries to decrease will cause net filtration of fluids into the interstitium. In addition to the Starling-Landis equation, one theory proposes that transcapillary fluid movement across the endothelium is more likely due to a local difference in the hydrostatic and COP across the endothelial surface glycocalyx, rather than a general difference in the hydrostatic and oncotic pressure between the plasma and tissue (Chappell et al. 2008). Nonetheless, decreases in COP may be an important cause of tissue edema and hypotension, secondary to the filtration of fluid out of the vasculature. It has been suggested that reducing crystalloid administration during intestinal surgeries in horses may reduce post-operative ileus that occurs secondary to intestinal edema (Doherty 2009). However, in addition to reducing crystalloid administration, it may be possible to prevent the formation of intestinal edema by administering colloids to increase the COP. For example, in humans, intestinal edema becomes apparent intra-operatively when the COP decreases to 15 mmHg or below; however, edema formation can be prevented when patients are administered 10% HES or albumin (Prien et al. 1990; Haynes et al. 2003). Interestingly, dogs that are not administered crystalloids during anesthesia have similar decreases in COP and TP when compared to dogs that are given crystalloids (Wright & Hopkins 2008) suggesting anesthesia itself will cause changes in these values. Many sources recommend that COP remain above 20 mmHg to prevent intestinal and other tissue edema (Schüpbach et al. 1978; Lundsgaard-Hansen & Pappova 1981). The COP of the horses in the current study not only decreased below this level during anesthesia, but had pre-anesthetic COP values below this level; therefore this was not a realistic expectation.

Similar to Boscan et al. (2007), we found that in the LRS group, COP and TP decreased in a linear fashion throughout general anesthesia; concurrent HES administration failed to attenuate this decrease, as the slope of the regression lines between groups was not statistically different. The volume of LRS administration in each group was not included in the comparative analysis. The fact that removing the volume of LRS administration in each group from the regression analysis did not change the outcome suggests that the volume of LRS administered could not be used to predict changes in COP in the current study. This is consistent with a previously reported study in dogs (Dismukes et al. 2010). Although the administration of HES administered IV was hypothesized to attenuate the typical decline in COP values seen during anesthesia, we may have used an inadequate volume of HES which was additionally diluted out by the horses' blood volume and crystalloids. This may have resulted in very little oncotic effect of HES in our study. This dose was chosen based on an attempt to mimic clinical situations such as horses undergoing anesthesia for colic surgery. These patients typically receive aggressive crystalloid administration with or without additional colloids. If this volume of HES was effective at attenuating the decline in COP in

healthy horses, it would be possible that this information could be extrapolated to horses with certain disease processes, such as colic. Also, compared to typical HES administration at 5 mL kg^{-1} , the cost in clinical situations could be lessened. Indeed, a similar rate of HES administration ($2.0\text{--}2.5 \text{ mL kg}^{-1} \text{ hour}^{-1}$) was given to un-anesthetized, hypoproteinemic horses and HES increased COP significantly for 6 hours after administration (Jones et al. 2001). The horses in that study, however, were not anesthetized, were hypo-proteinemic prior to HES administration, and received a larger total volume ($8\text{--}10 \text{ mL kg}^{-1}$). Thus, it is possible that had we continued HES at our rate, resulting in a larger total volume, we may have attenuated the decreases in COP in the LRS/HES group. It is also possible that had we administered a lower rate of crystalloids, we may have attenuated the decreases in COP and TP with our current rate of HES.

In addition, there were significant differences between the LRS and LRS/HES groups throughout the study. The horses in the LRS/HES group had a lower COP throughout anesthesia than horses in the LRS group. From the onset of the study, several individual horses in the LRS/HES group had COP values below the normal reference interval for our laboratory ($22\text{--}25 \text{ mmHg}$). All animals were clinically normal on physical examination, with TP values within reference intervals for our laboratory ($5.2\text{--}8.2 \text{ g dL}^{-1}$). Since globulins, fibrinogen and pH can all influence COP in addition to total protein (TP), it is possible that had we measured these variables, a cause for the differences in COP between groups would have been more evident. Although we have no clear explanation for this difference in COP, what is apparent is that the slopes of lines between the groups were the same, indicating that HES had no effect on change in COP over time. Though a larger sample size within groups may have brought the overall COP values closer together, we anticipate that the slopes would remain the same due to the already robust data.

The TP for pre- and post-anesthesia time points between groups were not statistically different. One study found that TP contributes to only 70.5% of the COP (Boscan et al. 2007); it is possible for there to be statistically significant differences in the COP between groups, while having similar TP values in both groups. Similarly, in our study, plasma was used to measure COP, but serum used for TP. Since serum is essentially plasma without clotting factors, fibrinogen was not included as part of the measured TP, but was included as part of the measured COP thus limiting comparisons between COP and TP in our study. However, the TP and COP were measured in the same manner across all horses; thus comparisons within each treatment group are valid. Similar to COP, the TP steadily decreased over the course of general anesthesia and the slope of the regression lines between groups was not statistically different. The TP of most horses in the current study decreased below the reference interval ($5.2\text{--}8.2 \text{ g dL}^{-1}$). In the HES group, we might expect the TP to decline further due to additional dilution from the administration of LRS/HES. The degree of plasma expansion resulting from the administration of HES is variable, but it may expand by more than the volume given (Smiley 1992; Silverstein et al. 2005). In dogs given 450 mL HES IV, plasma volume increased by greater than 650 mL within 30 minutes (Silverstein et al. 2005). Nonetheless, plasma expansion may decrease TP due to dilution. Ponies given HES had a greater reduction in TP when compared to ponies that received only saline (Jones et al. 1997). It is possible that the horses in our study did not experience a sufficient volume expansion to dilute TP due to the small volume of HES administered (2.5 mL kg^{-1} , total volume).

Because osmolality (OSM) is involved in transcellular fluid homeostasis and is a measure of the impact of fluid administration on hemodilution and electrolyte concentrations, we included it in our study. OSM refers to the number of osmoles per kilogram of solvent. In physiologic fluids, the main substances that contribute to the OSM are sodium, potassium, chloride, bicarbonate, urea and glucose (DiBartola et al. 2006). The number of each of these

osmotically active substances in the intracellular and extracellular spaces will influence the fluid volume in each of these compartments (DiBartola et al. 2006). Serum OSM did not change in the LRS/HES group over the course of anesthesia; pre- and post-anesthetic samples were similar, which is consistent with the administration of the isotonic fluids used in our study. The OSM of LRS and HES is 273 mmHg and 310 mmHg (Bateman & DiBartola 2006), respectively. OSM was significantly higher post-anesthesia in the LRS group when compared to pre-anesthesia values. We speculate that this difference may be indirectly related to xylazine administration for recovery. In the current study, 43% of the LRS/HES horses received xylazine for recovery, while 71% of the LRS horses received xylazine. In dogs administered xylazine, OSM remains increased from 2 to 5 hours after administration (Talukder et al. 2009). The mechanism for this is unknown and is most likely multifactorial, but increased serum glucose concentrations, decreased plasma vasopressin and increased plasma atrial natriuretic peptide have been previously implicated in horses as well as other species (Trim & Hanson 1986; Talukder et al. 2009).

In conclusion, COP and TP decreased linearly during general anesthesia of healthy horses, with LRS administration as well as LRS plus 6% HES administration. The addition of HES at a volume of 2.5 mL kg⁻¹ over 1 hour did not attenuate these decreases in COP values throughout the anesthetic period. Further studies are necessary to evaluate the appropriate volumes of HES and crystalloids to administer in combination that will attenuate the decrease in COP. Additionally, the decreases in COP and TP associated with general anesthesia, standard crystalloid fluid administration alone and in combination with the volume of HES administered in this study, approached critical levels that have been associated with tissue edema formation in some species.

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Figure 1.

Plasma colloid osmotic pressure concentrations in healthy anesthetized horses administered $7.5 \pm 1.1 \text{ mL kg}^{-1} \text{ hour}^{-1}$ lactated Ringer's solution (LRS) ($\circ$, solid regression line) or $7.8 \pm 1.0 \text{ mL kg}^{-1} \text{ hour}^{-1}$ LRS and 2.5 mL kg^{-1} hetastarch (HES) given over 1 hour ($\blacksquare$, dashed regression line; $*p < 0.05$ between treatment groups, $\#p < 0.05$ versus pre-anesthesia within the treatment group). For time points pre-anesthesia through 60 minutes and post-anesthesia, $n = 14$ total; 7/7, LRS/(LRS/HES), 90 minutes $n = 12$; 6/6, 120 minutes $n = 9$; 5/4, 150 minutes $n = 6$; 3/3, 180 minutes $n = 5$; 3/2, 210 minutes $n = 2$; 1/1, 240 minutes $n = 1$; 0/1. The sample sizes are the same for all figures.

Figure 2.

Serum total protein concentrations in healthy anesthetized horses administered $7.5 \pm 1.1 \text{ mL kg}^{-1} \text{ hour}^{-1}$ Lactated Ringer's solution (LRS) ($\circ$, solid regression line) or $7.8 \pm 1.0 \text{ mL kg}^{-1} \text{ hour}^{-1}$ LRS and 2.5 mL kg^{-1} hetastarch given over 1 hour ($\blacksquare$, dashed regression line; # $p < 0.05$ versus pre-anesthesia within the treatment group).

Figure 3.

Serum osmolalities (OSM) in healthy anesthetized horses administered $7.5 \pm 1.1 \text{ mL kg}^{-1} \text{ hour}^{-1}$ Lactated Ringer's solution (LRS) ($\circ$, solid regression line) or $7.8 \pm 1.0 \text{ mL kg}^{-1} \text{ hour}^{-1}$ LRS and 2.5 mL kg^{-1} hetastarch (HES) given over 1 hour ($\blacksquare$, dashed regression line; $**p < 0.05$ versus LRS pre-anesthesia and LRS/HES post anesthesia; $\bullet$, superimposed data symbols).