SCIENTIFIC ARTICLE

Effects of total parenteral nutrition associated with glutamine, enteral fluid therapy with or without glutamine, and fluid therapy on the acid-base and electrolyte balance of horses starved after exploratory laparotomy

Efeitos da nutrição parenteral total associada à glutamina, fluidoterapia enteral com ou sem glutamina, e fluidoterapia no equilíbrio ácido-base e eletrolítico de equinos sob inanição após laparotomia exploratória

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Abstract

This study aimed to evaluate the effects of the total parenteral nutrition associated with glutamine, enteral fluid therapy with or without glutamine, and fluid therapy on the acid-base and electrolyte balance of horses starved after exploratory laparotomy. Sixteen healthy male and female adult horses of mixed breed, aged between 4 and 14 years, and having a mean body weight of 248.40 ± 2.28 kg and a body score index of 3-4 (scale of 1-5) were divided into four groups with four animals per group. After an adaptation period of 30 days, they were randomly divided into four experimental groups: enteral fluid therapy, enteral fluid therapy associated with glutamine, total parenteral nutrition associated with glutamine, and parenteral fluid therapy. The experiment was further divided into two phases: Phase 1 and Phase 2. In Phase 1, an exploratory laparotomy was performed, treatments were administered to the groups and the horses received no food or water other than those given to their respective groups. In Phase 2, the animals were re-fed. Each phase had a total duration of 144 h. Venous blood samples were collected every 24 h throughout the experimental period for blood gas and electrolyte analyses. The following parameters were evaluated: pH, partial pressure of carbon dioxide, total carbon dioxide, bicarbonate, base shift, anion gap, sodium, potassium, chloride, total calcium and magnesium. Completely randomized designs with a 4 × 7 factorial scheme (groups × harvest time) in Phase 1 and a 4 × 6 factorial scheme (groups × harvest time) in Phase 2 were used with four replications. All values were considered significant when $p \leq 0.05$ (95% probability). Blood pH, bicarbonate concentration, and base shift in the PARGL group decreased, indicating metabolic acidosis. Changes in the acid-base and electrolyte balance were more intense in the PARGL group than in the other groups. These results demonstrated the need to monitor blood gas and electrolyte balance in horses with food restriction under nutritional support or prolonged fluid therapy so that such changes are promptly corrected.

Keywords: equine, electrolyte imbalances, fluid therapy, metabolic acidosis, parenteral nutrition.

Resumo

Este estudo teve como objetivo avaliar os efeitos da nutrição parenteral total associada à glutamina, fluidoterapia enteral com ou sem glutamina e fluidoterapia no equilíbrio ácido-base e eletrolítico de equinos submetidos à inanição após laparotomia exploratória. Dezesseis cavalos adultos saudáveis, machos e fêmeas, sem raça definida, com idade entre 4 e 14 anos, com peso corporal médio de 248,40 ± 2,28 kg e índice de escore corporal de 3 a 4 (escala de 1 a 5) foram divididos em quatro grupos com quatro animais por grupo. Após um período de adaptação de 30 dias, foram divididos aleatoriamente em quatro grupos experimentais: fluidoterapia enteral, fluidoterapia enteral associada à glutamina, nutrição parenteral total associada à glutamina e fluidoterapia parenteral. O experimento foi ainda dividido em

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duas fases: Fase 1 e Fase 2. Na Fase 1, os tratamentos foram administrados aos grupos, a laparotomia exploratória foi realizada e os cavalos não receberam alimentos ou água além daqueles dados aos seus respectivos grupos. Na Fase 2, os animais foram realimentados. Cada fase teve uma duração total de 144 h. Amostras de sangue venoso foram coletadas a cada 24 h durante todo o período experimental para análises gasométricas e eletrolíticas. Foram avaliados os seguintes parâmetros: pH, pressão parcial de dióxido de carbono, dióxido de carbono total, bicarbonato, desvio de base, anion gap, sódio, potássio, cloreto, cálcio total e magnésio. Delineamentos inteiramente casualizados com esquema fatorial 4 × 7 (grupos × época de colheita) na Fase 1 e esquema fatorial 4 × 6 (grupos × época de colheita) na Fase 2 foram utilizados com quatro repetições. Todos os valores foram considerados significativos quando p≤0,05 (95% de probabilidade). O pH sanguíneo, a concentração de bicarbonato e o desvio de base no grupo PARGL diminuíram, indicando acidose metabólica. As alterações no equilíbrio ácido-base e eletrolítico foram mais intensas no grupo PARGL do que nos outros grupos. Esses resultados demonstraram a necessidade de monitorar o equilíbrio hemogasométrico e eletrolítico em equinos com restrição alimentar sob suporte nutricional ou fluidoterapia prolongada para que tais alterações sejam prontamente corrigidas.

Palavras-chave: equino, desequilíbrios eletrolíticos, fluidoterapia, acidose metabólica, nutrição parenteral.

Introduction

Decreased appetite and/or inability to eat commonly occur under different conditions, resulting in malnutrition, compromised immune function, and impaired tissue repair (Bailey et al., 2016; Carr, 2018; Di Filippo et al., 2021; Hospes & Bleul, 2007; Melo et al., 2008).

Nutritional support, enteral or parenteral, is a therapeutic resource that helps patients recover from and avoid the risk of malnutrition; It has gained importance for reducing hospitalization time, optimizing response to clinical-surgical treatments, promoting tissue repair, and improving immune function (Bæk et al., 2020; Lawson et al., 2021).

Nutritional support should be considered for horses with increased metabolic rates, such as growing animals, individual horses with a history of malnutrition or hypophagia, patients with metabolic disorders, and those with diseases that result in an increased metabolic rate (Carr, 2018).

The use of parenteral nutrition in horses has been rarely studied although it has been described mainly in conference proceedings, individual case reports, retrospective studies, and review articles. It can be beneficial in ensuring adequate nutrient supply, particularly during critical illness or recovery from surgical procedures. However, many veterinarians reluctantly implement it because of not only the complexities of formulation, administration, and clinical monitoring but also the potential complications and expenses experienced by clients (McKenzie, 2015).

Therefore, this study aimed to evaluate the effects of total parenteral nutrition (TPN) associated with glutamine, enteral fluid therapy with or without glutamine, and fluid therapy on the acid-base and electrolyte balance of horses starved after exploratory laparotomy.

Materials and methods

Sixteen healthy male and female adult horses of mixed breed, aged between 4 and 14 years, with a mean body weight of 248.40 ± 2.28 kg and a body score index of 3 to 4, scale of 1–5 (Carroll & Huntington, 1988), were divided into four groups, and four horses were included in each group.

The horses that received endo-and ectoparasiticide were housed in paddocks and fed daily with commercial feed (1 kg/100 kg BW), Tifton hay (1 kg/100 kg BW), chopped elephant grass (*Pennisetum purpureum*), water, and mineral salt ad libitum. After an adaptation period of 30 days, they were randomly divided into four experimental groups (ENTFL, ENTGL, PARGL, and PARFL groups) in accordance with previously described methods (Melo et al., 2021).

For the ENTFL group, horses were administered electrolyte-infused enteral fluid therapy (5.7 g NaCl; 3.78 g $NaHCO_3$, 0.37 g KCl, and 10 g glucose/liter of water). For the ENTGL group, the horses were given enteral fluid therapy with electrolytes (5.7 g NaCl, 3.78 g $NaHCO_3$, 0.37 g KCl, and 10 g glucose/liter of water) associated with glutamine (L-glutamine, Ajinomoto do Brasil Indústria e Comércio de Alimentos Ltda, Laranjal Paulista/SP, Brazil).

A maintenance rate of 60 mL/kg was established to calculate the total volume of fluid to be administered to the ENTF and ENTGL groups over a 24-hour period (Dias et al., 2019; Melo et al., 2010). The total calculated volume of fluid was divided by 12 and administered by gravity flow every 2 h using an 11 mm × 16 mm nasogastric tube. Glutamine (ENTGL) was administered at a

dose of 0.5 g/kg body weight. The calculated total amount of glutamine was divided by 12 and administered in a diluted form in enteral fluid therapy every 2 h. The volume of fluid administered (ENTFL and ENTGL groups) and the amount of glutamine (ENTGL group) were adjusted daily according to the weight of the animal.

For the PARGL group, the horses received TPN associated with glutamine. TPN was prepared from equal amounts of solutions of amino acids (10% Aminoven, Fresenius Kabi, Barueri/SP, Brazil), lipids (20% Lipovenos, Fresenius Kabi), and 50% glucose (Fresenius Kabi). The proportions were 33.33% amino acids, 33.33% lipids, and 33.33% of 50% glucose to meet the energy requirements for daily maintenance. Glutamine was intravenously administered as a 1.5% sterile solution (15 g/L) at a dose of 0.5 g/kg of weight.

The total amount of TPN and the amount of glutamine to be administered were adjusted daily according to the animal's body weight. Both solutions were administered as continuous infusions via venous access into the right external jugular vein. The rate of administration (mL/h) was calculated by dividing the total infused volume by 24. The appropriate amount of intravenous fluid therapy with lactated Ringer's solution was administered to complete the daily maintenance requirement.

For the PARFL group, the horses were administered with parenteral fluid therapy. The volume of the fluid administered was 60 mL/kg BW. Half of it was supplied using lactated Ringer's solution, and the other half was provided via a 0.9% sodium chloride saline solution. Then, 50% glucose was provided in a diluted form in a saline solution at a dose of 1.5 g/kg BW. Both solutions were administered as continuous infusions via venous access into the right external jugular vein.

Venous access for the infusion of TPN (PARGL group) and parenteral fluid therapy (PARFL group) was obtained using a double lumen catheter (Duocath – 12F, Intra Special Catheters, Germany) with a coaxial size of 12 gauge and a length of 20 cm.

This study was divided into two phases: Phase 1 and Phase 2. In Phase 1, treatments were administered depending on the groups, exploratory laparotomy was performed, and the horses were given no food or water other than those described in their groups. In Phase 2, the horses were re-fed. On the first 2 days of Phase 1, TPN administered to the PARGL group provided only 50% and 75% of the maintenance energy needs, respectively. On the third day to the end of Phase 1, TPN provided 100% of these needs. In Phase 2, the horses in the groups were re-fed with Tifton hay, commercial concentrate, and water. Feeding was gradually reintroduced. On the first day, 4 kg of Tifton hay was fed, divided into two 2 kg meals given 12 h apart, and added with 0.5 kg of concentrate. On the second day, the amount of hay was increased to 8 kg and provided in two meals of 4 kg each plus 1 kg of commercial concentrate. From the third day, the amount of food provided was the same as during the adaptation period. Each phase had a total duration of 144 h.

The animals underwent two flank laparotomies to simulate surgical stress and obtain intestinal samples used in a parallel study: one at the beginning and the other at the end of the first phase in accordance with a previously described protocol (Ferreira et al., 2022). Each laparotomy lasted an average of 60 min.

Venous blood samples were collected for blood gas analysis every 24 h during the experimental period (total of 13 samples). For this purpose, 1 mL of whole blood without bubbles and without an anticoagulant was collected from the left external jugular vein through a 3 mL syringe and analyzed immediately after collection.

Blood gas analysis was performed using portable automatic equipment (I-Stat system, Abott Laboratories, Brazil) with specific cartridges (I-Stat cartridge EC8+, Abbott Laboratories, Brazil). The following parameters were evaluated: pH, partial pressure of carbon dioxide (PCO_2), total carbon dioxide (TCO_2), bicarbonate (HCO_3^-), base shift, anion gap, sodium, potassium, and chloride.

Blood samples were obtained through a venipuncture in the external jugular vein and placed in a vacuum tube without an anticoagulant for measuring the concentration of total calcium (Ca^{2+}) and magnesium (Mg^{2+}). After clot retraction, blood was centrifuged at 3,000 rpm for 5 min, and serum was separated into 0.5 mL aliquots and frozen at –20 °C until analysis. Measurements were performed in a semi-automatic biochemical device (BA-88A biochemical analyzer, Química Básica Ltda, Belo Horizonte/MG, Brazil) by using specific kits (colorimetric kit for calcium and magnesium dosage, Química Básica Ltda, Belo Horizonte/MG, Brazil).

The experimental design was completely randomized with a 4 × 7 factorial scheme (groups × harvest time) in Phase 1 and a 4 × 6 factorial scheme (groups × harvest time) in Phase 2 with four replications. Data were tabulated in an Excel® spreadsheet, and their averages were compared using Duncan's test. All values were considered significant when $p \leq 0.05$ (95% probability). Data were statistically analyzed using SAS software (1997).

Results

The serum sodium concentration did not show significant group × time interaction ($p > 0.05$) and difference ($p > 0.05$) between the total number of groups in both phases and the total number of times in phase 2. However, a significant difference was observed ($p < 0.05$) in the total number of times in Phase 1 (Table 1). In the PARGL group, hyponatremia was observed between T_3 and T_5 and from T_{10} until the end of the experimental period.

Chloride ions did not exhibit a significant interaction between the groups × times ($p > 0.05$) and differences ($p > 0.05$) between the total number of groups and the total number of times in both experimental phases (Table 2). Although the chloride value decreased in the ENTGL, PARFL, and PARGL groups, this decrease did not cause differences between the groups possibly because of the low number of animals used in each group.

Potassium concentration had no significant interaction between groups × times ($p > 0.05$); however, the total times in both phases and the total number of groups in Phase 1 differed significantly ($p < 0.05$; Table 3). The results demonstrated that serum potassium values had a more pronounced decrease in the PARGL group compared to those of the other groups in Phase 1 although the mean values remained within the reference limits for the species. In Phase 2, the potassium concentration increased.

Table 1. Mean + standard error of serum sodium concentration (mEq/L) of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	136.25 + 1.43	135.25 + 0.94	138.25 + 0.85	137.50 + 1.04	136.81 + 0.57[a]
T_2	133.00 + 0.81	134.50 + 1.25	134.00 + 0.91	135.00 + 1.08	134.12 + 0.49[b]
T_3	132.75 + 1.25	133.50 + 1.75	134.50 + 1.84	131.75 + 1.65	133.12 + 0.77[b]
T_4	133.00 + 0.81	132.25 + 2.32	134.50 + 2.66	131.75 + 2.68	132.87 + 1.04[b]
T_5	133.25 + 1.54	133.50 + 2.12	132.75 + 2.56	130.25 + 1.79	132.43 + 0.98[b]
T_6	132.25 + 0.62	131.00 + 1.68	134.00 + 2.16	132.25 + 1.93	132.37 + 0.81[b]
T_7	133.25 + 0.75	132.66 + 1.45	133.50 + 2.53	133.75 + 0.47	133.33 + 0.69[b]
Total	133.39 + 0.43	133.25 + 0.63	134.50 + 0.75	133.17 + 0.70	
Phase 2 - Refeeding					
T_8	133.00 + 2.04	131.33 + 1.20	131.75 + 1.54	132.25 + 0.62	132.13 + 0.68
T_9	134.25 + 2.78	133.66 + 1.20	133.25 + 2.56	133.00 + 2.04	133.53 + 1.05
T_{10}	133.00 + 2.41	134.00 + 1.15	134.50 + 1.65	131.66 + 2.40	133.35 + 0.94
T_{11}	130.00 + 3.39	132.33 + 1.66	133.75 + 1.70	129.66 + 4.84	131.50 + 1.42
T_{12}	131.75 + 4.73	133.66 + 2.60	133.00 + 1.68	131.33 + 4.17	132.42 + 1.58
T_{13}	135.66 + 1.33	134.00 + 1.52	132.25 + 1.93	131.33 + 3.17	133.23 + 1.02
Total	132.82 + 1.17	133.16 + 0.61	133.08 + 0.70	131.65 + 1.04	

Reference value: 132.00 – 146.00 mEq/L. Source: Carlson (2006). Averages followed by different lowercase letters in the column differ ($p<0.05$ – Duncan's test).

Table 2. Mean + standard error of serum chloride concentration (mEq/L) of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	100.50 + 1.44	100.50 + 1.04	102.25 + 0.85	100.75 + 2.05	101.00 + 0.66
T_2	99.50 + 1.44	101.00 + 1.63	101.50 + 0.95	100.00 + 1.77	100.50 + 0.69
T_3	100.75 + 0.85	98.75 + 1.31	100.75 + 2.65	99.75 + 2.01	100.00 + 0.85
T_4	100.50 + 0.28	97.00 + 1.73	98.50 + 2.78	96.75 + 2.28	98.18 + 0.97
T_5	99.50 + 1.55	96.50 + 2.10	97.50 + 3.01	99.00 + 4.14	98.12 + 1.32
T_6	99.50 + 1.84	93.00 + 3.24	98.25 + 2.17	99.00 + 2.48	97.43 + 1.30
T_7	99.75 + 2.09	96.33 + 1.85	98.75 + 2.65	100.50 + 0.95	99.00 + 0.98
Total	100.00 + 0.50	97.62 + 0.82	99.64 + 0.83	99.39 + 0.84	
Phase 2 - Refeeding					
T_8	98.75 + 2.89	98.33 + 2.18	97.00 + 2.67	102.00 + 2.04	99.06 + 1.23
T_9	101.50 + 3.86	101.00 + 2.64	97.25 + 2.68	100.50 + 2.17	100.00 + 1.39
T_{10}	98.50 + 2.78	100.66 + 2.02	98.25 + 1.88	98.00 + 2.64	98.78 + 1.09
T_{11}	97.50 + 3.92	100.33 + 2.72	98.25 + 2.05	96.66 + 3.84	98.14 + 1.46
T_{12}	99.50 + 4.85	101.00 + 1.73	99.00 + 1.68	97.33 + 4.70	99.21 + 1.63
T_{13}	104.66 + 1.33	98.00 + 2.51	97.25 + 2.65	96.00 + 4.00	98.84 + 1.53
Total	99.86 + 1.38	99.88 + 0.85	97.83 + 0.84	98.70 + 1.21	

Reference value: 99.00 – 109.00 mEq/L. Source: Carlson (2006).

Table 3. Mean + standard error of serum potassium concentration (mg/dL) of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	3.90 + 0.04	3.85 + 0.21	3.95 + 0.22	3.65 + 0.16	3.83 + 0.08^{a}
T_2	3.65 + 0.15	3.70 + 0.19	3.80 + 0.26	3.47 + 0.12	3.65 + 0.09^{a}
T_3	3.52 + 0.14	3.35 + 0.19	3.30 + 0.17	3.22 + 0.17	3.35 + 0.08^{b}
T_4	3.35 + 0.06	3.22 + 0.16	3.17 + 0.11	2.67 + 0.06	3.10 + 0.08^{b}
T_5	3.37 + 0.14	3.00 + 0.30	3.27 + 0.13	2.90 + 0.17	3.13 + 0.10^{b}
T_6	3.57 + 0.25	2.92 + 0.31	3.22 + 0.11	2.85 + 0.21	3.14 + 0.12^{b}
T_7	3.45 + 0.32	3.26 + 0.12	3.27 + 0.09	2.82 + 0.23	3.20 + 0.11^{b}
Total	3.54 + 0.07^{A}	3.33 + 0.09^{B}	3.42 + 0.07^{AB}	3.08 + 0.08^{C}	
Phase 2 - Refeeding					
T_8	3.32 + 0.23	3.56 + 0.52	3.55 + 0.18	3.10 + 0.16	3.37 + 0.13^{b}
T_9	3.60 + 0.18	3.70 + 0.40	3.47 + 0.14	3.55 + 0.23	3.57 + 0.10^{ab}
T_{10}	3.87 + 0.12	3.83 + 0.38	3.50 + 0.26	3.70 + 0.10	3.72 + 0.11^{ab}
T_{11}	3.95 + 0.32	3.66 + 0.12	3.87 + 0.24	3.73 + 0.18	3.82 + 0.11^{ab}
T_{12}	4.02 + 0.18	4.03 + 0.16	3.72 + 0.15	3.73 + 0.13	3.87 + 0.08^{a}
T_{13}	4.00 + 0.00	3.46 + 0.17	4.00 + 0.05	3.06 + 0.37	3.66 + 0.13^{ab}
Total	3.78 + 0.09	3.71 + 0.12	3.68 + 0.08	3.46 + 0.10	

Reference value: 2.4 – 4.7 mEq/L. Source: Carlson (2006). Averages followed by different uppercase letters in the row and lowercase letters in the column differ ($p < 0.05$ – Duncan's test).

Magnesium concentration did not have significant interactions between groups × times and differences ($p > 0.05$) between total times and total number of groups in both phases (Table 4). Although this concentration decreased, it did not cause differences between the times throughout the experimental period.

The total calcium concentration (Table 5) showed no significant interaction between groups × times ($p > 0.05$) and differences ($p > 0.05$) between the total times in both phases and the total number of groups in Phase 2. However, it had a significant difference ($p < 0.05$) in the total number of groups in Phase 1.

Blood pH did not have a significant interaction between the time groups × time ($p > 0.05$) and any difference between the total number of times and the groups in Phase 2. In Phase 1, the total number of groups and the total number of times significantly differed ($p < 0.05$; Table 6). pH decreased in all groups up to T_3, and this decrease was more pronounced in the PARGL group than in the other groups. This decrease was followed by a slight increase in all groups except the PARGL group. In Phase 2, the responses of the groups varied considerably over time.

PCO_2 showed no significant interaction between groups × times ($p > 0.05$) and no differences between the total number of groups in Phase 2 and the total number of times in both phases. However, there was a significant difference ($p<0.05$) in the total number of groups in Phase 1 (Table 7). Values close to or above the reference limits for the species were observed in the ENTGL and PARFL groups between T3 and T7, with concentrations returning to the reference values after the end of Phase 1.

The concentration of TCO_2 did not show significant interaction between groups × times ($p>0.05$) in both phases and difference between the total number of groups and the total number of times in Phase 2. The total number of groups and the total number of times significantly differed in Phase 1 ($p < 0.05$; Table 8). Despite these differences, the values remained within the reference limits for the species throughout the experimental period.

Table 4. Mean + standard error of serum magnesium concentration (mg/dL) of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Tempos	Grupos experimentais				Total
	ENTFL	ENTGL	PARFL	PARGL	
			Fase 1 - Inanição		
T_1	2.10 + 0.15	2.62 + 0.12	2.17 + 0.17	2.37 + 0.22	2.31 + 0.09
T_2	2.00 + 0.15	2.30 + 0.38	1.75 + 0.19	2.05 + 0.24	2.02 + 0.12
T_3	1.95 + 0.20	2.37 + 0.47	2.05 + 0.25	1.72 + 0.15	2.02 + 0.14
T_4	1.92 + 0.30	1.95 + 0.29	2.00 + 0.27	2.00 + 0.25	1.96 + 0.12
T_5	5.07 + 3.4	1.92 + 0.27	1.85 + 0.30	1.87 + 0.31	2.68 + 0.94
T_6	2.25 + 0.27	2.02 + 0.28	1.85 + 0.35	1.72 + 0.17	1.95 + 0.13
T_7	1.75 + 0.32	2.26 + 0.33	2.00 + 0.07	1.65 + 0.24	1.89 + 0.12
Total	2.43 + 0.48	2.20 + 0.11	1.94 + 0.08	1.91 + 0.09	
			Fase 2 - Realimentação		
T_8	2.10 + 0.24	6.36 + 3.83	1.97 + 0.23	2.35 + 0.37	2.98 + 0.80
T_9	2.30 + 0.33	2.00 + 0.20	2.00 + 0.27	2.72 + 0.41	2.27 + 0.16
T_{10}	2.35 + 0.29	2.36 + 0.28	1.90 + 0.27	6.90 + 5.23	3.20 + 1.09
T_{11}	2.42 + 0.26	2.13 + 0.35	2.15 + 0.27	2.93 + 0.69	2.39 + 0.19
T_{12}	2.40 + 0.18	2.26 + 0.41	1.85 + 0.16	2.73 + 0.57	2.28 + 0.16
T_{13}	2.26 + 0.21	1.93 + 0.38	2.32 + 0.18	2.30 + 0.62	2.21 + 0.16
Total	2.30 + 0.09	2.84 + 0.66	2.03 + 0.09	3.24 + 0.76	

Reference value: 2.2 – 2.8 mg/dL. Source: Carlson (2006).

Table 5. Mean + standard error of serum total calcium concentration (mg/dL) of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	7.12 + 0.25	7.37 + 0.75	8.87 + 1.36	8.17 + 0.51	7.88 + 0.41
T_2	7.70 + 0.24	8.15 + 0.22	9.07 + 1.07	7.92 + 0.30	8.21 + 0.29
T_3	7.80 + 0.18	8.20 + 0.14	8.55 + 0.48	7.97 + 0.40	8.13 + 0.16
T_4	7.72 + 0.12	7.65 + 0.57	8.50 + 0.89	7.40 + 0.30	7.81 + 0.27
T_5	7.80 + 0.12	7.80 + 0.72	9.37 + 1.44	7.77 + 0.43	8.18 + 0.41
T_6	7.32 + 0.31	7.90 + 0.42	9.00 + 1.26	7.60 + 0.30	7.95 + 0.35
T_7	7.90 + 0.12	8.10 + 0.43	8.92 + 1.50	6.77 + 0.08	7.91 + 0.42
Total	7.62 + 0.08^B	7.87 + 0.18^B	8.90 + 0.40^A	7.66 + 0.14^B	
Phase 2 - Refeeding					
T_8	7.37 + 0.33	7.66 + 0.49	9.52 + 1.34	6.92 + 0.34	7.88 + 0.44
T_9	7.80 + 0.25	7.63 + 0.48	8.47 + 1.46	7.65 + 0.53	7.90 + 0.39
T_{10}	7.80 + 0.45	7.40 + 0.20	8.22 + 1.19	10.13 + 2.54	8.33 + 0.62
T_{11}	7.62 + 0.44	8.26 + 0.17	8.12 + 1.04	7.56 + 0.46	7.89 + 0.31
T_{12}	7.65 + 0.61	7.83 + 0.55	7.77 + 0.99	7.20 + 0.15	7.62 + 0.32
T_{13}	7.43 + 0.18	8.10 + 0.32	8.05 + 0.98	7.50 + 0.61	7.79 + 0.31
Total	7.62 + 0.15	7.81 + 0.15	8.36 + 0.44	7.77 + 0.42	

Reference value: 9.6 – 13.6 mg/dL. Source: Carlson (2006). Means followed by different capital letters on the line differ ($p < 0.05$ – Duncan's test).

Table 6. Mean + standard error of blood pH of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	7.45 + 0.00	7.45 + 0.00	7.43 + 0.01	7.45 + 0.00	7.45 + 0.00^a
T_2	7.45 + 0.02	7.42 + 0.02	7.41 + 0.00	7.46 + 0.00	7.43 + 0.00^{ab}
T_3	7.41 + 0.02	7.40 + 0.02	7.39 + 0.00	7.38 + 0.02	7.40 + 0.01^c
T_4	7.45 + 0.00	7.41 + 0.02	7.40 + 0.02	7.42 + 0.03	7.42 + 0.01^{abc}
T_5	7.46 + 0.00	7.42 + 0.01	7.40 + 0.02	7.40 + 0.00	7.42 + 0.00^{abc}
T_6	7.46 + 0.01	7.44 + 0.01	7.41 + 0.02	7.41 + 0.01	7.43 + 0.00^{ab}
T_7	7.44 + 0.03	7.45 + 0.00	7.40 + 0.02	7.37 + 0.01	7.41 + 0.01^{bc}
Total	7.44 + 0.00^A	7.42 + 0.00^{AB}	7.41 + 0.00^B	7.42 + 0.00^B	
Phase 2 - Refeeding					
T_8	7.45 + 0.03	7.49 + 0.04	7.45 + 0.00	7.37 + 0.03	7.44 + 0.01
T_9	7.44 + 0.03	7.41 + 0.02	7.43 + 0.01	7.43 + 0.02	7.43 + 0.01
T_{10}	7.43 + 0.00	7.46 + 0.01	7.43 + 0.00	7.45 + 0.01	7.44 + 0.00
T_{11}	7.43 + 0.00	7.49 + 0.05	7.46 + 0.01	7.47 + 0.04	7.46 + 0.01
T_{12}	7.44 + 0.00	7.43 + 0.00	7.47 + 0.02	7.43 + 0.02	7.44 + 0.00
T_{13}	7.44 + 0.00	7.42 + 0.00	7.48 + 0.02	7.43 + 0.01	7.44 + 0.01
Total	7.44 + 0.00	7.45 + 0.01	7.45 + 0.00	7.43 + 0.01	

Reference value: 7.32 – 7.45. Source: Carlson (2006). The mean followed by different uppercase letters in the row and lowercase letters in the column differ ($p < 0.05$ – Duncan's test).

Table 7. Mean + standard error of the partial pressure of CO_2 (mEq/L) of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	44.72 + 1.53	44.92 + 1.10	45.75 + 2.50	45.50 + 1.91	45.22 + 0.82
T_2	42.42 + 2.33	44.62 + 2.61	43.82 + 1.28	40.57 + 1.28	42.86 + 0.96
T_3	44.35 + 2.60	46.45 + 4.37	45.57 + 2.83	43.97 + 1.88	45.08 + 1.39
T_4	42.13 + 1.06	45.70 + 4.38	47.50 + 2.95	42.83 + 1.27	44.83 + 1.51
T_5	43.96 + 1.93	47.30 + 5.06	46.95 + 2.56	42.63 + 0.14	45.48 + 1.59
T_6	41.93 + 0.67	47.42 + 4.23	48.30 + 4.22	39.46 + 1.68	44.79 + 1.86
T_7	44.06 + 1.91	45.16 + 1.24	48.12 + 3.79	42.06 + 2.17	45.10 + 1.38
Total	43.42 + 0.68^{AB}	45.97 + 1.26^{AB}	46.57 + 1.04^{A}	42.55 + 0.67^{B}	
Phase 2 - Refeeding					
T_8	44.56 + 2.62	40.46 + 4.07	45.20 + 3.28	42.40 + 3.00	43.31 + 1.54
T_9	44.53 + 1.92	45.83 + 2.73	46.67 + 4.71	42.36 + 1.51	44.99 + 1.56
T_{10}	44.03 + 1.21	39.70 + 1.41	47.60 + 3.17	40.10 + 1.77	42.85 + 1.30
T_{11}	41.90 + 0.41	40.46 + 1.18	44.56 + 3.12	39.83 + 3.82	41.69 + 1.21
T_{12}	41.83 + 0.49	40.50 + 2.45	44.03 + 1.76	41.46 + 2.40	41.95 + 0.91
T_{13}	42.20 + 0.60	46.10 + 2.90	43.13 + 2.62	41.96 + 2.37	43.45 + 1.19
Total	43.23 + 0.61	42.17 + 1.11	45.27 + 1.27	41.35 + 0.92	

Reference value: 38.00 – 46.00 mEq/L. Source: Carlson (2006). The averages followed by different capital letters on the line differ ($p<0.05$ – Duncan's test).

Table 8. Mean + standard error of total CO2 (mEq/L) of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	33.00 + 1.22	32.50 + 1.04	32.00 + 1.22	33.50 + 1.19	32.75 + 0.54^{a}
T_2	31.00 + 0.91	30.20 + 0.89	29.50 + 1.19	30.50 + 1.44	30.30 + 0.52^{bc}
T_3	28.87 + 0.82	30.25 + 0.94	29.27 + 1.02	26.90 + 0.98	28.82 + 0.52^{c}
T_4	30.33 + 0.88	30.75 + 1.93	31.25 + 1.93	30.00 + 2.08	30.64 + 0.82^{bc}
T_5	32.66 + 1.85	32.50 + 2.32	30.77 + 1.47	28.00 + 0.00	31.07 + 0.92^{ab}
T_6	31.00 + 0.57	33.50 + 2.10	32.25 + 1.25	26.00 + 1.00	31.00 + 1.01^{abc}
T_7	31.33 + 1.33	32.66 + 1.33	31.25 + 0.85	26.00 + 1.00	30.38 + 0.85^{bc}
Total	31.14 + 0.46^{A}	31.73 + 0.59^{A}	30.90 + 0.48^{A}	28.90 + 0.68^{B}	
Phase 2 - Refeeding					
T_8	30.75 + 2.89	32.33 + 1.20	33.00 + 2.04	28.66 + 4.17	31.61 + 1.15
T_9	32.00 + 1.15	30.66 + 0.33	32.12 + 3.59	30.00 + 1.73	31.26 + 1.11
T_{10}	30.66 + 0.88	29.33 + 0.33	33.36 + 2.60	30.00 + 2.08	30.84 + 0.87
T_{11}	29.33 + 0.33	32.33 + 2.96	33.43 + 3.17	30.33 + 2.33	31.35 + 1.16
T_{12}	29.33 + 0.66	28.00 + 2.08	33.66 + 2.02	29.00 + 2.88	30.00 + 1.10
T_{13}	30.00 + 0.00	31.00 + 2.00	33.66 + 2.72	29.50 + 2.56	31.13 + 1.12
Total	30.58 + 0.41	30.61 + 0.71	33.14 + 1.00	29.58 + 0.95	

Reference value: 24.00 – 32.00 mEq/L. Source: Carlson (2006). Averages followed by different uppercase letters in the row and lowercase letters in the column differ ($p<0.05$ – Duncan's test).

HCO_3^- exhibited no interaction between time and group in both phases ($p > 0.05$) and had no difference between the total times in Phase 2. However, the total number of times in Phase 1 and the total number of groups in both experimental phases differed significantly ($p < 0.05$; Table 9).

The baseline deviation did not show a significant interaction between the group and time ($p>0.05$). It also showed no significant differences between the total number of groups and the total times in Phase 2. However, the total number of groups and the total number of times in Phase 1 significantly differed ($p < 0.05$; Table 10).

The anions gap did not have a significant interaction between time and group ($p>0.05$) and no significant difference ($p > 0.05$) between the total number of groups and the total times of the phases in both phases (Table 11). Although the groups and times did not differ, anion gap varied between the groups. Anion gap increased in the PARGL group and suddenly decreased after the horses were re-fed. The other groups also showed a numerical decrease in anion gap values after the start of re-feeding, with lower mean values observed at T_8 in the ENTFL group and at T_9 in the other groups. This numerical decrease was followed by an increase in the mean values of all groups until T_{10}.

Table 9. Mean + standard error of bicarbonate concentration (mEq/L) of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	31.50 + 1.10	31.35 + 1.00	30.77 + 1.24	32.30 + 1.16	31.48 + 0.52[a]
T_2	29.47 + 0.83	28.97 + 0.90	27.97 + 1.05	29.47 + 1.49	28.97 + 0.51[b]
T_3	28.35 + 0.25	28.82 + 0.77	28.02 + 1.04	26.30 + 0.50	27.87 + 0.40[b]
T_4	28.93 + 0.88	29.35 + 1.89	29.92 + 1.71	28.70 + 2.04	29.28 + 0.78[b]
T_5	31.33 + 1.66	30.67 + 2.16	29.42 + 1.31	26.93 + 0.17	29.65 + 0.84[b]
T_6	29.33 + 0.72	32.20 + 1.95	30.87 + 1.24	24.76 + 0.83	29.61 + 0.98[b]
T_7	29.93 + 1.48	31.46 + 1.19	29.95 + 0.90	24.90 + 1.05	29.13 + 0.85[b]
Total	29.82 + 0.40[A]	30.36 + 0.56[A]	29.56 + 0.46[A]	27.84 + 0.66[B]	
Phase 2 - Refeeding					
T_8	30.13 + 1.19	31.00 + 1.16	31.55 + 1.82	23.83 + 1.05	29.31 + 1.08
T_9	31.80 + 0.75	29.16 + 0.43	31.22 + 3.19	26.73 + 0.84	29.84 + 1.07
T_{10}	30.03 + 1.55	28.23 + 0.28	31.73 + 2.43	28.50 + 1.96	29.62 + 0.85
T_{11}	28.13 + 0.52	31.10 + 2.99	31.70 + 2.95	29.13 + 2.18	30.01 + 1.10
T_{12}	28.53 + 0.33	27.36 + 1.95	32.20 + 2.08	27.96 + 2.71	29.01 + 1.01
T_{13}	28.70 + 0.30	30.13 + 1.61	32.43 + 2.64	28.23 + 2.21	29.98 + 1.03
Total	29.60 + 0.45[A]	29.50 + 0.66[A]	31.76 + 0.92[A]	27.40 + 0.79[B]	

Reference value: 20.00 – 28.00 mEq/L. Source: Carlson (2006). The averages followed by different uppercase letters in the row and lowercase letters in the column differ from each other ($p < 0.05$ – Duncan's test).

Discussion

Blood gas analysis and electrolyte measurement are important laboratory tests for characterizing and evaluating the intensity of hydroelectrolyte and acid-base imbalances in different clinical situations; they also enable veterinarians to institute appropriate therapeutic interventions (Ribeiro Filho et al., 2007) or monitor a patient's response to established therapies.

This study showed that hyponatremia developed in the PARGL group in both phases. Hyponatremia is usually associated with cases involving intense sodium loss, such as enterogastric

Table 10. Mean + standard error of base deviation of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	7.75 + 1.03	7.50 + 1.04	6.75 + 1.37	8.50 + 1.19	7.62 + 0.54^{a}
T_2	5.50 + 0.86	4.50 + 1.19	3.50 + 1.25	5.75 + 1.70	4.81 + 0.62^{bc}
T_3	3.97 + 0.83	4.00 + 0.40	3.50 + 1.25	1.20 + 0.77	3.16 + 0.49^{c}
T_4	4.66 + 1.20	4.75 + 1.97	5.00 + 1.95	5.33 + 1.85	4.92 + 0.82^{bc}
T_5	7.33 + 1.66	6.25 + 2.09	4.75 + 1.43	2.33 + 0.33	5.21 + 0.87^{b}
T_6	5.66 + 0.88	8.25 + 1.88	7.50 + 0.86	1.66 + 2.33	6.07 + 0.98^{ab}
T_7	5.66 + 1.76	7.00 + 1.00	5.25 + 0.75	- 0.66 + 1.20	4.38 + 0.96^{bc}
Total	5.78 + 0.46^{A}	6.00 + 0.58^{A}	5.17 + 0.51^{A}	3.65 + 0.78^{B}	
Phase 2 - Refeeding					
T_8	6.66 + 2.02	7.66 + 1.45	7.75 + 1.79	- 1.83 + 1.45	5.38 + 1.30
T_9	6.66 + 1.76	4.66 + 0.66	7.00 + 3.26	4.66 + 2.02	5.84 + 1.10
T_{10}	5.33 + 1.20	4.33 + 0.33	7.33 + 2.60	5.00 + 2.08	5.50 + 0.83
T_{11}	4.66 + 0.33	8.00 + 3.60	8.33 + 3.17	5.66 + 2.40	6.66 + 1.23
T_{12}	5.00 + 0.57	3.33 + 2.02	8.33 + 2.33	3.66 + 3.17	5.08 + 1.12
T_{13}	5.50 + 0.50	5.66 + 1.33	9.00 + 2.64	4.00 + 2.64	6.09 + 1.10
Total	5.64 + 0.49^{A}	5.61 + 0.77^{A}	7.90 + 0.96^{A}	3.61 + 0.98^{B}	

Reference value: - 2.00 – 4.00 mEq/L. Source: Carlson (2006). The mean followed by different uppercase letters in the row and lowercase letters in the column differ ($p < 0.05$ – Duncan's test).

Table 11. Mean + standard error of the anion gap (mEq/L) of horses under total parenteral nutrition associated with glutamine (PARGL), enteral fluid therapy with (ENTGL) or without glutamine (ENTFL), and fluid therapy (PARF) submitted to starvation after exploratory laparotomy.

Times	Experimental Groups				Total
	ENTFL	ENTGL	PARFL	PARGL	
Phase 1 - Starvation					
T_1	8.00 + 0.40	7.00 + 2.00	9.00 + 0.91	7.80 + 0.52	7.95 + 0.54
T_2	7.75 + 0.47	8.25 + 0.75	8.00 + 1.47	8.75 + 1.25	8.18 + 0.48
T_3	6.75 + 0.94	9.25 + 0.47	8.50 + 0.64	8.66 + 0.66	8.18 + 0.38
T_4	7.33 + 0.33	9.25 + 1.37	9.00 + 0.70	8.66 + 0.66	8.64 + 0.46
T_5	7.00 + 0.57	9.25 + 1.03	9.00 + 0.91	9.33 + 0.33	8.71 + 0.50
T_6	7.66 + 0.88	9.00 + 0.91	7.97 + 1.06	11.00 + 1.00	8.85 + 0.55
T_7	7.00 + 1.15	7.66 + 1.20	8.25 + 0.62	11.00 + 1.00	8.46 + 0.59
Total	7.37 + 0.25	8.55 + 0.43	8.53 + 0.32	9.13 + 0.39	
Phase 2 - Refeeding					
T_8	7.00 + 1.00	5.00 + 2.08	7.25 + 1.10	8.33 + 2.33	8.75 + 0.50
T_9	6.00 + 0.57	7.33 + 0.88	6.00 + 2.08	6.66 + 1.76	6.91 + 1.04
T_{10}	7.66 + 0.66	9.00 + 1.00	8.66 + 0.66	9.66 + 1.66	7.66 + 0.94
T_{11}	7.00 + 1.00	8.66 + 1.20	8.33 + 1.76	7.66 + 1.20	8.36 + 0.80
T_{12}	7.33 + 1.20	8.33 + 0.33	5.33 + 1.76	9.33 + 2.96	6.92 + 0.78
T_{13}	7.50 + 1.50	8.25 + 0.75	6.33 + 0.88	11.00 + 2.08	6.92 + 0.72
Total	7.05 + 0.35	7.16 + 0.78	7.25 + 0.59	8.77 + 0.79	

Reference value: 6.00 – 15.00 mEq/L. Source: Carlson (2006).

reflux, diarrhea, profuse sweating, and adrenal insufficiency (Carlson, 2006); however, none of these etiological factors were identified in the present study. Hyponatremia manifested in the PARGL group likely because of the supply of lower amounts of sodium than that in the other groups. In the PARGL group, water was provided mainly by an electrolyte-free glutamine solution and TPN, and the remaining maintenance requirement was provided by a lactated Ringer's solution. Therefore, providing large amounts of free water would cause a decrease in serum electrolyte levels. However, studies in humans have shown that the total amount of sodium and fluids administered during TPN does not influence the onset of hyponatremia because the kidneys in physiological situations can eliminate excess water and thus maintain homeostasis (Gómez-Hoyos et al., 2019).

Na^+ is also reduced probably because of the occurrence of false hyponatremia resulting from an increase in triglyceride, total protein, and glucose values in the PARGL group (unpublished data). Hypertriglyceridemia and/or intense hyperproteinemia produce a falsely low Na^+ because lipids or proteins occupy a significantly higher volume in blood samples and because Na^+ is present only in the aqueous phase. Severe hyperglycemia causes a reduction in the measured serum Na^+ concentration of approximately 1.6 mEq/L for every 100 mg/dL increase in glucose concentration. When glucose concentration increases, osmotic forces are generated, causing water to move from the intracellular fluid to the extracellular fluid; consequently, plasma Na^+ concentration becomes diluted (Carlson, 2006). In the other groups, the supply of isotonic polyonic solutions failed to prevent the decrease in Na^+ concentration although no hyponatremia occurred.

Serum potassium levels decreased in Phase 1 due to decreased intake of this electrolyte during the starvation phase. Although the polyonic solution used in the ENTFL and ENTGL groups contained potassium, the amount supplied was insufficient to prevent this decrease in circulation. This decrease could also be attributed to increased hormone release, such as insulin and catecholamines. Excitement and pain, which are common in horses exposed to stress, surgical or not, trigger the release of catecholamines, leading to hyperglycemia and a consequent decrease in potassium values (Di Fillippo et al., 2008). However, stress-associated hyperglycemia cannot be considered a probable cause, since only the groups that received 50% glucose (PARFL and PARGL) developed hyperglycemia; conversely, glucose concentration remained stable in the ENTFL and ENTGL groups. The potassium concentration in the PARGL group decreased markedly due to the development of a hyperglycemic condition associated with the provision of TPN in Phase 1. Once the food supply was restored, the potassium concentration increased and reached values similar to the initial levels.

The total calcium levels remained relatively constant throughout the study period although they were below the normal values for horses. However, the absence of a significant difference ($p>0.05$) at the beginning of the study (T1) demonstrated the homogeneity of the experimental groups. The results obtained in the present study were similar to those observed by other researchers who did not observe changes in calcium concentrations during a 10-day starvation period in a group of horses (Baetz & Pearson, 1972).

The magnesium ion response observed in our study partly corroborated the data of Baetz and Pearson (1972), who did not identify a change in magnesium concentration during the first 6 days of a 10-day starvation period in horses. Regardless of the absence of a significant difference, the magnesium concentration most remarkably decreased in the PARGL group although it decreased below the normal range in the other groups in at least one part of Phase 1. Magnesium concentration probably decreased due to the absence of dietary intake associated with the provision of magnesium-free fluid therapy in Phase 1. The small number of animals used per group and the variability of the response in each group and individual resulted in data overlap, preventing the identification of differences.

In addition to the absence of dietary intake (Stewart, 2011), hypomagnesemia development is closely associated with systemic inflammation and cytokine release (Sugiura et al., 2000). Thus, in the present study, hypomagnesemia might be initially associated with an inflammatory process triggered by laparotomy and surgical manipulation for obtaining the samples. However, the return of its concentration to values within the normal range or close in the refeeding phase, mainly in the ENTFL, PARFL, and PARGL groups, suggested that the absence of ingestion was the main cause of the decrease in magnesium concentration in Phase 1. This decrease often follows a

decrease in potassium concentration (Sugiura et al., 2000), and this finding was consistent with the results of the present study.

When animals starve, their pH likely decreases as a result of lipid catabolism. This phenomenon probably justified the decrease in pH in all groups up to T_3. Blood pH and HCO_3^- concentration can be used to identify the development of metabolic acidosis but not the development of acidemia in the PARGL group (DiBartola, 2006). Metabolic acidosis caused by the infusion of parenteral nutrition components is frequently observed during TPN in humans. Although the specific cause of this acidosis remains unclear, studies have indicated that it is associated with metabolic abnormalities such as thiamine deficiency and excessive lactic acid formation induced by the administration of large amounts of glucose and synthetic L-amino acids (Welbourne & Nissim, 2004).

In metabolic acidosis, the kidneys do not remove excess hydrogen ions and do not recover a sufficient amount of bicarbonate in the presence of normal PCO_2, verifying the decrease in bicarbonate and the maintenance of PCO_2 concentration in this study. Hyperventilation is a compensatory mechanism of metabolic acidosis. A reduction in blood pH stimulates the respiratory centers, and the resulting hyperpnea excretes excess CO_2 from the body, resulting in a decrease in TCO_2, as observed in the present study, but without hyperpnea.

Taking into account the physiological relationship between blood pH and blood potassium concentration, the potassium concentration in the PARGL group expectedly decreased when pH decreased. For every 0.1 unit drop in pH, potassium concentration increases by 0.2–1.7 mEq/L (Rose & Post, 2001); however, this relationship was not observed in the present study, and both parameters decreased in Phase 1. The variability in the degree of hyperkalemia is related to the presence of other factors that can alter potassium homeostasis. The effect of potassium deficiency in the PARGL group was superior to that of metabolic acidosis on potassium homeostasis. The refeeding phase was characterized by an increase in pH, indicating metabolic alkalosis in some cases.

HCO_3^- decreased significantly in the PARGL group, although it did not differ significantly in internal averages due to the small number of animals per group and the great variability of the data, with values that overlapped between groups.

Amino acid metabolism in metabolic acidosis primarily focuses on glutamine, the predominant extracellular amino acid, and glutamate, the most significant intracellular amino acid. Metabolic acidosis, diagnosed as reduced plasma HCO_3^- concentration as observed in this study, occurs because of the increased production of nonvolatile fatty acids derived from the incomplete oxidation of glucose-producing lactic acid and fatty acid-producing ketone bodies and the complete oxidation of sulfuric amino acids and phospholipids, which produce sulfuric acid and phosphoric acid, respectively. Thus, metabolic acidosis can develop under all catabolic conditions, such as starvation and surgical injury (Zhang et al., 2003).

In response to metabolic acidosis, the kidneys reabsorb HCO_3^- to the same extent as they produce acids to stabilize the body's alkaline reserves. For further HCO_3^- production, glutamine is extracted from the circulation by the kidneys and metabolized to ammonia and HCO_3^- (Zhang et al., 2003). Although this route of HCO_3^-production is important in cases of metabolic acidosis, the intravenous supply of glutamine at the dose used in this study could not prevent the decrease in HCO_3^-concentration and consequently the development of metabolic acidosis.

In the ENTGL and PARFL groups, an increase in PCO_2 between T_3 and T_7 likely corresponded to respiratory acidosis, which is indicated by values greater than 46 mmHg (Ribeiro Filho et al., 2007). Respiratory acidosis usually occurs as a compensatory mechanism of metabolic alkalosis or as a primary alteration in pulmonary disorders (Pinto et al., 2018; Ribeiro Filho et al., 2007). In animals that experience such disorders during these periods, respiratory acidosis is secondary or compensatory to metabolic alkalosis. Similar results have been obtained when intravenous lactate Ringer's solution or enteral fluid therapy is used for the treatment of experimentally induced impactions (Pinto et al., 2018).

Conclusions

Changes in the acid-base and electrolyte balance were more intense in the PARGL group than in the other groups even though such changes also occurred in the other groups. More studies

are needed to determine the optimal formulation of TPN for horses. Despite the promising results of this study, its use should not be discouraged because it has numerous clinical benefits. These results demonstrate the need to monitor blood gas and electrolyte balance in horses with food restriction under nutritional support or prolonged fluid therapy so that changes are promptly corrected.

Ethics statement

This study was approved by the Animal Experimentation Ethics Committee (CETEA/UFMG) under number 34/2008.

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Conflict of interests

The authors declare no conflicts of interest in the preparation, execution, and dissemination of the results of this study.

Authors' contributions

UPM, MSP, CF, FOPL, VAG - Development of methodology; preparation and writing the initial draft. UPM - Writing, Review and Editing manuscript. MSP - Statistical analysis.

Availability of complementary results

Non complementary information.

The study was carried out at horse's stud in Escola de Veterinária da UFMG (EV/UFMG), Belo Horizonte, MG, Brazil.

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