Parenteral nutrition in the mature horse

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Summary

Parenteral nutrition is an important component of the management of critically ill horses unable or unwilling to eat. It provides dextrose, amino acids, vitamins and minerals and, in some cases, lipids for nutritional support until enteral nutrition can be re instituted. It can also be used as a supplement to enteral nutrition, where horses are not ingesting at least 80% of digestible energy (resting) requirements for more than 2–3 days. This review discusses the indications, applications, monitoring and complications of parenteral nutrition in mature horses.

Rationale for implementation of parenteral nutrition

Background and indications for parenteral nutrition

Enteral vs. parenteral nutrition in critical illness

For decades, EN has been regarded as superior to PN. In human medicine, parenteral nutrition has been delay until EN is not possible (Heidigger et al. 2008). Arguments against PN included the possibility of metabolic complications such as hyperglycaemia and hypertriglyceridaemia, endocrine abnormalities, immunological dysfunction, infectious complications and GI mucosal atrophy (Kudsk et al. 1992; Hill et al. 1995). In a recent meta-analysis, a compilation of 11 studies comparing EN and PN, for the first time PN was shown to have a significant reduction in mortality (odds ratio: 0.51, 95% confidence interval: 0.27–0.97, P = 0.04) (Simpson and Doig 2005). Other studies have also supported the notion that PN is not associated with increased mortality despite an increase in infections (Braunschweig et al. 2001; Heyland and Samis 2003; Gramlich et al. 2004; Peter et al. 2005). Based on these results, there has been a slight shift in how PN is viewed. Instead of deciding between enteral and parenteral as the route for a patient’s feeding, PN is now viewed as a supplement to enteral feeding when 100% of the desired calories cannot be provided enterally. Current recommendations in human medicine include the initiation of enteral feeding as soon as possible whenever the GI tract is functioning, with early parenteral nutritional support as a supplement to ensure adequate provision of calories (Heiddegger et al. 2008). Rather than an all or nothing decision, the use of PN or EN has been modified to include both modes together, with the goal of early and complete provision of nutrition (Heiddegger et al. 2008).

How these principles apply to sick horses is unknown. These are no prospective studies comparing the effects of PN vs. EN in horses. The place for PN in equine medicine is when EN is not tolerated, or when it is only partially tolerated. One prospective study evaluating PN following small intestinal resection and anastomosis in 15 mature horses showed that horses receiving PN had lower markers of catabolism and starvation, including urea, total bilirubin and triglyceride concentrations than horses in the starved group. They also had higher blood glucose and insulin concentrations (Durham et al. 2004). The authors concluded that PN improved the overall nutritional status of those post operative horses. Another study evaluating the clinical effects of PN in these same 15 horses showed that horses receiving PN had higher catheter scores (more signs of catheter site swelling or phlebitis), but no other significant clinical effects (Durham et al. 2003).
**Indications for use of PN in horses**

Specific indications for PN in horses include oesophageal obstruction, persistent reflux, ileus and dysmotility such as those with post operative ileus or duodenitis-proximal jejunitis syndrome. Parenteral nutrition is also indicated in horses with hypertriglyceridaemia or those with hyperlipaemia from negative energy balance and/or stress, especially those breeds and signalments that are predisposed to lipid derangements (Dunkel and McKenzie 2003; Durham 2006). These include ponies, miniature horses, donkeys and mules, pregnant or lactating mares, obese horses and those with endocrine disorders such as pituitary pars intermedia dysfunction (PPID) or metabolic syndrome. Horses with dysphagia or cachexia in which indwelling nasogastric feeding tubes are not feasible would also benefit from PN. Horses with a body condition score (BCS) of ≥3/9 that are anorexic should also be considered candidates for early PN. Horses with circulatory shock, such as those with severe systemic inflammatory response syndrome or those with sepsis, should not be force fed, as GI perfusion abnormalities may be present in such horses. These animals should also be provided with parenteral nutritional support.

Any horse with prolonged anorexia would benefit from PN. Long-term nasogastric tube feeding has potential side effects of nasal, pharyngeal and upper GI trauma, and pulmonary aspiration (Hardy et al. 1992). Oesophagogastrotomy feeding can also be associated with complications, such as strictures, infection and fistulas (Stick et al. 1981).

**When to implement PN**

There are no strict guidelines for timing of initiation of PN. The optimal timing of nutritional intervention in sick horses is unknown, and probably varies with the individual horse and disease process. In general, PN should be considered in horses with good body condition after 3–7 days of intolerance of feeding or anorexia, with dextrose supplementation occurring sooner. Underweight horses and grossly obese horses should be supported with parenteral nutrition earlier than this; the former group lacks the reserves to tolerate further malnutrition, and the latter group is at risk for hypertriglyceridaemia and hyperlipaemia. Miniature horses, ponies and donkeys may develop hyperlipidaemia or hyperlipaemia within 24–48 h of fasting (Rush Moore et al. 1994; Haliebeek and Beynen 2001).

**How to administer parenteral nutrition to horses**

**Practical means of determining energy requirements**

The digestible energy requirements of horses occur in 2 forms: maintenance (DEm) and resting (DER).

**TABLE 1: Calculation of daily digestible energy requirements for horses**

<table>
<thead>
<tr>
<th>Horse</th>
<th>DEm (Mcal/day)</th>
<th>DER (Mcal/day)</th>
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<tbody>
<tr>
<td>Horses ≤600 kg</td>
<td>DEm (Mcal/day) = [bwt x 0.03] + 1.4</td>
<td>DER (Mcal/day) = (bwt x 0.021) + 0.975</td>
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<tr>
<td>Horses &gt;600 kg</td>
<td>DEm (Mcal/day) = [bwt x 0.0383] + 1.82 – [0.000015 × bwt²]</td>
<td>DER (Mcal/day) = (bwt x 0.04 × bwt x 0.792)</td>
</tr>
<tr>
<td>Lactating mares</td>
<td>Mares ≤300 kg: Initial 3 months post partum: DEm (Mcal/day) = DEm + (0.03 x bwt x 0.792)</td>
<td>DER (Mcal/day) = (bwt x 0.03 x bwt x 0.792)</td>
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<tr>
<td></td>
<td>Latter 3 months post partum: DEm (Mcal/day) = DEm + (0.02 x bwt x 0.792)</td>
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<td>Mares &lt;300 kg: Initial 3 months post partum: DEm (Mcal/day) = DEm + (0.04 x bwt x 0.792)</td>
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‘Maintenance’ requirements estimate the requirement of a healthy horse with leisure (nonworking/riding) activity. ‘Resting’ requirements are those of a stall-confined horse with virtually no activity. Calculations of digestible energy for resting and maintenance needs are shown in Table 1.

Most ill horses are stall-confined, and therefore provision of resting digestible energy needs should be the initial goal when providing PN. Very few disease states cause an increase in daily energy requirements in human patients. In recent years, several studies have found reduced mortality and hospital complications, such as pneumonia and longer lengths of stay, when calorie underfeeding was performed (Le Gall et al. 1993; Ibrahim et al. 2002; Villet et al. 2005). It has been suggested by these studies that somewhere between 25 and 66% of calculated energy requirements should be the goal of nutritional support in the critically ill. The caloric requirements of critically ill horses are unknown, but horses with endotoxaemia or sepsis may not have increased caloric requirements as is the case with critically human patients (Grau and Bonet 2009). The reasons for the benefits of permissive underfeeding are unknown, but animal studies have shown that restrictive energy intake is associated with decreased inflammatory cytokines, improved metabolic profiles, and increased survival (Jeejeebhoy 2004). Anorexic horses do not have energy losses associated with digestion, fermentation and absorptive processes, and this will lower daily energy demands. Therefore, it is reasonable to assume that idle, critically ill horses with anorexia have reduced energy requirements.

For a 500 kg horse, the DER is 11.5 Mcal/day. To accomplish calorie restriction (permissive underfeeding) 80% of this value should be the initial target for provision of calories with PN in sick horses with inactivity. Because every
individual horse has unique nutritional requirements, this is only a starting point. Daily adjustments to the rate of PN provision should be made based on serial reassessment of bodyweight, body condition, activity level, clinical status, biochemical indices and disease process. If PN is well tolerated, and activity level increases, the provision can be increased to DEr. Once horses become active as their clinical status improves, or if bodyweight is not maintained through provision of DEr, then the caloric administration should be increased to DEm, which is approximately 16.4 Mcal/day for a 500 kg horse.

Eighty percent of DEr is suggested as the initial caloric target because overfeeding of calories can predispose to hyperglycaemia, hyperlipaemia, hyperinsulinaemia, hepatic dysfunction, immune dysfunction, hypercapnia, and possibly increased inflammation in man and laboratory animals (Sternberg et al. 2000; Mechanick and Brett 2002; Grau and Bonet 2009). Many critically ill human patients actually have lower energy expenditure than healthy subjects, largely due to inactivity in the former group (Sternberg et al. 2000; Grau and Bonet 2009). Current recommendations in human critical care include provision of adequate or slightly increased nitrogen intake (amino acids) with slight under provision of calories (Martindale et al. 2009).

A study of 4 healthy horses showed that PN was tolerated well for 10 days (Hansen et al. 1988). Feed and water were withheld and yet 94% of bodyweight was maintained. The horses were administered 32.2–35.8 kcal/kg bwt/day, which is similar to DEm (16.3–17.9 Mcal/day). No haematological or biochemical derangements occurred over the 10 days, except for a decrease in blood urea nitrogen (BUN) and triacylglycerol. Two horses developed mild diarrhoea.

Determining protein requirements

Critical illness may result in protein catabolism as a result of the release of cytokines combined with increased secretion of catabolic hormones (Chrousos 1995; Grau and Bonet 2009). Based on this, ensuring adequate to slight overfeeding of amino acids or protein is recommended. Daily protein requirements for horses can be estimated as 0.5–1.5 g/kg bwt as crude protein. To allow for protein sparing, a nonprotein calorie-to-nitrogen ratio of 100–150 kcal/g of nitrogen should be provided in PN.

Formulations and components of PN

There are 3 forms of PN available for use in horses:

1. Parenteral dextrose supplementation

Dextrose can be supplied alone for provision of supplemental calories to horses with short-term (<72 h) anorexia, or to those with partial EN. The primary reasons for use of dextrose-only PN include cost restrictions and when only short-term calorie supplementation is required, as with a horse off feed for <72 h or one that is partially anorexic. Dextrose administration rates of 0.5–2 mg/kg bwt/min can be provided depending on the desired calorie provision. A rate of 1.7 mg/kg bwt/min is commonly used and usually well tolerated, while higher rates may result in hyperglycaemia. A continuous rate infusion (CRI) of 1.7 mg/kg bwt/min is provided as a 5% dextrose solution (50 g/l of crystalloid) administered at 1 l/h for a 500 kg horse. The solution contains 170 kcal/l (3.4 kcal/g of dextrose) and is usually well tolerated, except in insulin resistant horses. This solution would provide 4080 kcal/day, which is approximately 35.5% of DEr for a 500 kg horse. The osmolality of 5% dextrose in water is 250 mOsm/l and is additional to that of commercial crystalloids if dextrose is added to these fluids instead.

It should be noted that horses receiving only dextrose and no amino acid supplementation will experience muscle breakdown due to protein malnutrition. If horses are anorexic and intolerant of feeding for >3 days, a protein (or amino acid) source should be added (see below). Horses supplemented with dextrose, but no EN, should be administered B complex vitamins because GI production of vitamins may be compromised during anorexia. B vitamins are necessary for carbohydrate metabolism; for example, thiamine is necessary for thiamine pyrophosphate, a component of pyruvate dehydrogenase.

2. Lipid-free PN (dextrose-amino acid formulation)

This PN formula consists of only amino acid and dextrose solution, in a 50:50 volume of 50% dextrose and 8.5% amino acids (Travasol or Aminosyn 8.5%; in UK: Aminoven 25%) (see Fig 1). There is a commercially available dual chambered product (total volume 1 l) that is easily mixed by removing a clamp partition between the two chambers (Aminosyn II 4.25% /in 25% dextrose)2. The 50% dextrose contains 1.7 kcal/ml whereas the 8.5% amino acid solution

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contains 0.34 kcal/ml. Parenteral nutrition formulas without the lipid component have gained in popularity in recent years. Lipid-free formulas are indicated for short-term use (<7 days) because fatty acid deficiency may result after this time. Linoleic acid is considered the only essential fatty acid in horses (Lewis 1995). In addition to being less costly than lipid-containing formulas, PN without lipids may be less immunosuppressive in human patients (Heyland et al. 1998). In one meta-analysis, lipid-free PN formulations used in human patients resulted in a decrease in medical complications as compared to those containing lipids (Heyland et al. 1998). In one meta-analysis, lipid-free PN formulations used in human patients resulted in a decrease in medical complications as compared to those containing lipids (Heyland et al. 1998). This formula is indicated in horses with lipid derangements, such as those with hyperlipaemia, or in those with serum triglyceride concentrations >2.0 g/l (2.3 mmol/l).

This lipid-free formulation provides 1.02 kcal/ml of DE and 0.04 g/ml of amino acids. The formula is hypertonic, with an osmolarity of 1690 mOsm/l and should therefore be diluted with sterile water (in a 1:3 ratio for water:PN) if used in a peripheral vein. For a 500 kg horse, the rate of administration would be 470 ml/h (80% of this rate should be the initial ultimate goal) and to lower the osmolarity 150 ml/h of sterile water can be piggy-backed into the PN (Table 2). The nonprotein calorie:gram nitrogen ratio of this formula is 129; it provides 457 g of amino acids per day.

TABLE 2: Calculation of parenteral nutrition (PN) rates for a 500 kg horse

1. PN formulation without the lipid component:
   1500 ml 50% dextrose
   1500 ml 8.5% amino acid
   3000 ml total into PN bag
   This formulation provides:
   1.02 kcal/ml DE
   0.0425 g/ml amino acids
   Approximate osmolarity = 1690 mOsm/l
   To meet DE requirements for a 500 kg horse:
   11,500 kcal/day = 1.02 kcal/ml x 11,274.5 ml/day = 470 ml/h
   *Start at 25% of this rate and gradually increase over 24 h
   Dilute with sterile water: 150 ml sterile water/h piggy-backed to above
   This will provide 457 g protein/day (0.9 g/day)

2. PN formulation including lipids:
   1000 ml 50% dextrose
   1500 ml 8.5% amino acid
   500 ml 20% intralipid
   3000 ml total into PN bag
   This formulation provides:
   1.07 kcal/ml DE
   0.0425 g/ml of amino acids
   0.033 g/ml of lipid
   Approximate osmolarity = 1317 mOsm/l
   To meet DE requirements:
   11,500 kcal/day = 1.07 kcal/ml x 10,748 ml/day = 448 ml/h
   *Start with 25% of this rate and gradually increase over 24 h
   This will provide 457 g protein/day and 358.3 g lipid/day
   (0.7 g/kg bwt/day)

3. Lipid-containing PN (dextrose-amino acid-lipid formulation)

This is the formula of choice for long-term (>7 days) PN administration (see Fig 2). It includes 3 components: 50% dextrose, 8.5% amino acids, and 10–20% lipid solutions (Intralipid 20%)1,3. A formulation used by the author is as follows:

1000 ml 50% dextrose + 1500 ml 8.5% amino acids + 500 ml 20% lipid

The caloric content of 20% Intralipid alone is 2 kcal/ml. The formula provides 1.07 kcal/ml of DE. It provides 0.04 g/ml of amino acids and has an osmolarity of 1317 mOsm/l, lower than the nonlipid formulation because
Vitamins and minerals

Vitamins, especially those that are water soluble, may become limiting with anorexia. These should be administered along with PN unless the horse is receiving concurrent partial nutrition enterally. B complex vitamins (thiamine 12.5 mg/ml; niacinamide 12.5 mg/ml; pyridoxine 5 mg/ml; d-panthenol 5 mg/ml; riboflavin 2 mg/ml; cyanocobalamin 5 µg/ml) should be supplied at a rate of 1–2 ml/45 kg daily, diluted in fluids or PN. These, as well as vitamin K, can become limiting due to limited GI production associated with anorexia, and are important cofactors for aerobic metabolism. Vitamin C should be supplied at a rate of 20 mg/kg bwt/day enterally whenever possible. Electrolytes, including sodium, potassium, chloride, calcium, magnesium and phosphorus should be supplied through crystalloids. Potassium can be added to crystalloids containing sodium and chloride at a rate of 20–40 mEq/l (10–20 ml/l of 15% KCl [2 mEq/ml]) or higher in the form of potassium chloride. Potassium phosphate can also be used. Potassium supplementation should not exceed 0.3 mEq/kg bwt/h. Magnesium can be added to fluids at a rate of 3 mEq/l (approximately 1.5 ml/l of a 25% solution [approximately 2 mEq/ml] of MgSO4), but some fluids (Normosol and Plasmalyte) already contain magnesium at these concentrations and therefore do not require supplementation unless hypomagnesaemia is present. Calcium can be supplemented as 23% calcium gluconate diluted in fluids (50 ml/l) at a rate of 1 ml/kg bwt/day (1 mEq/kg bwt/day of calcium). Phosphorus can be supplemented at a rate of 0.01 mmol/kg bwt/h as sodium- or potassium phosphate. Fat-soluble vitamins (A, D, K) and trace minerals are stored in the body, and therefore should be added only for long-term PN administration (>7 days) and when no EN is possible. Vitamins and minerals formulated for PN use are available as commercial human products. Even though vitamin E is fat soluble, it may be helpful if provided early in the course of PN (12 iu/kg bwt/day enterally), as it has antioxidant properties.

Preparation and administration of parenteral nutrition

Components of PN should be mixed aseptically (Fig 3). Currently there are pre-made commercial PN products available, consisting of dextrose and amino acid solutions, that are easily mixed with removal of a clamp between chambers, without having to open or manually mix components (Aminosyn II 4.25%/in 25% dextrose)². Intravenous lines should be changed daily, and a new bag should be utilised each time PN is mixed. Vitamins and minerals can be added to crystalloids to minimise the number of injections into the PN solution. Lipids should be added to the bag last, as the acidic pH of dextrose solutions will destabilise the emulsions, whereas the presence of the amino acid solutions aids in buffering.

Parenteral nutrition can be supplied through the jugular or cephalic veins in horses. The limit of hypertonicity that these veins can tolerate is unknown. Endothelial injury and subsequent phlebitis or thrombosis as a result of chronic exposure to hypertonic solutions is of concern. To minimise these risks, the osmolality of PN formulations should be considered. The osmolality of lipid-containing formulations is in the range of 1300–2100 mOsm/l, depending on the formulation. The one described above (Table 2) is approximately 1300 mOsm/l and seems to be well tolerated in large veins. If much higher, then sterile water can be added to lower the osmolality. The author adds approximately one-third the volume of the PN solution as sterile water when using lipid-free (dextrose-amino acid only) formulations, which have an osmolality of 1690 mOsm/l. Adding sterile water in a 1:3 ratio will lower the osmolality to 1268 mOsm/l.

Double or triple lumen catheters consisting of minimally thrombogenic material, such as polyurethane, are ideal for use with PN (Fig 4). The additional lumen(s) allows for dedicated ports strictly for PN administration, without having to break lines or inject other medications into the PN lines. Examples include Arrow® or Mila® multilumen catheters.

Amino acid solutions and B vitamins are light sensitive, and should be protected from daylight until just before or throughout administration, respectively. Artificial lighting may be less of an issue.

Parenteral nutrition should be initiated at one quarter of the target rate, which is based on 0.8 × DEr as the first target. This is to allow for insulin and other physiological adaptations time to adjust to the PN. The rate should then

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