

Case Report

Suspected primary lactose intolerance in neonatal foals

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Summary

The intestine of neonatal mammals must be able to secrete lactase enzyme to hydrolyse lactose in its mother's milk. Failure to secrete lactase results in failure to digest lactose. This results in osmotic diarrhoea, weight loss, failure to thrive, lethargy, colic and abdominal distension. Lactose intolerance may occur secondarily to intestinal bacterial infection. Primary lactose intolerance is recognised in human infants. Here we report 2 cases of suspected primary lactose intolerance in foals. The foals responded well to oral administration of exogenous lactase enzyme.

Introduction

The ability of the neonatal intestine to digest lactose is a basic and essential function. The high concentrations of lactose in mare's milk must be paralleled by a correspondingly high activity of lactase within the foal's small intestine. In normal foals there is a natural reduction in lactase secretion at around 4–6 months of age and by the time of weaning it is usually insignificant. Horses over 3 years of age are unable to hydrolyse lactose (Roberts 1975).

Failure of neonates to digest lactose as a result of lactase enzyme deficiency means that this source of carbohydrate is not of use to the foal. The clinical consequences are osmotic diarrhoea, weight loss, failure to thrive, lethargy and often recurrent or persistent mild colic accompanied by abdominal distension. Lactose intolerance has been reported secondarily to intestinal bacterial infection with *Clostridium difficile* (Weese *et al.* 1999) and rotaviral infection (Sweeney 1987) that causes damage to mucosal enzyme systems. In such cases the lactose intolerance is often transient in nature, resolving during the convalescent period after the infection. Here we report 2 foals with suspected primary lactose intolerance.

Case details

Clinical findings

Case 1

A 6-day-old Thoroughbred cross Irish Draught filly foal, born at 340 days gestation and weighing 45 kg was referred for evaluation of diarrhoea present since birth and colic for the previous 14 h. On presentation the filly showed mild signs of abdominal pain. It was ambulatory and feeding, although dull and depressed. Body condition score was 3/9. The abdomen was distended and it was passing pale-orange, watery diarrhoea. Heart rate was 100 beats/min, respiratory rate 40 breaths/min and rectal temperature 38.6°C. It was approximately 20% dehydrated, with PCV 42% and total plasma solids of 55 g/l. Other parameters were within reference limits. Total leucocyte count was $6.2 \times 10^9/l$ (reference range [rr] 5.5–12.5 $\times 10^9/l$). Blood glucose was 4.7 mmol/l and all electrolytes were within normal limits. Serum IgG was determined to be greater than 8 g/l by enzyme immunoassay (SNAP foal IgG test)¹. No pathogens were identified in the samples of blood and faeces submitted for aerobic and anaerobic culture and sensitivity, faecal egg count, viral isolation and clostridial toxin detection.

Rehydration therapy was initiated immediately via the administration of i.v. 5% glucose (Glucose 40% injection)², in lactated Ringer's solution (Isolec)³, at 8 ml/kg bwt/h initially to treat dehydration and then at 4 ml/kg bwt/h for maintenance. Metronidazole at 15 mg/kg bwt *per os* q. 8 h (Metronex)⁴ and ceftiofur at 5 mg/kg bwt i.v. q. 12 h (Excenel)⁵ were administered until negative faecal cultures were returned on Day 3.

Due to the history of diarrhoea and failure to thrive since birth, and the clinical evidence of abdominal distension and colic, lactose intolerance was suspected. Confirmatory diagnosis via expired breath hydrogen analysis, as used in human infants, was not available. An oral lactose tolerance test (Martens *et al.* 1985) was not performed due to the risk of further compromising the filly's health, since the lactose tolerance test requires fasting for 12 h and the withholding of i.v. glucose supplementation. Oral lactase therapy, 4 drops

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q. 4 h (Colief)⁶ was administered. This proprietary lactase enzyme formulation is a neutral yeast lactase preparation, obtained from the controlled fermentation of *Kluyveromyces lactis* with a specific activity at 37°C of 50,000 µmol/min/g. The dose of 4 drops/4 h was extrapolated from that advised for use in human infants (Kanabar *et al.* 2001). By 4 h after the first lactase administration the foal ceased to show signs of colic or bloating and diarrhoea resolved within 24 h. The filly began to gain weight, reaching 48 kg 5 days after admission, and was discharged at that stage.

The diagnosis of primary lactose intolerance was based on the presence of diarrhoea since birth, the absence of any aetiological agent, and the rapid response to lactase therapy. The foal was prescribed lactase drops until weaning, initially on a 6 hourly basis with a view to increasing the dosing interval overnight as the filly matured.

Follow-up information was obtained from the referring veterinary surgeon 2 months following discharge and from the owner 9 months following discharge. It was reported that the filly had begun to resent administration of lactase so the treatment had been stopped on a number of occasions. This resulted in a rapid recurrence of the diarrhoea on each occasion and resolution when the lactase was again administered. Eventually the filly accepted regular drug administration and there were no further problems. The foal was weaned at 3 months of age and the owner was pleased with its growth and health at age 9 months.

Case 2

The following breeding season an 8-day-old Quarter Horse colt, born to term and with a history of persistent watery diarrhoea that had varied in severity since birth was presented for evaluation. The colt had not been pyrexia at any time, but had shown lethargy and signs of dehydration. Management by the referring veterinary surgeon included maintenance of hydration status through i.v. fluid therapy twice daily and stomach tubing with milk at regular intervals. Despite this therapy, the diarrhoea persisted and the foal deteriorated and was referred after 7 days of treatment.

At presentation the foal had profuse watery diarrhoea and was lethargic and anorectic, but able to stand. Heart rate was 70 beats/min, respiratory rate 20 breaths/min and rectal temperature 38.5°C. PCV was 34% and total plasma solids were 60 g/l. There was no evidence of dehydration. Blood glucose was 5.8 mmol/l. Serum IgG was determined to be >8 g/l by enzyme immunoassay (SNAP foal IgG test)¹. Haematology, biochemistry and fibrinogen were all within normal limits but venous (temperature corrected) blood gas analysis revealed severe acidaemia, secondary to metabolic acidosis (pH 6.77, rr 7.32–7.44) with base excess -28.4 mmol/l and anion gap 13.9 mmol/l. The foal showed hypokalaemia (3.2 mmol/l, rr 3.8–5.0 mmol/l), hypocalcaemia (2.06 mmol/l, rr 2.7–3.2 mmol/l) and hyperchloraemia (120 mmol/l, rr 90–103 mmol/l). Faeces and blood were submitted for bacterial, viral and toxin analysis as with *Foal 1*. All results were negative for pathogens.

Therapy consisted of maintenance administration (4 ml/kg bwt/h) of i.v. 5% glucose (Glucose 40% Injection)² in lactated Ringer's solution (Isolec)³. Due to the severity of acidaemia, bicarbonate was also administered to correct the plasma pH. The quantity of bicarbonate given was calculated using the equation base excess (mmol/l) x bodyweight (kg) x 0.41. Half the required amount of sodium bicarbonate (8.4%, Polyfusor⁷) was administered over 6 h, raising blood pH to 6.98. Intravenous fluid therapy with the remaining sodium bicarbonate was continued over an 18 h period resulting in a blood pH of 7.3 at the end of 24 h of therapy. Sodium penicillin G (10 mg/kg bwt i.v. q. 6 h, Crystapen)⁸ and ceftiofur (5 mg/kg bwt i.v. q. 12h, Excenel)⁴, were supplied for 48 h. Oral lactase therapy (Colief drops) was commenced, and by 2 h after the first administration of lactase, the diarrhoea had resolved and faeces remained normal throughout hospitalisation. Within 8 h the foal had improved in demeanour and begun to feed spontaneously. Management to discharge was then with oral lactase therapy alone and free access to the dam's milk.

The foal was discharged after 4 days hospitalisation, to remain on lactase therapy administered *per os* q. 6 h. Initially the foal made excellent progress but after 7 days the owner extended the overnight dosing interval from 6 to 10 h. The foal developed diarrhoea during these nights, but produced normal faeces during the day when dosing interval was every 6 h. Overnight dosing interval was therefore reduced to 6 h and at follow-up 2 months later, the owner reported no further problems.

Discussion

The rapid responses both to lactase administration and withdrawal in these foals, coupled with the presence of diarrhoea from birth and the lack of evidence of an infectious aetiology for the diarrhoea are consistent with primary lactose intolerance.

In man, primary lactose intolerance is rare in full term infants; congenital lactase deficiency is reported as a rare autosomal recessive disorder with excessive prevalence in Finland (16 cases in 17 years; Savilahti *et al.* 1983). However, the ability to secrete lactase is the last of the mechanisms for carbohydrate absorption to mature in the fetus (Mobassaleh *et al.* 1985) resulting in transient lactose intolerance being a significant problem in premature infants (Shulman *et al.* 1998, 2005). Failure to break down all the lactose in the feed allows significant amounts of lactose to enter the large bowel. It then becomes a substrate for lactobacilli and bifidobacteria in the colon, which break it down to produce lactic acid and hydrogen. The subsequent increase in breath hydrogen is an accepted indirect biomarker for hypolactasia (Levitt 1969). The rapid production of hydrogen in the lower bowel distends the colon, causing pain. The osmotic pressures generated by the lactose and lactic acid in the colon cause an influx of water, leading to further distension and acidic diarrhoea. Clinical signs in man are therefore similar to those seen in these foals, and include diarrhoea from birth, colic, bloating and failure to thrive.

Diagnosis is by a lactose tolerance test or breath hydrogen test. Management is either by addition of lactase to the milk, ingestion of lactase or feeding of lactose free formulas.

Preweaning lactase deficiency has been rarely reported in animals. Primary lactose intolerance has been reported in one calf (Olchoway *et al.* 1993). This case was managed by addition of lactase to its whole milk feed. Secondary lactose intolerance has however, been reported in the foal following intestinal infection with *Clostridium difficile* (Weese *et al.* 1999) and rotavirus (Sweeney 1987). The mechanism in these is likely to be diffuse mucosal damage of the small intestinal villi with the ability to digest lactose returning once mucosal damage has healed. In contrast, primary lactose intolerance is persistent.

The signs and response to treatment in these foals make a diagnosis of primary lactose intolerance likely. That increasing dose interval resulted in a recurrence of diarrhoea is equivalent to performing a lactose tolerance test. However, this cannot be certain without results of a controlled lactose tolerance test and hydrogen breath test. Furthermore, despite no infectious agent being detected it remains possible that these foals had secondary lactose intolerance, although the presence of clinical signs since birth and their duration until weaning make this less likely than a primary condition.

The dose of lactase used in this study was extrapolated from that used in man and was extremely effective in these cases. However, foals feed more frequently than human infants, and it may be that in other cases a more frequent dosing regime is required. Furthermore the enzyme was given to the foals rather than added to the milk, for ease of management. This was sufficient to produce the desired response in these cases, but in suspected cases that are refractory to treatment, it may be necessary to milk the mare and add the enzyme to the milk before bowl feeding the foal.

These case reports suggest that primary lactose intolerance should be a differential diagnosis for diarrhoea, colic and failure to thrive in the foal, particularly if the diarrhoea has been present since birth or the foal is premature or dysmature. Diagnosis may be made by response to treatment that is simple, inexpensive and rapidly successful in these cases. The recurrence of clinical signs when treatment is withdrawn illustrates the need for careful dosing and monitoring until the foal is weaned. The treatment is also advised for foals with secondary lactose intolerance. To our knowledge, there are no reported adverse reactions in children. Therapy with lactase is simple, affordable, effective and low risk.

Manufacturers' addresses

- ¹IDEXX Laboratories, Westbrook, Maine, USA.
- ²Arnold, Carson, California, USA.
- ³Ivex Pharmaceuticals, Larne, Co. Antrim, UK.
- ⁴Pharmacia and Upjohn, Peapack, New Jersey, USA.
- ⁵Pharmacia Animal Health, Tadworth, Surrey, UK.
- ⁶Crosscare Ltd., Dublin, Ireland.
- ⁷Fresenius Kabi, Bad Homburg, Germany.
- ⁸Schering Plough Animal Health, Harefield, Middlesex, UK.

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