

# Meconium retention in neonatal foals – Efficacy and safety of Macrogol 4000 on the release of meconium in foals in a Macrogol – A double blind placebo-controlled study

Amelie Brauch<sup>1</sup>, Ingrid Vervuert<sup>2</sup>, Tanja Randow<sup>3</sup> and Monica Venner<sup>4</sup>

<sup>1</sup> Animal Clinic, Haar, Germany

<sup>2</sup> Institute of Animal Nutrition, Nutrition Diseases and Dietetics, Faculty of Veterinary Medicine, University of Leipzig, Germany

<sup>3</sup> Veterinary practice Otten & Roth, Gettorf, Germany

<sup>4</sup> Equine Clinic, Destedt, Germany

**Summary:** Meconium retention is one of the most frequent diseases in neonate foals. The aim of this study was to evaluate the safety and efficacy of Kinderlax<sup>®</sup>, a high-molecular polyethylenglycol, in the prevention of meconium retention in neonate foals. For this we compared Kinderlax<sup>®</sup> as an add-on preparation to the usual enema application, in a double-blind placebo-controlled study. In total 79 healthy male foals were included into the study and were randomly allocated to either the placebo-group (n = 42) or the Kinderlax<sup>®</sup>-group (n = 37). One hour after birth 150 mL of colostrum and 50 mL of water was orally administered once to the foals. For the foals in the Kinderlax<sup>®</sup>-group, 12 g Kinderlax<sup>®</sup> (0.24 g/kg) were dissolved in water and administered orally before the colostrum, as a previous test with the human dosage of 0.32 g/kg had induced signs of colic in 8 foals. Both groups were administered an enema of 120 ml 4 % diluted acetylcysteine as a standard procedure in the prevention of meconium retention. Over 18 hours the foals were regularly checked for signs of dehydration and meconium retention. At two hours after birth a transabdominal ultrasonographic examination of the jejunum and duodenum was performed. 10 hours after birth, during the new-born-check, blood-samples were taken. Faecal samples were collected according to a standardized protocol four times during the study. For this, diapers were fixed on the hind quarters of the foals. To prevent the urine from mixing with the faeces, only male foals were included and a hole for the prepuce was cut into the diaper. Directly after collecting, the faeces samples were visually examined and the pH value was evaluated. Samples were frozen until further analysis of dry matter and crude ash. No foals showed signs of dehydration at any time. There were no significant differences between the groups as to the findings in the ultrasonographic examination or the faeces samples. Concentration of serum immunoglobulins were higher in the Kinderlax<sup>®</sup>-group compared to the placebo group although there was no difference in the quality of colostrum of the mares between both groups. In total eleven foals showed signs of meconium retention (14 %), eight were in the placebo-group and three in the Kinderlax<sup>®</sup>-group. However, this difference was not significant. No foals showed any signs of adverse effects related to the application of Kinderlax<sup>®</sup>. In this study Kinderlax<sup>®</sup> showed no advantage in the prevention of meconium retention in the dosage of 12 g. However, in a preliminary study, 16 g Kinderlax<sup>®</sup> was associated with moderate to severe signs of colic. A higher dosage or repeated administration of Macrogol might be a better option and should be investigated in the future.

**Keywords:** foal, macrogol 4000, polyethylenglycol, meconium retention, treatment, prevention

**Citation:** Brauch A., Vervuert I., Randow T., Venner M. (2020) Meconium retention in neonatal foals – Efficacy and safety of Macrogol 4000 on the release of meconium in foals in a Macrogol – A double blind placebo-controlled study. *Pferdeheilkunde* 36, 4–10; DOI 10.21836/PEM20200101

**Correspondence:** PD Dr. Monica Venner PhD, Pferdekl. Destedt, Trift 4, 38162 Destedt, Germany; mvenner@gmx.de

**Received:** October 26, 2019 | **Accepted:** November 26, 2019

## Introduction

### *Meconium retention in foals*

Meconium consists of swallowed allantoic fluid, cellular debris and gastrointestinal secretion which accumulate in the small colon and rectum and is passed usually shortly after birth (Bernard 2004). In foals the meconium's colour is usually of a dark shade and its consistency is firm to pasty. The meconium should be passed within 24 hours after birth (Prange 2013). When the passage of meconium is completed, the faeces change to a lighter colour and softer consistency which is called milk stool (McCue 2006, Prange 2013). If there is no milk stool after 12–36 hours after birth, there is meconium retention (McCue 2006).

There are two kinds of meconium retention, depending on which segment of the gut is affected by the impaction. It is a low impaction if it is related to the small colon or rectum near the pelvic inlet. In the case of a high impaction the colon transversum or the colon dorsal dextrum is affected (Prange 2013). Because of a narrower pelvic canal colt foals are at a higher risk to develop meconium retention than filly foals of about two third to one third (McCue 2006).

Although the use of preventive enemas is common, meconium retention is still one of the most frequent diseases in neonate foals (McCue 2006, Prange 2013, Graßl et al. 2017) with up to 3% affected foals (Prange 2013). It can lead to mild to severe abdominal pain (Bernard 2004). Affected foals show restlessness, straining to defecate und elevate or swish their

tail (Chaffin and Cohen 1999, Prange 2013). With time the symptoms increase to more severe colic signs (Prange 2013). The usual therapy consists of repeated enemas and fluid therapy, oral laxatives and analgesics (Pusterla et al. 2004, Prange 2013). Nevertheless, some foals will need a laparotomy.

There are two kinds of enemas, which are usually used in foals to improve passage of meconium. One is a commercial enema of sodium phosphate, which should not be administered frequently because of the risk of hyperphosphatemia and irritation of the rectum mucosa. The other is just warm soapy water. If this treatment fails, an acetylcysteine-bicarbonate enema can be used (Prange 2013).

After being successfully used in infants with meconium plugs, acetylcysteine enemas have been introduced into the therapy of meconium retention in foals (Pusterla et al. 2004). It decreases the firmness of the meconium by cleaving disulphide bonds in mucoproteins (Pusterla et al. 2004). Also, it is hypertonic and leads to fluid invasion into the bowel (Pusterla et al. 2004).

In addition to the enemas, analgesics such as metamizol or butorphanol should be applied as well as intravenous fluid. Supplementary to the enemas, mineral oil can be given via nasogastric tube. But because it is not known if mineral oils interfere with the uptake of immunoglobulins and other nutrients, they should not be given to very young foals, if not absolutely necessary (McCue 2006).

If the conservative therapy is not successful, surgery is the last option (Hughes et al. 1996, McCue 2006, Prange 2013). The prognosis for abdominal surgery in young foals varies in literature. Horses in general have a high tendency of forming adhesions (Hughes et al. 1996), which is even higher in young foals (Vatistas et al. 1996). If enterotomy is necessary, survival rate is lower (Scharner et al. 2015).

Foals with meconium retention have a high incidence of bladder rupture which may be the result from excessive straining to defecate (Pusterla et al. 2004). Another risk in foals with meconium retention is an insufficient immunoglobulin transfer because the foals may not nurse as much as healthy foals (McCue 2006).

Because still up to 3% of all new-born foals have meconium retention (Prange 2013) and because of the possible severe consequences a better prevention is needed.

### *Polyethylene glycol*

Polyethylene glycol (PEG) or macrogol is a linear polymer which is neither metabolized by the intestinal microbiota (De Giorgio et al. 2011, Wang et al. 2012) nor is it absorbed (Wang et al. 2012). It belongs to the group of osmotic laxatives (Koppen et al. 2015). It retains water in the intestine via hydrogen connections (Koppen et al. 2015). This has two effects, first it softens the stool by bringing in water. Second it increases the volume of the stool and by this it increases peristalsis due to distension of the colonic wall (De Giorgio et al. 2011). There are different kinds of PEG in use, depending on

its molecular weight Macrogol 3350 or Macrogol 4000, and the addition of electrolytes or not.

In children, PEG is used for treatment of chronic functional constipation (Koppen et al. 2015). Many studies have shown it to be superior to lactulose (Voskuij et al. 2004, Dupont et al. 2005, Candy and Belsey 2008, Treepongkaruna et al. 2011, Wang et al. 2012), to milk of magnesia and placebo (Gordon et al. 2016). In comparison to enemas it showed the same effectiveness, but it is preferred because of its less invasive nature (Koppen et al. 2015). It is well accepted because of its tastelessness and safety with no electrolyte or fluid imbalances following its use (Dupont et al. 2005, De Giorgio et al. 2011). Common side effects are diarrhoea, abdominal pain and bloating (De Giorgio et al. 2011, Wang et al. 2012, Koppen et al. 2015).

The dose of PEG depends on the aim to be achieved. For constipation, the dose is higher, about 1–1.5 g/kg/d (Koppen et al. 2015). The maintenance dose is lower and varies between different studies from 0.5 g/kg/d (Dupont et al. 2006) or 0.2–0.8 g/kg/d (Koppen et al. 2015).

Although enemas are common as prevention, meconium retention is still a problem in foals. This study was based on the hypothesis that PEG might be effective to prevent meconium retention in foals.

## **Material and Methods**

### *Study protocol: animals*

88 male foals of Warmblood mares of one German stud were included in the study. They were all healthy foals from healthy mares which were drinking from the mare within 3 hours after birth. The birth had to be physiologic and in time ( $330 \pm 10$  days). The foals were kept with their mares in individual boxes on straw.

The protocol was approved by the State Authority of Mecklenburg-Vorpommern.

The used compound was Kinderlax<sup>®</sup>, which contains Macrogol 4000 without any additives. It is a powder and should be administered dissolved in water.

### *Preliminary test*

Before the start the appropriate dosage was tested. 16 g Kinderlax<sup>®</sup> in 50 ml water was administered per baby bottle in the first hour after birth in 8 foals. For a foal with a body weight of 50 kg, the preliminary dosage was 20% less than the recommended dose of 0.4 g/kg bodyweight for infants. All foals showed moderate to severe signs of colic and had loose faeces. Because of this result, the dose was reduced to 12 g per 50 kg foal.

Furthermore, different diaper constructions were tested to collect the faeces. To avoid mixing urine and faeces, a hole for the prepuce was cut into the diaper and only male foals were included.

*Study protocol*

To confirm the health of the foals before including them into the study, every foal was clinically examined 30 minutes after birth: habitus, sucking and swallowing reflexes, legs conformation were evaluated as well as possible malformations investigated.

The 88 included foals were divided into two groups: one Kinderlax®-group and a placebo-group. The study was randomized and double-blinded according to the treatment.

One hour after birth, 12g Kinderlax® in 50ml water were administered via baby-bottle in the Kinderlax®-group. For a foal with a body weight of 50kg, the selected dosage was 0.24g/kg, which is approximately 50% less than recommended for infants.

The placebo-group was administered 50ml water at the same time, afterwards both groups received 150ml colostrum via baby-bottle.

For ethical reasons both groups received an enema as is common in meconium prophylaxis, so Kinderlax® was used as an add-on preparation.

At 2 hours after birth a transabdominal ultrasonographic examination of the duodenum and jejunum was performed from the left and right side of the abdomen. From each examination point (duodenum, jejunum right side, jejunum left side) 3 pictures and 3 short films of 5 seconds duration were saved for later evaluation. From each segment of the small intestine visualized the thickness of the wall, the dilatation, motility and contents were evaluated.

The foals were regularly checked for their state of hydration: at 2, 5, 10, 14 and 18 hours after birth. For this the humidity of the mucosa, the capillary filling time and the skin turgor were surveyed. Drop out criteria were defined in order to pro-

tect the foals from adverse reactions (Table 1). Foals with a score of 5 and higher were immediately excluded from the study as well if they had the score 3 in colic symptoms or appetite. The other foals were treated symptomatically.

At 10 hours after birth, the new-born check was performed. This included a clinical examination with the body temperature, an adpection of the umbilical region, auscultation of the heart, trachea and lung, palpation of the joints, the mandibular lymph nodes, the testis, and a rectal, digital exploration of possible meconium. In addition a blood sample was taken to count the white blood cells and the concentration of immunoglobulins. Serum was frozen for further analysis.

*Faeces samples*

At two hours after birth the diapers were tightened on the foals (see Fig. 1). To prevent a mixing of urine and faeces only male foals were included and a hole for the prepuce was cut into the diaper. The diapers were changed at 5, 10, 14 and 18 hours after birth and the collected faeces were visually examined and the pH was evaluated. Subsequently faeces were frozen until analysis.

*Visual examination of the faeces*

Scores were given for their form and consistency at each time. If no sample was collected, the time point was rated with 0.

*pH value*

The pH value was evaluated for the samples at 5 and 18 hours post natum within 10 hours after collecting. Until then the samples were stored in a fridge. To evaluate the pH value 5–10g faeces were mixed with distilled water at the ratio of 1:2 in a glass. Then a sensor was put into the glass and left until it showed a constant value.

Before this the sensor had been standardized in solutions with the pH of 4 and 7.

Table 1	Drop out criteria	Abbruchkriterien
Appetite	0 = normal 1 = slightly reduced 2 = moderate reduced 3* = anorexia	
Dehydration status	0 = < 5% 1 = 5–7% 3 = 8–12% 4 = > 12%	
Colic symptoms	0 = none 1 = mild 2 = moderate 3* = severe	
Tenesmus	0 = none 1 = swishing with the tail, mild straining to defecate 2 = repeated, moderate straining 3 = long persistence in the posture for defecating with intensive straining	
Faeces	0 = physiologic 2 = watery diarrhoea	

\* sole drop out criterion



**Fig. 1:** Colt foal with diaper construction | Hengstfohlen mit Windelkonstruktion

### Dry matter analysis of the faeces

A defined amount of faeces (4.5–5.5 g) was dried in a drying oven at 105°C for 3 hours then the weight was re-weighted again. Analysis were performed in triplicate.

### Crude ash analysis of the faeces

To evaluate the crude ash content of the faeces, 5–10 g faeces were annealed at 600°C for 7 hours in the muffle furnace. The ashes had to be white or light brown, leaving only the inorganic parts. The ash was re-weighted. Analysis were performed in triplicate.

### Meconium retention

During the whole study, all foals were closely watched for any signs of meconium retention.

A treatment protocol existed which was to be followed, if a foal showed signs of meconium retention.

### Statistics

The data were analyzed using the statistical software program (STATISTICA, version 12, StatSoft GmbH, Hamburg, Germany). The data were analyzed for normal distributions using the Shapiro-Wilks test. ANOVA with repeated measurements was performed to analyze dry matter and ash content in feces for the different sampling points and groups. Normal distributed data were subjected to t-test for independent groups. Nonparametric data were analyzed using the Mann-Whitney U test. Correlations among variables were examined by calculating Spearman's correlation coefficients. Statistical significance was set to  $P < 0.05$ .

## Results

In total, 88 foals were included into the study, from which 9 foals were excluded. Five foals needed too much time to drink on their own, two mares did not tolerate the examinations of their foals, one foal showed hyperthermia and tachypnea and for one foal, the study protocol was not followed correctly.

Finally, 42 foals were included in the placebo-group and 37 in the Kinderlax®-group.

### Clinical signs of meconium retention

Of the 79 foals 14% (11 foals) showed signs of meconium retention. Of these only 4 showed severe signs, 6 showed mild to medium signs and one showed absence of defecation. Eight of these foals belonged to the placebo-group and 3 to the Kinderlax®-group. However, this was no significant difference ( $p = 0.161$ ).

5,1% (4 of the 79 foals) of the foals needed intensive care because of meconium retention (Table 2).

### Exclusion of foals before the end of the study

5 foals in the placebo-group were excluded because of severe clinical signs of meconium retention and only 2 in the Kinderlax®-group. Because of the low number of excluded animals no significant difference could be determined.

### New-born examination 10h post natum

During this examination all parameters of all foals were physiologic except for one foal with an umbilical hernia and one foal with a haematoma of the umbilicus. For safety reasons a digital rectal exploration was performed during this examination.

The diaper-construction caused no irritations on the umbilicus or elsewhere for the foals.

### Haematocrit

10h after birth the average haematocrit for all foals was  $44.6 \pm 8.4\%$ , with  $45.2 \pm 10.7\%$  for the placebo-group and  $43.4 \pm 4.3\%$  for the Kinderlax®-group with no significant difference ( $p = 0.239$ ).

### White blood cell count

The white blood cell count (WBC) ranged between  $3.4 \times 10^9/L$  and  $18.0 \times 10^9/L$  (mean average  $\pm$  SD:  $9.6 \pm 2.4 \times 10^9/L$ ). In the placebo-group it ranged from  $3.4 \times 10^9/L$  to  $18.0 \times 10^9/L$  (mean average  $\pm$  SD:  $9.6 \pm 2.6 \times 10^9/L$ ), in the Kinderlax®-group from  $4.8 \times 10^9/L$  to  $13.2 \times 10^9/L$  (mean average  $\pm$  SD:  $9.5 \pm 2.2 \times 10^9/L$ ). There was no significant difference ( $p = 0.945$ ). 11.9% of the foals of the placebo-group had WBC out of the reference values of  $5.0$  to  $13.0 \times 10^9/L$ . In the Kinderlax®-group 5.4% of the animals were outside of the reference

**Table 2** Appearance and severeness of the symptoms in total and divided in groups | Auftreten und Schweregrad der einzelnen Symptome insgesamt und bezogen auf die Gruppenzugehörigkeit

		Placebo-group	Kinderlax®-group	Total
Tenesmus	mild	2	1	3
	moderate	2	0	2
	severe	4	1	5
Colic symptoms	mild	0	0	0
	moderate	1	0	1
	severe	2	1	3
Inappetence	mild	2	0	2
	moderate	2	1	3
	severe	1	0	1
No Faeces		1	1	2
Watery diarrhoea		0	0	0

values. Within two days all foals that had WBC out of range, were physiologic without any treatment.

### Serum immunoglobulins

In the placebo-group the serum concentration of total globulins ranged from 2.4 g/dL to 4.2 g/dL (mean  $\pm$  SD: 3.1  $\pm$  0.4 g/dL) which correlates to 950  $\pm$  320 mg/dL immunoglobulins. In the Kinderlax<sup>®</sup>-group the concentration varied between 2.5 g/dL and 4.1 g/dL (mean  $\pm$  SD: 3.4  $\pm$  0.5 g/dL). The serum IgG value was significantly higher in the Kinderlax<sup>®</sup>-group ( $p = 0.0197$ ).

The IgG concentration of the colostrum of the mares was measured by refractometry and the values ranged from 35.1 g/L to 116.7 g/L (71.5  $\pm$  22.5 g/L). There was no significant difference in the IgG concentration of colostrum between both groups ( $p = 0.20$ ). There was no significant correlation between the concentration of immunoglobulins in the colostrum and the serum immunoglobulins of the foals ( $R^2 = 0.194$ ).

### Sonographic examination of the small intestine

#### Duodenum

In the placebo-group the pictures of two foals could not be evaluated because of insufficient quality. Of the findings 82.5% were physiologic, the non-physiologic findings in this group were a combination of dilatation and a thickened wall. In the Kinderlax<sup>®</sup>-group, one foal was excluded because the duodenum could not be identified in the pictures. In this group 88.9% of the findings were physiologic, the non-physiologic findings were dilatations. There was no significant correlation between the group and the sonographic findings ( $p = 0.458$ ).

#### Jejunum

In both groups one foal was excluded because of insufficient material.

The physiologic findings were found in 26.8% of the placebo-group and 16.7% of the Kinderlax<sup>®</sup>-group. The non-physiologic findings were mostly hypomotile and dilated intestinal loops with hyper- or hypoechogenic ingesta (Tab. 3). There were no significant differences between the groups ( $p = 0.283$ ).

#### Hydration

No foal showed any signs of dehydration during the whole study and there were no significant differences between both groups.

#### Examination of faeces samples

The texture of the faeces showed no significant differences between both groups.

The older the foals became the wider the range in the findings became but with a tendency to become softer the older the

foal. After 18 hours only 9% of the foals had typical faeces for milk-nutrition. In total 4 foals showed severe signs of meconium retention during or after the study.

#### Dry matter

With increasing age there was a significant decrease of dry matter in the faeces from 5 h p.n.: 36.3  $\pm$  7.1%, 10 h p.n.: 31.6  $\pm$  6.0%, 14 h p.n.: 28.1  $\pm$  5.5%, 18 h p.n.: 25.6  $\pm$  5.2% in all groups with no significant difference between groups.

The mean average for dry matter in faeces was at all points lower in the placebo group than in the Kinderlax<sup>®</sup>-group. However, this difference was not significant.

#### Crude ash

Crude ash content did not change over time and groups.

#### pH value

pH in faeces decreased from a median 7.12 (25/75 Q: 6.87/7.39) 5 h p.n. to a median 6.89 (25/75 Q: 6.71/7.02) 18 h p.n. without significant differences between treatment groups.

## Discussion

In children macrogol is shown to be safe and effective for the treatment of acute constipation and long term treatment of chronic obstipation (De Giorgio et al. 2011, Treepongkaruna et al. 2011, Wang et al. 2012). It is superior to other laxatives such as lactulose or magnesium milk and less invasive than enemas (Gordon et al. 2016).

To the authors knowledge, in foals comparable studies are missing so far. In order to evaluate whether PEG could improve to prevent meconium retention in neonatal foals, macrogol was used as an add-on to an enema, which is common in the prevention of meconium retention and compared to a placebo-group as control.

**Table 3** Number of foals in which sonography revealed findings of the jejunum | Anzahl an Fohlen bei denen abweichende Befunde des Jejunums in der ultrasonografischen Untersuchung beobachtet wurden

	Placebo-group	Kinderlax <sup>®</sup> -group
Divergent wall thickness	2	3
Dilatation	27	28
Motility	Hypomotility	23
	Hypermotility	0
Ingesta	Hypoechogenicity	11
	Hyperchogenicity	1
	Inhomogeneity	12
		16
		1
		9

During the whole study no foal showed any signs of adverse effects, dehydration or abnormal vital parameters. The leucocyte count of 11 foals belonging to both groups was out of range, but normalized within two days without any treatment. Therefore, no side effects on the WBC was noted.

The sonographic findings of the jejunum and duodenum turned out to be without any significant difference between both groups. Also, the findings of the visual and laboratory testing of the faeces samples showed no difference, fecal pH values and dry matter content dropped in both groups due to the change from meconium to milk faeces.

In total 11 foals showed signs of meconium retention, 8 of the placebo-group and 3 of the Kinderlax®-group. 3 foals in the placebo-group and 1 in the Kinderlax®-group required intensive treatment. Because of the low number of foals with symptoms, this difference was not significant and the outcome reflects the range of biological variation.

In conclusion in this double-blinded, placebo-controlled study in new-born foals no advantage of macrogol for the prevention of meconium retention in foals was found.

The dosage used in this study was approximately 50% lower than the lowest recommended dose in children. This might be a reason why macrogol proved ineffective in the prevention of meconium retention in this study. However, in our preliminary test with a dosage of 16 g per foal all foals showed moderate to severe signs of colic, so the use of higher doses at once in foals is not advisable. The repeated administration of the dosage used here might be an option resulting in a better effect. Furthermore, there are no studies about macrogol in human infants. The intestine barrier in new-born foals is not as tight as in older ones because of the need of absorbing immunoglobulins. This may lead to a higher absorption rate of macrogol in new-born foals than in children which would reduce the active concentration in the intestine further.

In this study macrogol showed no additional effect in preventing meconium retention in foals.

## References

- Bernard W. (2004) Colic in the foal. *Equine Vet. Educ.* 16, 319–323
- Candy D., Belsey J. (2008) Macrogol (polyethylene glycol) laxatives in children with functional constipation and faecal impaction: a systematic review. *Arch. Dis. Child.* 94, 156–160; DOI 10.1136/adc.2007.128769
- Chaffin M. K., Cohen N. D. (1999) Diagnostic Assessment of Foals with Colic. *American Association of Equine Practitioners*, proceeding 45, 235–242
- De Giorgio R., Cestari R., Corinaldesi R., Stanghellini V., Barbara G., Felicani C., Di Nardo G., Cucchiara S. (2011) Use of macrogol 4000 in chronic constipation. *Europ. Rev. Med. Pharmacol. Sci.* 15, 960–966
- Dupont C., Leluyer B., Amar F., Kalach N., Benhamou P.-H., Mouterde O., Vannerom P.-Y. and a Multicenter Group (2006) A Dose Determination Study of Polyethylene Glycol 4000 in Constipated Children: Factors Influencing the Maintenance Dose. *J. Pediatr. Gastroenterol. Nutr.* 42, 178–185
- Dupont C., Leluyer B., Maamri N., Morali A., Joye J.-P., Fiorini J.-M., Abdelatif A., Baranes C., Benoît S., Benssoussan A., Boussioux J. L., Boyer P., Brunet E., Delorme J., Francois-Cecchin S., Gottrand F., Grassart M., Hadji S., Kalidjian A., Languépin J., Leissler C., Lejay D., Livon D., Lopez J. P., Mougnot J. F., Risse J. C., Rizk C., Roumaneix D., Schirrer J., Thoron B., Kalach N. (2005) Double-Blind Randomized Evaluation of Clinical and Biological Tolerance of Polyethylene Glycol 4000 Versus Lactulose in Constipated Children. *J. Pediatr. Gastroenterol. Nutr.* 41, 625–633
- Graßl M., Ulrich T., Wehrend A. (2017) Inzidenz und Letalität häufiger neonataler Erkrankungen beim Fohlen während der ersten 10 Tage post natum in einer Veterinärklinik. *Tierärztl. Praxis G* 45, 5
- Gordon M., MacDonald J. K., Parker C. E., Akobeng A. K., Thomas A. G. (2016) Osmotic and stimulant laxatives for the management of childhood constipation (Review) *Cochrane Database System. Rev.* 8. Art. No.: CD009118; DOI 10.1002/14651858.CD009118.pub3
- Hughes F. E., Moll H. D., Slone D. E. (1996) Outcome of surgical correction of meconium impaction in 8 foals. *J. Equine Vet. Sci.* 16, 172–175
- Koppen I. J. N., Lammers L. A., Benninga M. A., Tabbers M. M. (2015) Management of Functional Constipation in Children. *Therap. Pract. Pediatr. Drugs* 17, 349–360; DOI 10.1007/s40272-015-0142-4
- McCue P. (2006) Meconium Impaction in Newborn Foals. *J. Equine Vet. Sci.* 26, 152–155
- Pusterla N., Magdesian K. G., Maleski K., Spier S. J., Madigan J. E. (2004) Retrospective evaluation of the use of acetylcysteine enemas in the treatment of meconium retention in foals: 44 cases (1987–2002). *Equine Vet. Educ.* 16, 133–136
- Prange T. (2013) Small colon obstructions in foals. *Equine Vet. Educ.* 25, 293–296; DOI 10.1111/eve.12040
- Scharner D., Dudziak N., Winter K., Brehm W. (2015) Laparotomie beim Fohlen – Auswertung von 98 Fällen (2001–2011). *Pferdeheilkunde* 31, 20–26; DOI 10.21836/PEM20150103
- Treepongkaruna S., Simakachorn N., Pienvichit P., Varavithya W., Tongpenyai Y., Garnier P., Mathiex-Fortunet H. (2011) A randomised, double-blind study of polyethylene glycol 4000 and lactulose in the treatment of constipation in children. *Europ. Rev. Med. Pharmacol. Sci.* 15, 960–966
- Vatistas N. J., Snyder J. R., Wilson W. D., Drake C., Hildebrand S. (1996) Surgical treatment for colic in the foal (67 cases): 1980–1992. *Equine Vet. J.* 28, 139–145
- Voskuil W., de Lorijn F., Verwijs W., Hogeman P., Heijmans J., Mäkel W., Taminiu J., Benninga M. (2004) PEG 3350 (Transipeg) versus lactulose in the treatment of childhood functional constipation: a double blind, randomised, controlled, multicentre trial. *Gut* 53, 1590–1594; DOI 10.1136/gut.2004.043620
- Wang Y., Wang B., Jiang X., Xu C., Shao C., Jia L., Huang Z., Xu X., Liu H., Shang I. (2012) Polyethylene glycol 4000 treatment for children with constipation: A randomized comparative multicenter study. *Experiment. therap. med.* 3, 853–856; DOI: 10.3892/etm.2012.491