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# Potential Use of Oxytocin as a Prokinetic Drug in Horse

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## ABSTRACT

**Objective:** To test the hypothesis that oxytocin could alter gastrointestinal motility and, therefore, be potentially useful as a prokinetic drug in the horse.

**Method:** On day 1, 200 barium-impregnated polyethylene spheres (diameter=3.2, weight=20mgr) were administered to each of 30 healthy, adult Warmblood horses via nasogastric intubation. During the next three days the following variables were recorded: gut motility, defecation frequency per day, weight of feces per defecation and intestinal transit time. On day 5, following the administration of barium spheres, horses were randomly separated in two even subgroups. The first subgroup received 0.07IU/kg of oxytocin intravenously while the second subgroup received 0.14IU/kg. During the next three days the same variables were recorded of each horse.

**Results:** Oxytocin administration led to a statistically significant increase in gut motility ($p<0.01$ for subgroup 1 and 2). That increase was transit, lasting for almost an hour post-administration and was more consistent for subgroup 2. As far as defecation frequency and fecal weight are concerned, it seems that oxytocin administration led to small but statistically significant increase in both subgroups which was noted only for the day of oxytocin's administration. Oxytocin administration led to a faster intestinal transit time in both subgroups ($p<0.001$). It is worth noting that although no statistically significant difference was found between the two subgroups in any of the variables, 3 horses of the second subgroup showed signs of abdominal discomfort that reached its peak 35 minutes post-administration and subsided spontaneously within 30 minutes.

**Conclusion:** Oxytocin could be useful as a prokinetic drug in cases of gastrointestinal disease as it increases gut motility, daily defecation frequency, fecal weight per defecation and intestinal transit time. Moreover, this effect was not found to be non-dose dependent, therefore the lower dose is recommended.

**Key words:** gut motility, horse, oxytocin, prokinetic drugs

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## INTRODUCTION

A multitude of equine disorders are associated with decreased or abnormal intestinal motility and horses may potentially benefit from primary or adjunctive pharmacological therapy to enhance motility [1]. These disorders include gastric impaction, pyloric stenosis, anterior enteritis, impactions of the ileum, caecum and large colon, grass sickness and post-operative ileus, among other less common disorders. The practitioner must decide if stimulating motility using prokinetic therapy is indicated based on physical examination parameters, exact or presumed diagnosis and known indications/contraindications [1]. A number of medications have been utilised by equine practitioners in attempts to promote motility of the GI tract caused by various conditions, such as parasympathomimetics, benzamides, sodium channel blockers, macrolide antimicrobials dopamine antagonists, a-adrenergic antagonists, and opioid antagonists [1]. Still, there is a vivid interest in discovering new substances in the treatment of the equine intestinal hypomotility.

Oxytocine is a centrally synthesized peptide of nine amino-acids that is critically involved in both central and peripheral aspects of mammalian attachments and survival [2,3]. Animal research has demonstrated oxytocin's unique role in induction or enhancement of uterine contractions at parturition, treatment of postpartum retained placenta, metritis, uterine involution after manual correction of prolapsed uterus, milk letdown or agalactia [4] as well as protective aggression against intruders, in aspects of social behavior and bonding between mother and infant and between mating pairs [5,6].

Recently, in humans, it has been hypothesized that oxytocin also contributes to the control of gastrointestinal (GI) motility [7]. Oxytocin is secreted into the blood in response to stimulation of endogenous cholecystokinin (CCK), to consumption of a fatty meal, and to exogenous CCK administration in women [8]. In contrast to what was found in animals till now [9-11], intravenous infusion of oxytocin stimulated colonic peristalsis and accelerated gastric emptying in healthy women [12,13]. Oxytocin relaxed the ileum and the caecum, while it had a contracting effect on the colon, both in vitro [14,15] and in vivo [9,10,16]. These effects may be explained by the fact that oxytocin and its receptors have been found throughout the GI tract, predominately on the myenteric plexus and interstitial cells of Cajal (ICCs) [17,18]. Clinically, women with constipation have shown improvement during lactation, a state in which the levels of oxytocin in plasma are high [19]. In an open based pilot trial, it was found that nasal inhalation of oxytocin increased stool frequency in constipated women [20].

The aim of this study was to test the hypothesis that oxytocin could alter gastrointestinal motility and, therefore, be potentially useful as a prokinetic drug in the horse.

## MATERIALS AND METHODS

In this study, 30 healthy, adult Warmblood horses (18 were geldings and 12 mares) were used. Their age ranged between 6 to 15 years. In order to acquire objective data, the trial was randomized, double-blinded and all data were collected by the same clinician. Throughout the period of the study, all 30 horses were kept under the same stable conditions with unlimited access to water. Each horse was regularly receiving 9 kg of alfa-alfa hay in three servings, at 8.00, at 13.00 and at 19.00. Governmental Ethical Committee approval was taken before starting the study.

In order to quantitatively record the normal bowel function, on day 1, 200 barium-impregnated polyethylene spheres (diameter=3.2, weight=20mgr) were administered to each horse via nasogastric intubation. During the following three days each horse was monitored (heart and respiratory rate) and gut motility was assessed by auscultation. Moreover, the following variables were recorded:

- Defecation frequency per day
- Weight of feces per defecation
- Intestinal transit time through the barium-impregnated polyethylene spheres. Counting of the barium-impregnated polyethylene spheres was done by fecal radiographic examination.

The second phase of the project started on day 5 and its aim was to assess the effect of oxytocin administration on gastrointestinal motility. In order to so, horses were randomly separated in two even subgroups. In both subgroups, the left jugular vein was aseptically catheterized and 200 barium-impregnated polyethylene spheres (diameter = 3.2, weight = 20mgr) were administered again to each horse via nasogastric intubation. The first 15 horses comprised the first subgroup and received 0.07IU/kg of oxytocin while the remaining 15 horses comprised the second subgroup and received 0.14IU/kg. Both dosages were diluted within 1lt of NaCl 0.9% and the administration lasted 20 minutes. During the next three days the same variables as before were recorded of each horse.

## RESULTS

### Gut motility

Before the administration of oxytocin, all clinical parameters (gut motility, heart rate and respiratory rate) were within normal limits. Horses were not influenced by the administration of the barium-impregnetated polyethylene spheres.

| | Day 1 | | Day 5 | | |
|---|---|---|---|---|---|
| Horse Number | Gut motility | Heart rate - Respiratory rate | Gut motility | Heart rate - Respiratory rate | |
| 1 | 2 | 36 - 12 | 4 | 40 - 12 | Subgroup 1 |
| 2 | 2 | 36 - 12 | 3 | 44 - 16 | |
| 3 | 3 | 36 - 12 | 4 | 36 - 12 | |
| 4 | 2 | 40 - 12 | 4 | 44 - 16 | |
| 5 | 2 | 40 - 12 | 4 | 40 - 12 | |
| 6 | 3 | 36 - 12 | 4 | 36 - 12 | |
| 7 | 2 | 36 - 12 | 3 | 44 - 16 | |
| 8 | 2 | 36 - 12 | 4 | 40 - 12 | |
| 9 | 3 | 36 - 12 | 3 | 44 - 16 | |
| 10 | 2 | 40 - 12 | 4 | 44 - 16 | |
| 11 | 2 | 40 - 12 | 3 | 40 - 12 | |
| 12 | 3 | 36 - 12 | 4 | 44 - 16 | |
| 13 | 2 | 40 - 12 | 3 | 44 - 16 | |
| 14 | 3 | 36 - 12 | 4 | 36 - 12 | |
| 15 | 2 | 36 - 12 | 3 | 44 - 16 | |
| 16 | 2 | 36 - 12 | 3 | 54 - 18 | Subgroup 2 |
| 17 | 3 | 36 - 12 | 4 | 60 - 18 | |
| 18 | 2 | 36 - 12 | 3 | 40 - 12 | |
| 19 | 2 | 36 - 12 | 3 | 36 - 12 | |
| 20 | 2 | 36 - 12 | 3 | 40 - 12 | |
| 21 | 3 | 36 - 12 | 4 | 52 - 18 | |
| 22 | 3 | 36 - 12 | 4 | 60 - 18 | |
| 23 | 2 | 36 - 12 | 3 | 36 - 12 | |
| 24 | 2 | 36 - 12 | 3 | 44 - 12 | |
| 25 | 2 | 40 - 12 | 3 | 40 - 12 | |
| 26 | 2 | 36 - 12 | 4 | 40 - 12 | |
| 27 | 2 | 36 - 12 | 3 | 40 - 12 | |
| 28 | 2 | 36 - 12 | 3 | 44 - 12 | |
| 29 | 3 | 36 - 12 | 4 | 60 - 18 | |
| 30 | 2 | 36 - 12 | 4 | 44 - 16 | |

**Table 1. Clinical parameters and gut motility before and after oxytocin administration**

As mentioned before, the first phase lasted for three days; horses were kept under the same stable conditions for two more days and were then divided in two even subgroups. The second phase of the project started on day 5 with the first subgroup receiving 0.07IU/kg of oxytocin and the second 0.14IU/kg. Horses were again monitored for the same parameters till day 7.

Data were analyzed by descriptive statistics, by Mann-Whitney U test for bowel motility and by Wilcoxon Signed-Ranks test for heart rate and respiratory rate. It is obvious that oxytocin administration led to a statistically significant increase in gut motility ($p<0.01$ for subgroup 1 and 2) (Table 1).

| | Day 1 | | Day 5 | | |
|---|---|---|---|---|---|
| Horse Number | Defecation frequency | Fecal weight (kgr) | Defecation frequency | Fecal weight (kgr) | |
| 1 | 4 | 5 | 4 | 6 | Subgroup 1 |
| 2 | 7 | 8 | 7 | 9,5 | |
| 3 | 5 | 11 | 7 | 15,5 | |
| 4 | 6 | 8,5 | 6 | 9,5 | |
| 5 | 6 | 9 | 6 | 9 | |
| 6 | 5 | 9,5 | 7 | 13,5 | |
| 7 | 6 | 8,5 | 7 | 9,5 | |
| 8 | 5 | 5 | 5 | 6,5 | |
| 9 | 6 | 7,5 | 6 | 7,5 | |
| 10 | 7 | 10,5 | 8 | 12,5 | |
| 11 | 5 | 8 | 6 | 9,5 | |
| 12 | 5 | 7,5 | 6 | 9,5 | |
| 13 | 6 | 8 | 6 | 8 | |
| 14 | 5 | 10 | 6 | 13 | |
| 15 | 7 | 9 | 8 | 11,5 | |
| 16 | 5 | 6 | 6 | 7,5 | Subgroup 2 |
| 17 | 7 | 8 | 9 | 10 | |
| 18 | 5 | 6 | 5 | 7,5 | |
| 19 | 6 | 9 | 7 | 10 | |
| 20 | 5 | 9 | 6 | 9 | |
| 21 | 7 | 11 | 7 | 14 | |
| 22 | 6 | 7,5 | 6 | 9 | |
| 23 | 5 | 5 | 7 | 7 | |
| 24 | 6 | 8 | 6 | 9,5 | |
| 25 | 7 | 11 | 7 | 15 | |
| 26 | 4 | 5 | 4 | 7 | |
| 27 | 7 | 7,5 | 8 | 9 | |
| 28 | 6 | 9 | 8 | 10 | |
| 29 | 6 | 10 | 6 | 10 | |
| 30 | 6 | 11 | 6 | 13 | |

**Table 2. Defecation frequency and fecal weight before and after oxytocin administration**

More specifically, for subgroup 1 almost all horses (14/15) increased their gut sounds; this increase in bowel movement lasted for approximately 60 minutes and no statistically significant difference was noted for consecutive measurements. The gut motility increase was more pronounced for subgroup 2, where all horses (15/15) responded to oxytocin administration. Moreover, for the second subgroup, although a statistically significant increase was not noted for respiratory rate and heart rate, it needs to be pointed out that 3 horses showed signs of abdominal discomfort that reached its peak 35 minutes post-administration and subsided spontaneously within 30 minutes. Although, those horses did show a marked increase in heart rate,

the later was not proven to be statistically significant. It is worth mentioning here that of these 3 horses 2 were geldings and 1 was a mare.

**Defecation frequency and fecal weight**

The defecation frequency and fecal weight were calculated for subgroups 1 and 2 (Table 2) and data were analyzed by Wilcoxon Signed-Ranks test.

For subgroup 1, as far as defecation frequency is concerned, it seems that oxytocin administration led to small but statistically significant increase (p=0.008) which was noted on Day 5. More specifically, 6 horses (40%) increased defecation frequency by 1, 2 horses (13.33%) by 2 while in 7 horses defecation frequency remained stable. After that period horses returned to their normal defecation frequency. The same result was found for fecal weight. Oxytocin administration led to a significant increase in fecal weight for one day in subgroup 1 (p=0.002). In total 12 horses (80%) increased their fecal weight by 1kgr (3/15), 1.5kgr (3/15), 2kgr (2/15), 2.5kgr (1/15), 3kgr (1/15), 4kgr (1/15) or 4 even 4.5kgr (1/15). That effect was not found after Day 5.

For subgroup 2, statistical analysis led to similar results as to subgroup 1. As far as defecation frequency is concerned, oxytocin administration led to a mild but relatively significant increase (p=0.015). Four horses (26.66%) increased defecation frequency by 1 and 3 (20%) by 2. That increased was recorded only for Day 5. After that period horses returned to their normal defecation frequency. The same result was found for fecal weight. Oxytocin administration led to a statistically significant increase in fecal weight for one day in subgroup 2 (p= 0.001). In total 13 horses (86.66%) increased their fecal weight by 1kgr (2/15), 1.5kgr (5/15), 2kgr (4/15), 3kgr (1/15), 4kgr (1/15). That effect was not found after Day 5.

**Intestinal transit time**

Data from both subgroups (Tables 3 and 4) were analyzed by Wilcoxon Signed-Ranks test and oxytocin administration led to a faster intestinal transit time which was expressed by faster appearance of barium spheres in the feces as well as a higher percentage of them in the feces 72 hours post-administration. That result was statistically significant for both subgroups (p<0.001). For subgroup 1, the first appearance of barium spheres was accelerated by 2hours (1/15), 3hours (8/15) or 4 hours (6/15). For the same subgroup the percentage of spheres found in the feces 72 hours post administration increased by 5% (1/15), 10% (8/15) or even 15% (6/15). Likewise, for subgroup 2 horses after oxytocin administration accelerated their intestinal transit time by 3 hours (9/15) or 4 hours (6/15); as far as the percentage of spheres found in the feces 72 hours post administration is concerned, that increased by 10% (10/15) or 15% (5/15).

| | Before oxytocin administration | | After oxytocin administration (0,07IU/kg) | |
|---|---|---|---|---|
| Horse Number | First appearance of barium spheres in the feces after administration (hours) | % of Barium spheres in feces 72 hours post administration | First appearance of barium spheres in the feces after administration (hours) | % of Barium spheres in feces 72 hours post administration |
| 1 | 9 | 80 | 6 | 95 |
| 2 | 11 | 80 | 8 | 95 |
| 3 | 11 | 90 | 7 | 100 |
| 4 | 13 | 80 | 9 | 90 |
| 5 | 10 | 75 | 7 | 90 |
| 6 | 15 | 90 | 11 | 100 |
| 7 | 9 | 80 | 6 | 90 |
| 8 | 12 | 80 | 9 | 90 |
| 9 | 10 | 90 | 7 | 100 |
| 10 | 10 | 90 | 6 | 100 |
| 11 | 13 | 80 | 9 | 95 |
| 12 | 12 | 80 | 8 | 95 |
| 13 | 11 | 80 | 9 | 90 |
| 14 | 13 | 90 | 10 | 95 |
| 15 | 12 | 80 | 9 | 95 |

**Table 3. Intestinal transit time of subgroup 1**

| | Before oxytocin administration | | After oxytocin administration (0,14IU/kg) | |
|---|---|---|---|---|
| Horse Number | First appearance of barium spheres in the feces after administration (hours) | % of Barium spheres in feces 72 hours post administration | First appearance of barium spheres in the feces after administration (hours) | % of Barium spheres in feces 72 hours post administration |
| 16 | 9 | 85 | 6 | 95 |
| 17 | 9 | 80 | 6 | 90 |
| 18 | 12 | 90 | 8 | 100 |
| 19 | 11 | 80 | 8 | 95 |
| 20 | 12 | 90 | 8 | 100 |
| 21 | 9 | 80 | 6 | 95 |
| 22 | 13 | 80 | 10 | 95 |
| 23 | 11 | 80 | 7 | 90 |
| 24 | 14 | 80 | 10 | 95 |
| 25 | 11 | 90 | 8 | 100 |
| 26 | 10 | 80 | 7 | 90 |
| 27 | 9 | 80 | 6 | 95 |
| 28 | 11 | 80 | 7 | 90 |
| 29 | 12 | 90 | 8 | 100 |
| 30 | 9 | 80 | 6 | 90 |

**Table 4. Intestinal transit time of subgroup 2**

It is worth noting that no statistically significant difference was found between the two subgroups.

**DISCUSSION**

Colic is considered by horse owners and equine veterinarians to be one of the most important (if not the most important) medical problems in horses [22]. The term colic comprises nearly 100 conditions recognized to result in abdominal pain [22]. Alteration of gastrointestinal motility is often the underlying cause for abdominal pain [23]. Gastrointestinal propulsive motility depends on a complex interaction between neural, hormonal, vascular, and neuromuscular pathways. Disruption of this intricate interaction leads to stasis of aboral movement of food material, also called ileus. Unfortunately, this is a common and often fatal problem in the horse. A variety of prokinetic agents have been used in the horse with variable success [23]. A number of medications have been utilized by equine practitioners in attempts to promote motility of the GI tract caused by various conditions, such as parasympathomimetics, benzamides, sodium channel blockers, macrolide antimicrobials, dopamine antagonists, a-adrenergic antagonists, and opioid antagonists. This lengthy list implies the lack of a single efficacious prokinetic medication for all motility disorders in the horse [1].

In this study an effort was made to investigate the potential use of oxytocin as a prokinetic drug in the horse. So far the only application of oxytocin in equine gastrointestinal disorders was to relax the esophagus in cases of esophageal obstruction [24]. As mentioned before, though, in humans, it is hypothesized that oxytocin contributes to the control of gastrointestinal motility, as and its receptors have been found throughout the GI tract, predominately on the myenteric plexus and interstitial cells of Cajal [7,8,12,13,17,18]. So, the aim of this study was to clinically evaluate the response of the equine gastrointestinal tract to oxytocin administration.

In order to do so, 30 animals have been studied. Their normal clinical parameters and intestinal motility have been recorded and they were, then, divided in two subgroups. The first subgroup received a relatively low dose of oxytocin (0,07IU/kg) while a high dose of the same substance (0,14IU/kg) was administered to the second one. The optimal dose of oxytocin and route of administration for induction remains controversial. Some researchers and clinicians promote the use of low doses of oxytocin as being more physiological and less likely to induce untoward delivery complications [25]. Still, the slow intravenous injection is reported to have fewer complications and it is commonly used in equine practice [26]; that method of administration was chosen in the present study.

Oxytocin's prokinetic effect was evaluated through clinical auscultation but also through defecation frequency, fecal weight and most importantly through administration of barium – impregnated polythelene spheres.

As far as auscultation is concerned, it was found that intestinal motility increased in both subgroups. That increase started straight after the oxytocin administration and lasted for approximately one hour. Both subgroups responded to oxytocin administration in a similar way, although in the second subgroup the increase was slightly more pronounced and more dependable as all horses altered their sounds. It has to be noted here though, that with the higher dose horses became agitated, as it is expressed by the increased in heart and respiratory rate. Moreover, 3 horses showed signs of abdominal discomfort. Although it was expected that mares would be more prone to suffering from colic following administration of oxytocin, no such predisposition was found in this study. These signs responded spontaneously; still, as no statistically significant difference in gut motility was found between subgroups, one would advise in favor of the lower dose which manages to increase gut sounds without producing any side effects to the horse.

Similar results were found when analyzing results for defecation frequency and fecal weight. The response to oxytocin was mildly positive with both groups marginally increasing the numbers of defecations and fecal weight for the first day of administration. Again, no substantial difference was noted between the two subgroups which shows that oxytocin effect was not dose dependent, at least not for the concentrations used in this study.

Finally, similar results were seen when evaluating horses' response to oxytocin administration as far as its ability to accelerate intestinal transit time is concerned. Although, it seems that there is a higher response to higher dosage, no statistically significant result was found between subgroups.

In general, it is obvious that oxytocin can increase gut motility in healthy equines. This effect is transient and lasts for approximately one hour post administration. This positive effect on the intestine is similar to what was seen in humans where recently oxytocin and oxytocin receptor mRNA has been found in full-thickness biopsies of human gastrointestinal tract, predominantly on the myenteric plexus and interstitial cells of Cajal [17,18]. Therefore, it is likely that oxytocin in both horses and humans exerts its actions on the gut via receptors on smooth muscle cells or receptors in the enteric nervous system. Binding of oxytocin to its cognate receptor induces smooth muscle contractions in mammary myoepithelial cells and uterus myometrium [27]. It is tempting to speculate that the same intracellular signal cascade takes place in the smooth muscle cells of the gut [13]. Furthermore, systemically administered oxytocin is transported across the blood–brain barrier and may thus act directly upon oxytocin receptors in the central nervous system [28], which may influence the efferent impulses to the gut [13]. Systemically administered oxytocin may also induce the release of other neurotransmitters and/ or peptides in the gut in the same way as it stimulates atrial natriuretic peptide (ANP) secretion from the heart and nitric oxide (NO) production in vascular endothelial cells [13]. That thought is supported by the fact that so far no one was able to demonstrate any oxytocin receptors in the rat GI tract. This might explain why the effects evoked by oxytocin on gastric and intestinal motility in rat are suggested to be mediated by release of cholocystokinin (CCK) and CCK receptors, which in turn leads to motility inhibition in the proximal GI tract [29]. The latter also applies in horses and has been used clinically in esophageal obstructions [24], so it can be speculated that oxytocin exerts its prokinetic effect on the equine gastrointestinal tract in a similar way as in other species. Moreover, CCK is produced by endocrine cells in the proximal small intestine and is released into the blood [30]. The question is how oxytocin mediates this release of CCK, and the oxytocin receptor antagonist atosiban inhibits the release [29], if no oxytocin receptors are present in the GI tract [18]. Theoretically, intraperitoneal oxytocin and atosiban injections may cross the blood–brain barrier [31] and exert central effects by activating respective inhibit vagal neurons in the dorsal vagal complex that are involved in the regulation of CCK secretion [32]. However, other, as yet unknown, mechanisms may be involved.

This study shows that like in normal rats and healthy humans, oxytocin administration did manage to increase intestinal motility in horses. Still, same like other prokinetic drugs, the effect of oxytocin in sick horses remains to be tested. In humans, although oxytocin has been shown to stimulate colonic motility in healthy women [13], it failed to improve gut function in constipated subjects which included patients with a comparable, advanced constipation. One pathological mechanism in constipation might be the lack of a proper reaction to physiological stimulus. There might be disturbances at the receptor level or in intracellular signal cascade pathways. Even if a substance has an effect on normal cells, it is not certain that it has any effect on pathological cells with an abnormal function [7]. The same problems arose with other prokinetic drugs where it has been postulated that intestinal ischemia, distention and leucocyte infiltration as well as peritoneal inflammation [1] often change the pharmacological properties of a drug or the gastrointestinal response to it. Another plausible explanation for oxytocin's failure to improve clinical symptoms in actual cases of constipation in humans could be related to the dose or route of administration. Perhaps, the short half-time of oxytocin, in combination with only two nasal administrations daily,

might explain the absence of effects on constipation in that study [7]. In our study, oxytocin was given intravenously at a relatively high doses and it did lead to a transient increase in gut motility and faster passage of spheres in both subgroups. As expected, that effect was short-term as the half-life of exogenous oxytocin is 6.8min [33]. Whether it can be clinically useful remains to be tested.

It is interesting to note that oxytocin had a tendency for a positive effect on abdominal pain and discomfort in humans and laboratory animals [34]. In rats, oxytocin has been shown in several studies to increase the threshold for peripheral pain [35,36]. Children suffering from recurrent abdominal pain exhibited lower plasma levels of oxytocin than healthy controls [37]. Oxytocin receptors have been found on dorsal roots ganglia, an important area for joint pain processing [38], and on enteric nerve plexa and nerve fibres in the bowel wall [7]. Oxytocin may thus act on peripheral afferent neurons. Furthermore, 1–2% of circulating oxytocin crosses the blood-brain barrier [39]. Inhaled oxytocin may therefore exert its effects also directly on central neurons. Under physiological conditions, oxytocin is released into the circulation in response to physical contact and massage [40] and a fatty meal [8]. Oxytocin is at the same time released centrally via neuronal projections emanating from the paraventricular nuclei of the hypothalamus [41]. The oxytocin, serotonin and dopaminergic systems are interconnected by these pathways [42,43]. In this study, oxytocin administration not only did it not produce analgesia but a few horses showed signs of abdominal discomfort as well. It has to be stressed once again that all horses in the present study were normal and not actual cases. Perhaps, in actual equine colic cases, oxytocin could show similar analgesic properties as it does in other species. Moreover, in rats and humans the administration of oxytocin produces antistress and antinociceptive effects that persist for several weeks after the administration [7]. If that applies to horses, it could also be proven beneficial in the treatment of equine gastrointestinal diseases. Again, that also waits to be investigated in future studies.

In conclusion, based on the results of this study it seems that oxytocin administration has a positive effect on gastrointestinal motility. Moreover, this effect was not found to be non-dose dependent as no statistically significant result was seen between subgroups. Both groups showed similar increase in intestinal motility, defecation frequency, fecal weight and intestinal transit time. Moreover, a non-negligible percentage (20%) developed signs of colic. Although these signs were transient, there is no reason why one should take such a risk. The exact mechanism of oxytocin's action of the gut, the presence of oxytocin receptors within the intestinal wall and its relation with cholecystokinin in the horse wait to be investigated in future studies.

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