

# Risk of post-anaesthetic colic in horses anaesthetised with two different anaesthetic protocols: single-centre retrospective study

Yleisanestesian jälkeisen ähkyn esiintyvyys kahdella eri anestesiaprotokollalla nukutetuilla hevosilla: retrospektiivinen tutkimus

## ► SUMMARY

Post-anaesthetic colic (PAC) has been reported as one of the most common peri-anaesthetic complication in horses. There is limited amount of information on the effects of anaesthetic regimes and the incidence of PAC. We analysed the medical records of horses anaesthetised at University of Helsinki Veterinary Teaching Hospital between January 2013 and December 2016. Horses anaesthetised for orthopaedic surgeries, castrations or phallectomies with isoflurane and either romifidine or lidocaine constant rate infusion (CRI) were included in the study. Uni- and multivariable analyses were used to investigate the relationship between the PAC and the following risk factors: lidocaine or romifidine CRI, acepromazine, type of opioids, local anaesthesia, type of NSAIDs and antibiotics, sex, age, weight, season, procedure, preoperative hospitalisation, positioning, time of surgery, duration of anaesthesia and the duration of postoperative hospitalisation. Significance was set at  $p < 0.05$ . There were 233 anaesthetic episodes of horses with isoflurane, of which 127 received a romifidine CRI and 106 a lidocaine CRI. Overall incidence of PAC was 6.87 % ( $N = 16 / 233$ ). Incidence of PAC was 3.77% ( $N = 4 / 106$ ) and 9.44% ( $N = 12 / 127$ ) in horses receiving lidocaine and romifidine CRI, respectively ( $p = 0.09$ ). Increasing body weight was identified as a predisposing risk factor for PAC ( $p = 0.047$ ; odds ratio of 1.8 for a 100 kg increase). Use of different opioids and acepromazine and preoperative hospitalisation were possible confounding factors. This study did not show differences in the incidence of PAC in horses anaesthetised with isoflurane and romifidine or lidocaine CRIs. However, further prospective studies are required to investigate the effect of different anaesthetic protocols for the incidence of PAC.

## ► YHTEENVETO

Nukutuksen jälkeinen ähky on yleisimpiä anestesia-komplikaatioita hevosilla. Erilaisten nukutusprotokollien vaikutusta nukutuksen jälkeisen ähkyn esiintyvyyteen hevosilla on tutkittu vain vähän. Kävimme läpi Helsingin Yliopiston Yliopistollisessa eläinsairaalsa 1.1.2013 – 31.12.2016 ortopediseen leikkaukseen, kastroitioon tai penisamputaatioon isofluraanilla ja joko lidokaiini ( $n = 106$ )- tai romifidiini-infuusiolla ( $n = 127$ ) nukutettujen hevosten potilastiedot. Käytimme yhden muuttujan analyysiä sekä monimuuttuja-analyysiä selvittääksemme nukutuksen jälkeisen ähkyn ja seuraavien tekijöiden välistä yhteyttä: lidokaiini- tai romifidiini-infuusio, asepromatsiiniesilääkitys, hevoselle käytetty opioidi, paikallispuudutuksen käyttö, hevoselle käytetty tulehduskipulääke ja antibiootti, ikä, paino, sukupuoli, asento leikkauksen aikana, leikkauksen vuorokaudenaika, sairaalassaolo ennen leikkausta, vuodenaika, toimenpide, anestesian kesto ja leikkauksen jälkeisen sairaalassaoloajan pituus. Nukutuksen jälkeisen ähkyn esiintyvyys oli 6,87 % ( $n = 16$ ). Esiintyvyys oli 3,77 % ( $n = 4$ ) lidokaiini-infuusiolla nukutetuilla hevosilla ja 9,44 % ( $n = 12$ ) romifidiini-infuusiolla nukutetuilla ( $p = 0,09$ ). Tutkituista tekijöistä ainoastaan hevosen suuri paino tunnistettiin nukutuksen jälkeiselle ähkylle altistavaksi riskitekijäksi (vetosuhte 1,8 jokaiselle 100 kg:n nousulle painossa). Eri opioidit, asepromatsiini-esilääkitys ja sairaalassaoloaika ennen leikkausta olivat mahdollisia sekoittavia tekijöitä. Emme todenneet merkitseviä eroja nukutuksen jälkeisen ähkyn esiintyvyydessä lidokaiini- ja romifidiini-infuusiolla ja isofluraanilla nukutettujen hevosten välillä. Tarvitaan lisää prospektiivisiä tutkimuksia, jotta voidaan paremmin selvittää eri nukutusprotokollien vaikutusta nukutuksen jälkeisen ähkyn esiintyvyyteen.

## INTRODUCTION

General anaesthesia in horses is often performed using a balanced anaesthetic technique (*i.e.* co-administration of intravenous agents to minimise the undesirable side effects of inhalant anaesthetics and to improve perioperative analgesia). The co-administration of an injectable agent as a constant rate infusion (CRI) in combination with volatile anaesthetic agent has been defined as partial intravenous anaesthesia (PIVA). Several injectable drugs have been investigated for their suitability for this purpose in a horse.<sup>1,2</sup> Among them, infusion of lidocaine (an amide-like local anaesthetic agent) during equine anaesthesia has gained attention due to the potential analgesic,<sup>3,4</sup> anaesthetic-sparing<sup>5,6</sup> and anti-inflammatory effects of this agent.<sup>7,8</sup> However, CRI of lidocaine has been associated with increased ataxia during the recovery phase of anaesthesia, leading to poorer quality of recovery compared to that achieved with alpha-2 adrenergic agonists (alpha-2 agonists).<sup>9</sup> For this reason, many anaesthetists have switched to PIVA techniques that include alpha-2 agonist. Romifidine is an alpha-2 agonist drug widely used in horses. It provides sedation and analgesia<sup>10</sup> with significantly less ataxia in a standing horse than other alpha-2-agonists detomidine and xylazine.<sup>11</sup> Romifidine CRI has been shown to decrease the amount of isoflurane needed for equine general anaesthesia,<sup>12,13</sup> albeit not consistently.<sup>14</sup> Additionally, the use of romifidine tends to improve the quality of recovery.<sup>14</sup> The cardiovascular side effects typical for alpha-2-agonists, such as decreased cardiac output and consequently reduced oxygen delivery, are a concern in alpha-2-agonist-CRI during general anaesthesia.<sup>15</sup> Moreover, romifidine, like other alpha-2-agonists, reduces gastrointestinal motility<sup>16</sup> and may thus exacerbate hypomotility associated with general anaesthesia.

Colic has been reported as a common complication after anaesthesia in horses,<sup>17</sup> with an incidence varying between 2.5% and 21.4% depending on the study.<sup>18-23</sup> The reported risk factors for increased risk of PAC are performing anaesthesia for surgical procedure (in contrast to diagnostic imaging), elective orthopaedic surgery and anaesthetising the horse out-of-hours.<sup>18-20</sup> Some studies have identified benzyl penicillin or ceftiofur as a risk

## TAKE HOME –MESSAGE

- Post-anaesthetic colic is among the most common peri-anaesthetic complication in horses and hence horses should always be monitored for colic signs after general anaesthesia.
- Heavier horses have increased risk of developing post-anaesthetic colic.
- Choosing either lidocaine or romifidine CRI with isoflurane did not have a statistically significant influence on incidence of post-anaesthetic colic.

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factor for PAC,<sup>20,22</sup> whereas controversy exists regarding morphine as a risk factor.<sup>18,20</sup> Certain breeds, such as Arabians and Thoroughbreds, may have increased risk for PAC.<sup>21,22</sup> Conversely, providing feed normally prior to anaesthesia may reduce the risk for PAC.<sup>23</sup>

Since there is a lack of consistency among the equine clinics included in the studies as to what factors may prevent or facilitate the development of post-anaesthetic colic in anaesthetised horses, our primary aim was to investigate retrospectively in a teaching equine hospital whether the incidence of PAC was higher in horses anaesthetised with isoflurane and an adjunctive CRI of romifidine than in horses that received an adjunctive CRI of lidocaine. The secondary aim was to investigate possible risk factors for PAC. Our hypothesis was that there is no significant difference in the incidence of PAC in horses anaesthetised with isoflurane and romifidine CRI compared with horses anaesthetised with isoflurane and lidocaine CRI.

## MATERIALS AND METHODS

### Study design

We conducted a retrospective observational study and reviewed all medical records of horses receiving general anaesthesia at the Veterinary Teaching Hospital of the University of Helsinki between 1 January 2013 and 31 December 2016. Foals less than 12 months of age and pregnant mares were excluded from the study as well as

horses undergoing surgery other than castration, arthroscopy, neurectomy or other minor elective orthopaedic or soft tissue surgery, and horses euthanised during surgery and horses anaesthetised with some other protocol besides isoflurane and either a romifidine or lidocaine CRI. If a horse had more than one general anaesthesia during the study period, each anaesthesia was recorded as a separate event. Out of all included anaesthetic episodes, 127 were performed with isoflurane (Attane<sup>a</sup>) and a romifidine (Sedivet<sup>b</sup>) CRI, and 106 with isoflurane and a lidocaine (Lidocain<sup>c</sup>) CRI.

The information obtained from the medical records were the horse's age (years), breed, body mass (kg) and sex (gelding, mare, stallion) as well as the time (daytime from 8 am to 4 pm, evening from 4 pm to midnight or night from midnight to 8 am) and date of surgery, recumbency during surgery (lateral vs. dorsal), type of antimicrobials and non-steroidal anti-inflammatory drugs given, the anaesthetic protocol used (romifidine vs lidocaine group), tranquilizers (acepromazine (Plegicil<sup>d</sup>) yes vs. no), the opioids given (levomethadone (L-Polamivet<sup>e</sup>), morphine (Morphin<sup>f</sup>) or butorphanol (Butordol<sup>g</sup>)), local anaesthetic techniques used (yes vs no), duration of anaesthesia (min), whether the horse had had previous general anaesthesia within the past week (yes vs no), the duration of hospitalisation (days) and whether the horse was hospitalised pre- and/ or postoperatively.

All horses underwent pre-anaesthetic assessment on the day of the surgery. All horses were sedated with either detomidine (Domosedan<sup>c</sup>) or romifidine prior to induction of general anaesthesia. After sedation, anaesthesia was induced by a rapid intravenous injection of racemic ketamine (Ketaminol<sup>e</sup>) at 2.2 mg/ kg and midazolam (Midazolam Hameln<sup>g</sup>) or diazepam (Stesolid Novum<sup>h</sup>) at 0.03–0.08 mg/ kg. General anaesthesia was maintained after endotracheal intubation with isoflurane in 100% oxygen delivered via a large-animal circle system and either a lidocaine (lidocaine group; loading dose 1.5 mg/ kg in 15 minutes, then maintenance at 3 mg/ kg/ h) or romifidine CRI (romifidine group; CRI 0.04 mg/ kg/ h). If the horse was not breathing spontaneously, mechanical ventilation was instituted (data not analysed). Intraoperative monitoring consisted of a clinical evaluation of the anaesthetic depth, electrocardiography,

**TABLE 1 TAULUKKO**

Results collected from patient data regarding perianaesthetic medications of horses anaesthetised with isoflurane and either lidocaine or romifidine constant rate infusion. NSAIDS = non-steroidal anti-inflammatory drugs.

Potilasohjelmasta poimitut tiedot isofluraanilla ja joko lidokaiini- tai romifidiini-infuusiolla nukutettujen hevosten saamista muista anestesiaan liittyvistä lääkityksistä.

Medication Lääkitys	Lidocaine group Lidokaiiniryhmä (n=106)	ROMIFIDINE GROUP Romifidiiniryhmä (N=127)	TOTAL Yhteensä (N=233)
<b>Opioidit Opioids</b>			
Butorphanol Butorfanoli	106	113	219
Levomethadone Levometaconi	0	11	11
Morphine Morfiini	0	1	1
No opioid Ei opioidia	0	2	2
<b>Acepromazine Asepromatsiini</b>			
Acepromazine Asepromatsiini	21	90	111
No acepromazine Ei asepromatsiinia	85	37	122
<b>Local anaesthesia Paikallisuudutus</b>			
Local anaesthesia Paikallisuudutus	5	39	44
No local anaesthesia Ei paikallisuudutusta	101	88	189
<b>Antimicrobial drugs Mikrobilääkkeet</b>			
Benzyl penicillin Bentsyylipenisilliini	64	28	92
Benzyl penicillin + gentamicin Bentsyylipenisilliini + gentamysiini	33	15	48
Procain penicillin Prokaiinipenisilliini	3	52	55
Procain penicillin + gentamicin Prokaiinipenisilliini + gentamysiini	5	30	35
Other antimicrobial Muu mikrobilääke	1	1	2
No antimicrobial Ei mikrobilääkettä	0	1	1
<b>NSAIDS Tulehduskipulääkkeet</b>			
Flunixin meglumine Fluniksiinimeglumiini	95	113	208
Meloxicam Meloksikaami	1	14	15
No NSAID Ei tulehduskipulääkettä	10	0	10

respiratory gases, pulse oximetry, invasive blood pressure and arterial blood gases. If hypotension (i.e. mean arterial pressure < 70 mmHg) was noticed, it was treated with a dobutamine (Dobutect<sup>1</sup>) CRI to effect (0.5–2 µg/ kg/ min). All horses received a balanced electrolyte solution (Ringer Lactate) intravenously during anaesthe-

sia. After the completion of the surgical procedure, the horses were transferred to a padded recovery box and allowed to recover from anaesthesia without assistance. Supplemental oxygen was provided via a nasal tube. Either intravenous detomidine (lidocaine group, standard dose 2.5 µg/ kg) or romifidine (romifidine group, standard

dose 20 µg/ kg) was given intravenously when the horse was extubated to provide additional sedation for the recovery phase. The horses were returned to their boxes in the stable within 30–60 minutes after standing up. If the horse was still clinically sedated, a muzzle was placed around the mouth to prevent attempts to eat shavings. About 6 hours after the anaesthesia, feeding with small amounts of hay was started, after which feeding was increased gradually. The horses were observed by a veterinary nurse. Clinical examination and recording of faecal output were carried out every 8 hours by veterinary students or veterinary nurses under supervision of a veterinarian for as long as the horse was hospitalised.

The surgical procedure types were also obtained and categorised as “arthroscopies” (which also included minimally invasive surgeries on structures other than articular ones, i.e. tendon sheath). They were further classified as “elective” or “septic”, in addition to “castrations”, “neurectomies” and “other surgeries”. If two procedures were performed during a single anaesthetic episode, the case was categorised according to the procedure that was believed to cause most nociception.

The season of the year when the surgery took place was also recorded. If surgery was carried out during November, December, January, February and March, the season was classified as “winter”, since horses are not pastured during these months in Finland. If the surgery took place during April and May, the season was classified as “spring”, since this is the transition time. Surgeries performed during June, July and August were entered into “summer” category, since horses are commonly pastured during these months. Surgeries that were performed during September and October were classified as “autumn”, which is the transition time from pasture to stable feeding.

The presence (yes) or absence (no) of signs of colic in the first 24 hours after recovering from general anaesthesia was recorded. Colic signs were defined as decreased appetite and faecal output as well as clinical signs of abdominal discomfort such as pawing, rolling, flank-watching and teeth-grinding. If a horse had showed signs of colic, the time between anaesthesia recovery and the onset of signs, as well as any further diagnosis, treatment and outcome were obtained from the medical records.

If the horse had been discharged from

**TABLE 2 TAULUKKO**

Combination of single categories with low frequencies that were used to evaluate the incidence of post-anaesthetic colic in horses anaesthetised with isoflurane and a constant rate infusion of either lidocaine or romifidine. Matalien esiintyvyyksien vuoksi tehdyt kategorioiden yhdistämiset tutkittaessa nukutuksen jälkeisen ähkyn esiintyvyyttä isofluraanilla ja lidokaiini- tai romifidiini-infuusiolla nukutetuilla hevosilla.

Variable Muuttuja	Categories Kategoriat	Action Toiminto
Antibiotics Antibiootit	All antibiotic treatment combinations without benzyl penicillin Kaikki antibioottiyhdistelmät ilman bentsyylipenisilliiniä	Combined to form the "Other antibiotics" category Yhdistettiin muodostamaan "Muut antibiootit"-kategoria
Procedure Toimenpide	All other procedures besides "septic arthroscopies" Kaikki muut toimenpiteet kuin "septinen artroskopia"	Combined Yhdistettiin
Breed Rotu	All other breeds besides "Standardbred", "Warmblood" and "Finnhorse" Kaikki muut rodut kuin "lämminväriäinen", "puoliverinen" ja "suomenhevonen"	Combined Yhdistettiin
Pre-op hospitalisation Sairaalassaolo Ennen Leikkausta	Numeric variable Numeerinen arvo	Dichotomized into the no hospitalisation vs hospitalisation variable Muokattiin kyllä/ ei-tyyppiseksi muuttujaksi
Opioids Opioidit	All other categories besides "Butorphanol" Kaikki muut paitsi "butorfanoli"	Combined to form the "Other" category Yhdistettiin muodostamaan "Muut"-kategoria
Positioning Asento	All other categories besides dorsal Kaikki muut paitsi selällään	Combined to form the "Other" category Yhdistettiin muodostamaan "Muut"-kategoria

hospital sooner than 24 hours after recovering from anaesthesia, we contacted the owner via telephone or e-mail and asked whether the horse had showed signs of colic as described in previous paragraph during the first day after surgery. If we could not reach the owner or the owner did not remember with certainty whether the horse had had colic signs or not, the case was excluded.

### Data analysis

Data were entered into a spreadsheet (Excel) and analysed statistically using commercially available software (SAS System for Windows, version 9.4<sup>b</sup>). If a category showed a low frequency (i.e.  $N < 25$ ), a category combination was made for data analysis purposes.

The effects of the pre-defined factors, such as age, body mass, sex, acepromazine, type of antibiotics, use of gentamicin (only horses using benzyl penicillin), anaesthesia protocol, type of opioids, local anaesthesia, type of NSAIDs, procedure, time of surgery, positioning, duration of anaesthesia, season, pre-operative hospitalisation and post-operative hospitalisation (days) were

analysed with univariable logistic regression models. The models included the incidence of colic as the response variable and the factor at hand as the sole fixed effect.

Explanatory variables with a  $p$ -value of  $< 0.1$  in the univariable analysis were included in a multivariable logistic regression model. The anaesthesia protocol (romifidine vs. lidocaine) was forced into the model as a fixed factor. Other explanatory variables were selected into the final model using a stepwise approach. In the stepwise selection process, a significance level of 0.15 was required to allow a variable into the multivariable model, and a significance level of 0.20 was required for a variable to stay in the multivariable model. Akaike Information Criteria (AIC) were used to assess the model fit. In the logistic regression, the results were quantified with odds ratios (OR) and their 95% confidence intervals (CIs).  $P$ -values of  $< 0.05$  were considered statistically significant.

### RESULTS

#### Overall incidence of colic and animals

A total of 638 general anaesthetic proce-

dures were carried out on horses within the study period. Out of these, 405 were excluded from further investigation due to following reasons: 65 anaesthesias were performed on horses less than 12 months old, 41 anaesthesias were executed with a protocol differing from both of the investigated protocols, 6 horses were euthanised on the surgical table or in the recovery box, 262 anaesthesias were done for a type of surgery other than castration, arthroscopy, neurectomy or other minor elective procedure, and the follow-up was lost for 30 horses that were discharged from hospital on the day of surgery. Out of the included 233 equine anaesthesias, there were 16 cases of post-anaesthetic colic, leading to an incidence of 6.87%.

The most common breed within the included population was Warmblood ( $N = 115$ , 49.4%), followed by Standardbred ( $N = 34$ , 14.6%) and Finnhorse ( $N = 28$ , 12.0%). The rest were ponies ( $N = 21$ , 9.01%), Icelandic horses ( $N = 7$ , 3.00%), Arabian horses ( $N = 6$ , 2.58%), Irish Cobs ( $N = 4$ , 1.72%) and miscellaneous breeds including Friesian horse, Appaloosa, American Bashkir curly horse, PRE (Pura Raza

**TABLE 3 TAULUKKO**

Univariate analysis of investigated post-anaesthetic colic risk factors in horses anaesthetised with isoflurane and a constant rate infusion of lidocaine or romifidine. If P-value was < 0.1, variable was included to multivariate analysis. \* = variable included to multivariate analysis.

Yhden muuttujan analyysi nukutuksen jälkeisen ähkyn riskitekijöistä isofluraanilla ja lidokaiini- tai romifidiini-infusiolla nukutuilla hevosilla. Jos P-arvo oli < 0.1, muuttuja otettiin monimuuttuja-analyysiin. \* = monimuuttuja-analyysiin otettu muuttuja.

Variable Muuttuja	Comparison Vertailu	Odds ratio Vetosuhde	95 % confidence Interval 95 % luottamusväli		P-value P-arvo
			Lower limit Alaraja	Upper limit Yläraja	
Age (years) Ikä (vuosia)	Age Ikä	1.047	0.950	1.153	0.354
Body mass (kg) Paino (kg)	100 kg increase 100 kg painonnousu	1.620	0.947	2.772	0.078*
Sex Sukupuoli	Gelding vs stallion Ruuna vs ori	1.739	0.469	6.446	0.408
	Mare vs stallion Tamma vs ori	2.353	0.724	7.643	0.155
Acepromazine Asepromatsiini	Yes vs No Kyllä vs ei	2.574	0.865	7.658	0.089*
Antibiotics Antibiootti	Other vs benzyl penicillin Muut vs bentsyylipenisilliini	1.583	0.572	4.379	0.376
Gentamicin Gentamysiini	No vs yes Ei vs kyllä	0.287	0.065	1.255	0.097
Protocol Protokolla	Romi vs Lido	2.661	0.832	8.509	0.099*
Opioids Opioidit	Other vs butorphanol Muut vs butorfanoli	4.322	1.072	17.424	0.040*
Local anaesthesia Paikallisuudutus	Yes vs No Kyllä vs ei	0.991	0.270	3.637	0.989
NSAID Tulehduskipulääke	Meloxicam vs flunixin Meloksikaami vs fluniksiini	0.919	0.113	7.473	0.937
Procedure Toimenpide	Septic arthroscopy vs Other Septinen artroskopia vs muu	2.170	0.750	6.279	0.153
Daytime / evening Vuorokaudenaika	Daytime vs Evening Päivä vs ilta	0.467	0.123	1.771	0.263
Positioning Asento	Other vs Dorsal Muu vs selällään	1.090	0.293	4.047	0.898
Duration of anaesthesia Nukutuksen Kesto	10 min increase 10 minuutin lisäys	1.023	0.854	1.225	0.808
Season of the year Vuodenaika	Spring vs autumn Kevät vs syksy	4.933	0.568	42.830	0.148
	Summer vs autumn Kesä vs syksy	0.822	0.050	13.599	0.891
	Winter vs autumn Talvi vs syksy	3.289	0.397	27.231	0.270
Hospitalised preop Sairaalahoidossa ennen leikkausta	Yes vs no Kyllä vs ei	2.417	0.866	6.748	0.092*
Hospitalised postop (days) Sairaalahoidossa leikkauksen jälkeen	1 day increase 1 päivän lisäys	1.074	0.943	1.223	0.284

Espanola) horse, a Shire horse and Trakehner horse. The median age of the horses was 4 years (range 1–24 years) and mean body mass 485 kg (SD ± 98.3 kg). Mares represented 24.5% of the population (N = 57), geldings 21.5% (N = 50) and stallions 54.1% (N = 126).

### Anaesthetic procedures

Different perianaesthetic drugs used in

horses are presented in Table 1. Before the induction of anaesthesia, all horses allocated to the romifidine group were sedated with either intravenous romifidine or detomidine, while all horses allocated to the lidocaine group received intravenous detomidine. It was not possible to differentiate reliably from all records whether the horses belonging to the romifidine group had received romifidine or detomidine as

a premedication nor the dose of alpha-2 agonist given and, hence, these data were not analysed.

The most common surgical procedure was castration (N = 110, 47.21%) followed by arthroscopy of septic joint (N = 53, 22.75%) and elective arthroscopy (N = 50, 21.46%). Rest of the procedures (N = 20, 8.58%) included penile tumour resections, neurectomies, splint bone fragment remov-

**TABLE 4 TAULUKKO**

Final multivariate analysis of post-anaesthetic colic risk factors in horses anaesthetised with isoflurane and a constant rate infusion of lidocaine or romifidine. *P*-value < 0.05 was considered statistically significant. \* = statistically significant value. Lopullinen usean muuttujan analyysi nukutuksen jälkeisen ähkyn riskitekijöistä isofluraanilla ja lidokaiini- tai romifidiini-infusiolla nukutetuilla hevosilla. *P*-arvoa < 0.05 pidettiin tilastollisesti merkitsevänä. \* = tilastollisesti merkitsevä arvo.

Variable Muuttuja	Comparison Vertailu	Odds ratio Vetosuhde	95 % Confidence Interval 95 % luottamusväli		P value P-arvo
			Lower limit Alaraja	Upper limit Yläraja	
Protocol Protokolla	Lido vs romi	0.502	0.143	1.759	0.282
Body Mass (Kg) Paino (Kg)	100 kg increase 100 kg painonnousu	1.804	1.008	3.358	0.047*
Opioids Opioidit	Butorphanol vs others Butorfanoli vs muut	0.293	0.067	1.284	0.103
Hospitalised preop Sairaalahoitossa ennen leikkausta	No vs Yes Ei vs kyllä	0.453	0.154	1.331	0.150

als and a cast change done under general anaesthesia. Vast majority of procedures (N = 208, 89.27%) were done during day-time. The next most common time was the evening (N = 24, 10.30%) and only one anaesthesia (0.43%) took place at night. The horse was most commonly placed in dorsal recumbency during anaesthesia (N = 182, 78.11%). Right lateral recumbency (N = 23, 9.87%) was slightly more common than left lateral recumbency (N = 19, 8.15%). Data regarding recumbency were missing on nine cases. Mean duration of anaesthesia was 83 minutes (SD ± 28.7 minutes).

Nearly half of the horses had anaesthesia during winter (N = 98, 42.06%). Spring was the next most common season (N = 51, 21.89%), followed by summer (N = 46, 19.74%) and autumn (N = 38, 16.31%). Only 11 horses (4.72 %) had had previous anaesthesia within the last 7 days. Nearly two thirds of the horses (N = 149, 63.95%) arrived at the hospital on the same day when they were anaesthetised and more than half of the horses (N = 135, 57.94%) left home on the same day when they were anaesthetised.

#### Evaluated factors and their association with postanaesthetic colic

Some of the evaluated categories within the study variables had very low frequencies. Therefore, the category combinations presented in Table 2 were made for data analysis purposes.

The ORs and 95% CIs for the investigated factors are presented in Table 3. In

the univariate analyses, five meaningful factors were detected with a *p*-value of < 0.1: anaesthesia protocol used (lidocaine vs romifidine CRI), the use of acepromazine, pre-operative hospitalisation, type of opioids (butorphanol vs others) and the horse's body mass. The use of gentamicin was explored only in the subgroup of horses that received benzyl penicillin. Romifidine CRI, use of acepromazine, pre-operative hospitalisation, use of other opioid than butorphanol and increasing body mass initially seemed to be potentially predisposing factors to post-anaesthetic colic.

The results of the multivariable logistic regression are presented in Table 4. The final model included all the possible factors from the univariable analysis results except the use of acepromazine, which did not meet the pre-defined requirements of the multivariable model. Based on AIC, a model with four predictors had the best model fit. Thus, the final model included the anaesthesia protocol, the type of opioids (butorphanol vs other), body mass (kg) and pre-operative hospitalisation (yes/ no) as fixed terms and PAC as the response. The only statistically significant effect was the body mass of the horse (*p* = 0.047; OR being 1.8, with a 95% CI of 1.01–3.36, for a 100 kg increase).

#### Follow-up

Out of the 16 PAC (lidocaine n = 4, romifidine n = 12) cases, three (all romifidine) resolved spontaneously without treatment and 13 (lidocaine n = 4, romifidine n = 9) were managed medically. The most com-

mon diagnosis was large colon impaction (n = 7, romifidine n = 4, lidocaine n = 3). The treatments of colic consisted mainly of fluid therapy (enteral or intravenous) – one horse also received lidocaine CRI, one received an additional dose of flunixin, another got gastric protectants and one horse required a plasma transfusion due to suspected colitis. In nine of the 13 horses treated medically, colic signs resolved within the next 24 hours. In one horse it took 36 hours for the signs to resolve and in two of the horses it took several days. One horse was treated at the stable by a local veterinarian. The time from the start of treatment to the end of colic signs is unknown for this horse.

#### DISCUSSION

Our single-centre retrospective study detected 16 episodes of PAC among 233 horses that received isoflurane anaesthesia with a romifidine or lidocaine CRI for orthopaedic or elective soft-tissue procedures. Thus, overall incidence of PAC was 6.87% in our study population. This incidence falls well in between the range of incidences reported in other studies.<sup>18-23</sup> Since the number of colic cases was low (n = 16) in our study, it was challenging to find meaningful risk factors for PAC. Although there was a propensity towards an increased risk of PAC when romifidine was used for anaesthesia maintenance in contrast to lidocaine, this factor did not reach statistical significance either in the univariate or in the multivariable logistic

regression analysis. The only factor that was associated with an increased risk of PAC in the multivariate analysis was the heavy weight of the horse.

Weight was a significant factor, almost doubling the risk of PAC (i.e. OR = 1.8) per each 100 kg increase. To our knowledge, this is the first time that such a finding is reported. In previous studies, no link between the horse's weight and incidence of PAC has been reported.<sup>18,20,21</sup> However, heavier horses have previously been reported to have high risk for poor recovery from anaesthesia.<sup>24</sup> It is unclear why heavier horses were at a higher risk of PAC, and, whilst the size of the horse is a factor beyond the control of a veterinarian, it is meaningful to recognise it as a risk factor for post-anaesthetic complications.

Intravenous lidocaine is commonly used in horses to treat postoperative ileus.<sup>25</sup> Intraoperative lidocaine infusions have been proposed as a preventive measure to minimize the risk of PAC in horses undergoing abdominal surgery.<sup>26</sup> Whether lidocaine effectively increases gastrointestinal motility in horses is under debate. Some in-vitro and in-vivo models have shown that lidocaine does not change the jejunal motility<sup>27,28</sup> or faecal output.<sup>29</sup> Other reports have found that lidocaine may affect ion channel activity in the equine jejunal smooth muscle and therefore enhance its contractility.<sup>30</sup> In contrast, one study showed a delayed gastrointestinal transit time after prolonged administration in healthy non-anaesthetised horses.<sup>31</sup> Nevertheless, to our knowledge, no retrospective or prospective study has been able to demonstrate that infusions of lidocaine effectively prevent PAC in horses undergoing non-abdominal surgeries.

Infusions of alpha-2 agonists have been introduced in equine anaesthesia in order to improve the quality of anaesthetic recoveries, among other beneficial effects.<sup>2</sup> However, alpha-2 agonists have been long known to decrease gastrointestinal motility in horses.<sup>32</sup> Similarly to other alpha-2 agonists, romifidine decreases small intestine, caecal and large intestine motility in healthy horses.<sup>16</sup> A post-infusion incidence of colic as high as 7.5% has been found in horses sedated with this agent for dental procedures.<sup>33</sup> However, in our study, it was unclear whether romifidine was a key factor in the development of PAC. The use of other sedative agents may have

acted as a confounding factor. While all horses that received a lidocaine CRI also received butorphanol as an opioid, some horses that received romifidine CRI also received levomethadone or morphine as a co-sedative agent.

In general, opioids have been associated with decreased gastrointestinal motility in horses.<sup>29,34</sup> As for morphine, it has been previously reported that its use may increase the risk of PAC.<sup>18</sup> However, other studies reported no statistically significant differences in the incidence of PAC in horses receiving morphine preoperatively.<sup>20,35</sup> Whether levomethadone may increase the incidence of PAC has not been studied. The commercial preparation of levomethadone licensed for equine use in Finland consists of a formulation that also contains fenpipramide, a parasympatholytic agent. Therefore, it may be expected that this formulation would also potentiate a delay in gastrointestinal motility. In our study, the use of opioids other than butorphanol (i.e. the  $\mu$ -agonists morphine or levomethadone) was significantly associated with an increase in PAC in the univariate analysis. Unfortunately, with the small number of PAC cases, it was not possible to differentiate whether the use of a romifidine CRI, the use of a full  $\mu$ -agonist opioid or the combination of these two, increases the risk for PAC. Moreover, the multivariate analysis further excluded these variables as significant factors in the development of PAC.

Since acepromazine has been shown to decrease gastric emptying time in ponies,<sup>36</sup> it could predispose horses to colic due to impaction. In our study, the univariate analysis showed a tendency towards an increased risk of PAC when acepromazine was given. However, the significant association was lost in the multivariate analysis. This is in agreement with previous reports, in which no association was found between acepromazine and an increased risk of PAC.<sup>19,20</sup> Interestingly, acepromazine has been associated with an overall reduced risk of death in anaesthetised horses.<sup>37</sup> Therefore, the use of acepromazine for anaesthetic premedication should be considered, keeping in mind the other potential beneficial effects of the drug. These include mild sedation or anxiolysis and decreased peripheral vascular resistance, which may improve peripheral perfusion.

In addition to anaesthetic drugs, chang-

es in management and the stress response related to anaesthesia and surgery are thought to be explanatory factors for PAC.<sup>19</sup> In our study, pre-anaesthetic hospitalisation tended to increase the risk of PAC. Therefore, it may be implied that treating the horses as outpatients (i.e. same-day surgery) may reduce the risk. However, when this variable was confronted with the confounders, no significant differences were found, which is in agreement with a previous retrospective study.<sup>19</sup> Interestingly, neither the post-anaesthetic hospitalisation affected the incidence of PAC in the present study. These findings suggest that the decision of patient admission and discharge should be based on other patient-related factors besides the potential risk of PAC.

Fasting horses for variable amount of time before anaesthesia is common practice in order to reduce risk for colic. Incomplete records prevented the evaluation of fasting as a risk factor, which is a limitation of the study. However, feed is routinely withdrawn for 12 hours before a non-urgent anaesthesia in our hospital. A prospective multicentre study reported that horses that are not fasted before anaesthesia tend to develop PAC.<sup>20</sup> Conversely, another study reported a PAC incidence of only 2.5% in non-fasted horses anaesthetised for elective non-abdominal procedures.<sup>23</sup> Further studies are necessary to investigate the role of fasting in PAC and as Bailey et al.<sup>23</sup> suggest, commonly employed preanaesthetic feeding protocols may need to be re-evaluated.

Due to the retrospective nature of our study, it was difficult to identify the potential confounding factors, such as other drugs given to the horse, the duration of anaesthesia and the type of surgical procedure. There were also cases where a part of data was missing. These were important limitations of the study together with the single-centre setting. The small number of colic cases may have biased some results and type II error may have occurred. Further multicentre prospective studies are warranted in order to gain more information on the effects of different anaesthetic protocols on the incidence of PAC.

We conclude that there was no significant difference in the risk of post-anaesthetic colic in horses anaesthetised with isoflurane and romifidine CRI compared with horses anaesthetised with isoflurane and lidocaine CRI.

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