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Abstract: The aim of this retrospective study was to determine if there was an association between the lowest arterial blood oxygen tensions (PaO2) measured during anaesthesia and post-operative incisional complications in horses. Clinical records of 278 horses undergoing ventral midline coeliotomy from 1 January 2010 to 31 December 2013 were examined.

The frequency of incisional complications was 32.0% (n = 89). In a multivariable model, intra-operative arterial blood oxygen tensions (PaO2) was not significantly associated with development of an incisional complication (P = 0.351). Using hypertonic (7.2%) saline (P = 0.028, OR 3.167, 95% CI 1.132-8.861), increasing total plasma protein concentration (TP) (P = 0.002, OR 1.061 per g/L, 95% CI 1.021-1.102), an intestinal resection (P < 0.001, OR 4.056, 95% CI 2.231-9.323), increasing body mass (P = 0.004, OR 1.004 per kg, 95% CI 1.001-1.006) and the use of penicillin alone compared with penicillin and gentamicin pre-operatively (P = 0.009, OR 4.145, 95% CI 1.568-10.958) increased the risk of incisional complications. The study was unable to demonstrate a link between low intra-operative PaO2 and increased risk of post-operative incisional complications.

Lack of association between arterial oxygen tensions in horses during exploratory coeliotomy and post-operative incisional complications: A retrospective study

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Abstract

The aim of this retrospective study was to determine if there was an association between the lowest arterial blood oxygen tensions (PaO_2) measured during anaesthesia and post-operative incisional complications in horses. Clinical records of 278 horses undergoing ventral midline coeliotomy from 1 January 2010 to 31 December 2013 were examined.

The frequency of incisional complications was 32.0% (*n* = 89). In a multivariable model, intra-operative arterial blood oxygen tensions (PaO_2) was not significantly associated with development of an incisional complication (*P* = 0.351). Using hypertonic (7.2%) saline (*P* = 0.028, OR 3.167, 95% CI 1.132-8.861), increasing total plasma protein concentration (TP) (*P* = 0.002, OR 1.061 per g/L, 95% CI 1.021-1.102), an intestinal resection (*P* < 0.001, OR 4.056, 95% CI 2.231-9.323), increasing body mass (*P* = 0.004, OR 1.004 per kg, 95% CI 1.001-1.006) and the use of penicillin alone compared with penicillin and gentamicin pre-operatively (*P* = 0.009, OR 4.145, 95% CI 1.568-10.958) increased the risk of incisional complications. The study was unable to demonstrate a link between low intra-operative PaO_2 and increased risk of post-operative incisional complications.

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Introduction

The survival of horses undergoing emergency abdominal surgery has improved in recent decades (Freeman et al., 2000). Post-operative complications at the incision site, such as drainage or oedema, are still common (Phillips and Walmsley, 1993; Mair and Smith, 2005; Freeman et al., 2012). In a previous study, 16% of horses undergoing emergency abdominal surgery developed an incisional complication (Proudman et al., 2002); other reported rates of incisional complication range from 7.4% to 42.2% (Freeman et al., 2000; Mair and Smith, 2005; Torfs et al., 2010; Durward-Akurst et al., 2013).

Risk factors associated with an increased likelihood of incisional complications include increasing heart rate on admission (French et al., 2002), increasing body mass and increasing age (Wilson et al., 1995), performing an enterotomy (Honnas and Cohen, 1997), use of polyglactin 910 to suture the linea alba (Honnas and Cohen, 1997), using staples rather than suture material for skin closure (Torfs et al., 2010), anaesthetic duration > 110 min (Smith et al., 2007) and poor anaesthetic recovery (Freeman et al., 2012). Factors thought to reduce the incidence of incisional complications include using two rather than three layers of sutures to close the abdomen (Colbath et al., 2014) and using a stent (Tnibar et al., 2013) or an abdominal bandage to cover the incision (Smith et al., 2007).

In a study by Costa-Farre et al. (2014), horses with intra-operative arterial blood oxygen tensions (PaO_2) < 80 mmHg (10.6 kPa) were significantly more likely to develop post-operative incisional complications than those with $PaO_2 \geq 80$ mmHg (10.6 kPa). A direct correlation has also been found between arterial and subcutaneous partial pressures of O_2 and incisional infection rates in human patients undergoing colorectal surgery (Greif et al., 2000). Higher rates of wound infection have been demonstrated in rabbits exposed to hypoxic conditions (14% inspired oxygen) for 21 days postoperatively, compared with normoxic conditions (21% inspired oxygen) (Hunt et al. 1975). We hypothesised that PaO_2 measured during anaesthesia would be associated with the development of post-operative incisional complications in horses.

Materials and methods

Inclusion criteria

Clinical records of horses admitted to the Philip Leverhulme Equine Hospital for investigation of colic from 1 January 2010 to 31 December 2013 were examined. Cases were included if they had undergone ventral midline coeliotomy for correction of gastrointestinal pathology and survived for at least 7 days post surgery. Any horses that underwent repeat coeliotomy, midline coeliotomy for a cause not related to the gastrointestinal tract, or where anaesthetic records did not include PaO_2 values, were excluded. Anaesthetic, surgical and post-operative management varied between cases and was determined by the anaesthetist and surgeon involved.

Ethical approval was granted from Veterinary Research Ethics Committee University of Liverpool, UK, on 15 October 2013, approval number VREC155

Definitions

An incisional complication was defined as positive bacterial culture from an incision site swab and/or the presence of the following clinical signs: marked oedema at the incision site, purulent discharge from the incision site and hypoechoic areas around the incision site on ultrasonographic examination, with accompanying pyrexia.

Data collected

The following data were recorded from each case: age, body mass, breed, sex, heart rate (HR), packed cell volume (PCV) and total plasma protein concentration (TP) at admission, clinical signs of systemic inflammatory response syndrome (SIRS) at admission (defined as HR > 50 beats per min (bpm) and PCV > 0.5 L/L), American Society of Anesthesiologists (ASA) grade, pre-anaesthetic medication, anaesthetic induction and maintenance agents and peri-operative administration of antimicrobial agents. Intra-operative data included use of vasopressors and inotropes, fluid therapy, analgesic infusions, dexamethasone administration, mean arterial blood pressure (MAP), highest arterial partial pressure of carbon dioxide ($PaCO_2$), lowest pH, lowest PaO_2 and duration of anaesthesia. Recovery score, anaesthetist, surgeon, whether surgery was performed out of hours, type of pathology, whether an intestinal resection and/or enterotomy was performed, suture materials for abdominal closure, presence of an incisional complication before discharge from the hospital and how this was defined were also recorded.

Anaesthetic and surgical technique

Anaesthetic protocol varied and was determined by the anaesthetist involved. After induction of anaesthesia, all horses had an orotracheal tube placed, were hoisted onto a padded operating table, positioned in dorsal recumbency and the endotracheal tube connected to a large animal circle breathing system. Inhalational anaesthetic agents were vaporised in 100% oxygen and all horses were mechanically ventilated throughout.

In all cases, the surgical site was clipped and prepared aseptically with chlorhexidine, followed by surgical spirit, and an adhesive drape was placed over the incision site. The pattern of abdominal closure and the suture material used to close the abdomen was determined by the surgeon involved; however, in all cases, suture material rather than staples were used to close the skin. All horses had an adhesive dressing and an abdominal bandage for recovery.

At the end of surgery, horses were disconnected from the anaesthetic breathing system, hoisted into a padded recovery box and positioned in right lateral recumbency. Oxygen was provided via a demand value until extubation and subsequently at 15 L/min via a nasopharyngeal tube. This was continued until horse head movement dislodged the tubing.

Until discharge from the hospital, incision sites were examined at least once daily. In horses showing clinical signs of infection, the decision to swab the incision site for bacterial culture and sensitivity was determined by the attending clinician.

Blood gas analysis

During anaesthesia, arterial blood samples were taken through a cannula placed in the mandibular branch of the facial artery, which also permitted invasive arterial blood pressure monitoring. Samples were collected anaerobically into heparinised syringes (PICO50; Radiometer) following withdrawal of approximately 1 mL of blood that was discarded, and analysed immediately using a bench top blood gas analyser (ABL77; Radiometer). The timing and frequency of blood gas analysis was not standardised, and the lowest recorded PaO_2 from each horse was used for data analysis.

Statistical analysis

Statistical analyses were performed using Minitab 16 (Minitab) and Stata 13 (Statacorp). Data were tested for normality using a Ryan-Joiner test. Parametric data are presented as means ± standard deviations (SDs); non-parametric data are presented as medians with interquartile ranges (IQR). Univariable analysis was performed with Pearson's χ^2 analysis for categorical variables and binary logistic regression for continuous variables. Variables with $P < 0.2$ were offered to a multivariable logistic regression model, using both forwards and backwards stepwise entry, with a P value of 0.20 for entry and 0.21 for removal, although the final model chosen by both procedures was the same. The possible effect of the interaction of anaesthetic duration and PaO_2 was tested by forcing it into the final model. The statistical significance of entering terms into regression models was assessed by changes in the Likelihood Ratio and the Wald Statistic used to obtain the P value of coefficients in the model, together with their confidence intervals (CIs). A P value < 0.05 was considered to be significant.

Results

Of 278 horses that met the inclusion criteria from 1 January 2010 to 31 December 2013 (Fig. 1), 89 (32%) developed an incisional complication; swabs were taken from 64 of these and all were positive on bacterial culture.

Demographic data

The ages of horses ranged from 2 months to 30 years, with a mean ± SD of 12.2 ± 5.7 years, which was not significantly different between groups. Body mass ranged from 48 to 750 kg, with a median of 532 (466-600) kg. The most commonly represented breeds were Thoroughbreds (*n* = 35; 12.6%) and Cobs (*n* = 35; 12.6%), followed by Welsh ponies (*n* = 33; 11.9%) and Warmbloods (*n* = 31; 11.2%); the remaining 144 horses consisted of multiple different breeds. There were 154 (55.4%) neutered males, 112 (40.3%) entire females and 12 (4.3%) entire males; these proportions were not significantly different between groups. The median pre-operative HR was 48 (40-60) bpm, the median PCV was 0.39 (0.34-0.43) L/L and the median TP was 68 (62-72) g/L; overall 21/278 (7.6%) horses had clinical signs of SIRS on presentation.

Anaesthetic and surgical management

Horses were graded ASA 4 or 5 in 89/278 (32%) cases. The most common pre-anaesthetic medication was xylazine and morphine (211/278; 75.9%). In 233/278 (83.8%) cases, anaesthesia was induced with ketamine and diazepam or midazolam. Maintenance of anaesthesia was with isoflurane (150/278; 54.0%), sevoflurane (126/278; 45.3%) or desflurane (2/278; 0.7%); none of these variables were significantly different between groups.

Peri-operative penicillin was used in 199/278 (71.6%) cases, while 44/278 (15.8%) cases received penicillin and gentamicin. Most horses, (242/278; 87%) were treated with vasopressors and/or positive inotropes due to hypotension; the agent most frequently administered was dobutamine (210/278; 75.6%). Drugs used were not significantly different between groups. All horses received intravenous fluid therapy, including Hartmann's solution (165/278; 59.3%), Hartmann's solution with supplemental potassium chloride (112/278; 40.3%) or dextrose in saline (1/278; 0.4%); in addition, 24/278 (8.6%) received hypertonic (7.2%) saline and 64/278 (23.0%) received synthetic colloids. Continuous infusion with lidocaine was used in 184/278 (66.2%) cases and dexamethasone was administered to 34/278 (12.2%) cases; there were no significant differences between groups.

Similarly, there were no significant differences between groups in the lowest MAP, the mean MAP, the lowest pH or the highest $PaCO_2$ measured during anaesthesia. The median duration of anaesthesia was 106 (90-132) min, the minimum duration was 50 min and the maximum duration was 240 min; recovery score was not significantly different between groups. The majority of horses dislodged the nasal tubing supplying oxygen in the early stage of recovery although exact timings and numbers of horses were not recorded.

Twelve anaesthetists and 10 surgeons were involved with the surgical procedures, Pathology affected the small intestine in 168/278 (60.4%) cases and the large intestine in 110/278 (39.6%) cases. Enterotomy was performed in 117/278 (63.7%) cases and resection was performed in 75/278 (27.0%) cases. Braided lactomer (Polysorb) was used to suture the linea alba in 270/278 (97.1%) cases and polypropylene (Prolene) was used to suture the skin in 263/278 (94.6%) cases.

Blood gas analysis

One to five arterial blood gas analyses were performed in each case; in 51/278 (18.4%) horses, only one arterial blood gas sample was taken; in all cases, the first sample was taken within 40 min of anaesthetic induction. There was no significant difference in the number (mean ± SD) of blood gas analyses between cases which developed incisional complications (2.57 ± 1.08) and cases which did not develop incisional complications (2.42 ± 1.04; P = 0.305). Of the horses sampled more than once, 45/233 (19.3%) initially had a PaO_2 ≥ 100 mmHg (13.3 kPa), which reduced to < 100 mmHg on subsequent samples.

Univariable and multivariable analysis

Categorical and continuous variables associated with outcome at P < 0.2 are shown in Tables 1 and 2, respectively. Table 3 lists the variables chosen in the final regression model. The stepwise model did not require PaO_2 and, when forced into the final model, was not significant (P = 0.351). The odds ratio (OR) for each unit increase in PaO_2 was 0.999 (95% confidence interval, CI, 0.996-1.002).

Anaesthetic duration was > 2 h in 97/278 (34.9%) cases and was not associated with an increased risk of incisional complication (P = 0.427). If lowest PaO_2 was divided into categories of < 80 mmHg (10.6 kPa) and ≥ 80 mmHg (10.6 kPa) (Costa-Farre et al., 2014), this also was not associated with outcome (P = 0.379). However, when the two terms were combined with a new categorical variable with four levels (PaO_2 < 80 mmHg and anaesthetic duration ≤ 2 h; PaO_2 < 80mmHg and anaesthetic duration > 2 h; PaO_2 ≥ 80 mmHg and anaesthetic duration ≤ 2 h; PaO_2 ≥ 80 mmHg and anaesthetic duration > 2 h), this variable was statistically significant (P = 0.041), but did not materially alter the direction, size and statistical significance of the other coefficients. The adjusted coefficients for these terms suggested that, regardless of the PaO_2 level, the highest risks occurred for anaesthetic duration ≤ 2 h and these were significantly greater than the risks of anaesthetic duration > 2 h (P < 0.05).

Discussion

This study found 32.0% of horses developed an incisional complication following ventral midline coeliotomy and gastrointestinal surgery, but we did not find a link between low PaO_2 during anaesthesia and increased post-operative incisional complications. Oxygen is essential for normal wound healing; it is needed for collagen production, angiogenesis, fibroblast production and epithelialisation (Gottrup et al., 2004). Reactive oxygen species mediate destruction of bacteria within leucocytes and this effect is correlated with increasing tissue partial pressure of oxygen (Hopf and Rollins, 2007). Tissue hypoxia will reduce the effectiveness of leucocytes, resulting in decreased production of interleukins 2 and 8 (Gottrup et al., 2004), which may contribute to the development of wound infections. Human surgical patients who were hyperoxaemic in the peri-operative period were less likely to develop incision site infections (Qadan et al., 2009). However, we were unable to demonstrate the same effect in horses undergoing gastrointestinal surgery.

In human studies, an increased fraction of inspired oxygen (FiO_2) is often provided post-operatively. Greif et al. (2000) showed that human patients receiving FiO_2 0.8 (PaO_2 206 mmHg, 27.5 kPa) intra-operatively and for 6 h post-operatively had significantly fewer surgical wound infections compared with patients receiving FiO_2 0.31 (PaO_2 114 mmHg, 15.2 kPa). In contrast, supplemental oxygen was provided post-operatively in the early recovery period, initially via demand value at the end of the endotracheal tube and after extubation via nasal insufflation. The majority of horses dislodged the nasal tube supplying oxygen early on during recovery. Provision of supplemental oxygen after horses leave the recovery box presents significant practical problems and was not provided during this study. Therefore one potential reason for the lack of association found in our study is that horses were not provided with a high enough FiO_2 post-operatively to affect development of incisional complications. This may be compounded by the fact that horses are frequently hypoxaemic in the immediate post-operative period (Mason et al., 1987; McMurphy and Cribb, 1989), due to impaired pulmonary function secondary to atelectasis (Nyman et al., 1990), coupled with reduced FiO_2. However PaO_2 was not measured in the post-operative period in any of the horses in our study.

Bacterial contamination of the wound may occur in the early post-operative period (Ingle-Fehr et al., 1997), indicating that post-operative arterial and tissue oxygen tensions may be important in preventing incisional infections. However, these data were not available, since it was standard practice to remove the arterial cannula at the end of surgery. Prospective studies where arterial blood gases are analysed during recovery and in the post-operative period could be performed to investigate this further.

Costa-Farre et al. (2014) studied horses undergoing general anaesthesia for exploratory coeliotomy and found that those with a PaO_2 < 80 mmHg (10.6 kPa), combined with an anaesthetic duration > 2 h, had the highest risk of surgical site infections. To compare our findings with Costa-Farre et al. (2014), we performed an additional analysis, in which the effect of the interaction of PaO_2 < 80 mmHg and anaesthetic duration > 2 h was forced into our multivariable model. Our statistical model did not require the main effects of PaO_2 < 80 mmHg or anaesthetic duration > 2 h, but the interaction term was statistically significant at $P = 0.041$. However, in contrast to the study by Costa-Farre et al. (2014), our findings suggest that a longer anaesthesia time is protective against incisional infections. This is unexpected, since previous veterinary studies have reported increased incisional complication rates for longer durations of anaesthesia (Costa-Farre et al., 2014; Smith et al., 2007) and similar findings have also been reported in the human literature (Curry et al., 2014).

The stress response to anaesthesia and the properties of anaesthetic drugs can adversely affect the immune response (Anderson et al., 2014). Longer anaesthesia may be associated with hypothermia, which is associated with increased incisional complication rates in human beings (Kurz et al., 1996). However, an anaesthesia time > 2 h alone was not significantly associated with outcome and became significant only when forced into a statistical model that did not require its inclusion in combination with PaO_2. Therefore, the clinical relevance of this finding is questionable.

Tissue partial pressure of oxygen depends on PaO_2, but this relationship can be affected by factors reducing perfusion, such as hypovolaemia, hypotension and peripheral vasoconstriction (Chang et al., 1983). In hypovolaemia, tissue oxygen tensions will be lower for a given PaO_2 compared with normovolaemia, as demonstrated experimentally in dogs (Gottrup et al., 1987). Horses undergoing colic surgery are likely to be hypovolaemic; therefore, PaO_2 values obtained during surgery may not reflect tissue oxygen tensions. Hypovolaemia occurs in these horses due to SIRS and sequestration of extracellular fluid into the intestinal lumen (Mair and Edwards, 2003). Despite aggressive fluid therapy during anaesthesia, volume deficits may not be totally resolved before recovery. In our study, risk factors indicating that horses were hypovolaemic were significantly associated with incisional complications, including increased TP and administration of hypertonic (7.2%) saline.

Hypertonic saline was most often used immediately pre-operatively to improve circulating volume in horses showing clinical signs of hypovolaemia. Higher than normal TP is also thought to be suggestive of hypovolaemia (Mair and Edwards, 2003). It is possible that these horses had low tissue oxygen tensions (regardless of PaO_2), which contributed to the development of incisional complications; however, since tissue oxygen was not measured, this cannot be proven. Other factors indicative of hypovolaemia, such as PCV, HR (Mair and Edwards, 2003) and MAP were not significantly associated with incisional complications in the multivariable model. Intra-operative MAP may have been affected by pre-operative fluid administration, intra-operative vasopressor and inotrope use, and ventilation; therefore values may not accurately indicate volume status. Although PCV and HR alone were not associated with incisional complications, clinical signs of SIRS, which includes cases with HR > 50 bpm and PCV > 0.5 L/L was significantly associated with incisional complications ($P < 0.001$) in univariable analysis. It did not remain significant following multivariable analysis, which may be due to the low numbers of animals with SIRS included (n = 21).

Horses that had intestinal resection were at increased risk of incisional complications. Bacterial contamination of the abdominal incision site following incision into the intestinal lumen may increase the risk of surgical site infection (Honnas and Cohen, 1997). Resection is often required for strangulating intestinal lesions. Ischaemic insult following vascular occlusion leads to compromise of the mucosal barrier and translocation of bacteria and endotoxin into the bloodstream (Moore et al., 1981), which may lead to SIRS and a greater degree of hypovolaemia than with lesions not requiring resection.

Increasing body mass was found to be associated with an increased risk of developing incisional complications, as reported previously (Wilson et al., 1995). Using penicillin alone compared to penicillin and gentamicin for peri-operative antimicrobial treatment increased the frequency of incisional complications (OR 4.145, 95% CI 1.568-10.958.). The combination of penicillin and gentamicin has an extended spectrum of activity compared with penicillin alone, particularly against Gram negative organisms (Haggett and Wilson, 2008), which may have reduced the frequency of incisional complications. Only 15.8% of horses received this combination, with the majority receiving penicillin alone (71.6%), it therefore may be useful to consider penicillin-gentamicin as perioperative antimicrobial treatment for horses undergoing exploratory coeliotomy and gastrointestinal surgery.

The retrospective nature of this study results in a number of major limitations. Varying anaesthetic protocols were employed, which may have affected the results, although no significant differences were found in pre-anaesthetic medication, induction or maintenance agents between groups. A wide variety of breeds were included and therefore breed could not be subjected to meaningful statistical analysis, in contrast with Costa-Farre et al. (2014), who studied predominantly Andalusian horses (35/84; 41.7%) and had a standardised anaesthetic protocol.

The number and timing of arterial blood gas analyses in our study was not standardised. The first sample was taken within 40 min of anaesthetic induction and the number of samples taken ranged from one to five. When multiple analyses were performed, 45/233 (19.3%) horses initially had PaO_2 values > 100 mmHg (13.3 kPa), which subsequently decreased to < 100 mmHg (13.3 kPa). Since 51/278 (18.4%) horses were sampled only once, a proportion of these may have developed hypoxaemia that went undetected, potentially affecting the results.

Some potentially important factors that could contribute to post-operative incisional complications, such as body temperature, were not analysed due to the lack of data. Hypothermia increases surgical site infections in human patients (Kurz et al., 1996) and body temperature decreases in horses under general anaesthesia (Edner et al., 2007). Future prospective studies should include measurement of body temperature.

The number of layers of sutures used to close the abdomen was not consistently reported in the clinical records. Use of two layer modified subcuticular closure of the abdomen significantly reduces incisional complication rates compared with three layer closure (Colbath et al., 2014). However, a previous study using data from the same hospital as our study found no difference in incisional complication rates between two and three layer closure (Coomer et al., 2007).

The definition of incisional complications was not limited to those cases that had a positive bacterial culture from an incision site swab. Previous studies have defined incisional infection as incisional drainage persisting > 12 h after surgery (Durward-Akurst, 2013), purulent discharge with heat, pain or swelling around the incision site (Mair and Smith, 2005) and serosanguineous/purulent discharge, with or without bacterial culture (Torfs et al., 2010). Whilst these may not all represent true bacterial infections, wound suppuration and oedema have been shown to increase the risk of further complications, such as incisional herniation and dehiscence (Gibson et al., 1989; French et al., 2002). Therefore, it was considered to include horses with these case definitions even if bacterial culture was not performed.

Conclusions

This study was unable to demonstrate a link between low intra-operative PaO_2 and increased risk of developing post-operative incisional complications in horses. Other factors that could indicate poor tissue oxygen tension including use of hypertonic saline, increasing TP and requiring an intestinal resection were associated with an increased risk. Further prospective studies are required to investigate an association between tissue oxygen indices during the early post-operative period and the incidence of post-operative incisional complications.

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

References

Anderson, S.L., Duke-Novakovski, T., Singh B., 2014. The immune response to anaesthesia: Part 2 sedatives, opioids, and injectable anaesthetic agents. Veterinary Anaesthesia and Analgesia 41, 553-566.

Chang, N., Goodson, W.H., Gottrup, F., Hunt, T.K., 1983. Direct measurement of wound and tissue oxygen tension in postoperative patients. Annals of Surgery 197, 470-478.

Colbath, A.C., Patipa, L., Berghaus, R.D., Parks, A.H., 2014. The influence of suture pattern on the incidence of incisional drainage following exploratory laparotomy. Equine Veterinary Journal 46, 156-160.

Coomer, R.P.C., Mair, T.S., Edwards, G.B.E., Proudman, C.J., 2007. Do subcutaneous sutures increase risk of laparotomy wound suppuration? Equine Veterinary Journal 39, 396-399.

Costa-Farre, C., Prades, M., Ribera, T., Valero, O., Taura, P., 2014. Does intraoperative low arterial partial pressure of oxygen increase the risk of surgical site infection following emergency exploratory laparotomy in horses? The Veterinary Journal 200, 175-180.

Curry, C.S., Smith, K.A., Allyn, J.W., 2014. Evaluation of anesthetic technique on surgical site infections (SSIs) at a single institution. Journal of Clinical Anesthesia 26, 601-605.

Durward-Akhurst, S.A., Mair, T.S., Boston, R., Dunkel, B., 2013. A comparison of two antimicrobial regimens on the prevalence of incisional infections after colic surgery. Veterinary Record 172, 287

Edner, A., Nyman, G., Essén-Gustavsson, B., 2007. Metabolism before, during and after anaesthesia in colic and healthy horses. Acta Veterinaria Scandinavica 49, 34.

Freeman, D.E., Hammock, P., Baker, G.J., Goetz, T., Foreman, J.H., Schaeffer, D.J., Richter, R.A., Inoue, O., Magid, J.H., 2000. Short- and long-term survival and prevalence of postoperative ileus after small intestinal surgery in the horse. Equine Veterinary Journal Supplement 32, 42-51.

Freeman, K.D., Southwood, L.L., Lane, J., Lindborg, S., Aceto, H.W., 2012. Post operative infection, pyrexia and perioperative antimicrobial drug use in surgical colic patients. Equine Veterinary Journal 44, 476-481

French, N.P., Smith, J., Edwards, G.B., Proudman, C.J., 2002. Equine surgical colic: Risk factors for postoperative complications. Equine Veterinary Journal 34, 444-449.

Gibson, K.T., Curtis, C.R., Turner, A.S., McIlwraith, C.W., Aanes, W.A., Stashak, T.S., 1989. Incisional hernias in the horse incidence and predisposing factors. Veterinary Surgery 18, 360-366.

Gottrup, F., Firmin, R., Rabkin, J., Halliday, B.J., Hunt, T.K., 1987. Directly measured tissue oxygen tension and arterial oxygen tension assess tissue perfusion. Critical Care Medicine 15, 1030-1036.

Gottrup, F., Gellet, S., Kirkegaard, L., Hansen, E.S., Johannsen, G., 2004. Continuous monitoring of tissue oxygen tension during hyperoxia and hypoxia: Relation of subcutaneous, transcutaneous and conjunctival oxygen tension to hemodynamic variables. Critical Care Medicine 16, 1229-1234.

Greif, R., Akca, O., Horn, E.P., Kurz, A., Sessler, D.I., 2000. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. New England Journal of Medicine 342,161-167

Haggett, E.F., Wilson, W.D., 2008. Overview of the use of antimicrobials for the treatment of bacterial infections in horses. Equine Veterinary Education 20, 433-448.

Hopf, H.W., Rollins, M.D., 2007. Wounds: An overview of the role of oxygen. Antioxidants and Redox Signalling 9, 1183-1192.

Honnas, C.M., Cohen, N.D., 1997. Risk factors for wound infections following celiotomy in horses. Journal of the American Veterinary Medical Association 210, 78-81.

Hunt, T.K., Linsey, M., Grislis, G., Sonne, M., Jawetz, E., 1975. The effect of differing ambient oxygen tensions on wound infection. Annals of Surgery 181, 35-39.

Ingle-Fehr, J.E., Baxter, G.M., Howard, R.D., Trotter, G.W., Stashak, T.S., 1997. Bacterial culturing of ventral median celiotomies for prediction of postoperative incisional complications in horses. Veterinary Surgery 26, 7-13.

Kurz, A., Sessler, D.I., Lenhardt, R., 1996. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. The New England Journal of Medicine 334, 1209-1215.

Mair, T.S., Edwards, G.B., 2003. Strangulating obstructions of the small intestine. Equine Veterinary Education 15, 192-199.

Mair, T.S., Smith, L.J., 2005. Survival and complication rates in 300 horses undergoing surgical treatment of colic. Part 2: Short-term complications. Equine Veterinary Journal 37, 303-309.

Mason, D.E., Muir, W.W., Wade, A., 1987. Arterial blood gas tensions in the horse during recovery from anaesthesia. Journal of the American Veterinary Medical Association 190, 989-994.

McMurphy, R.M., Cribb, P.H., 1989. Alleviation of postanesthetic hypoxemia in the horse Canadian Veterinary Journal 30, 37-41.

Moore, J.N., White, N.A., Berg, J.N., Trim, C.E., Garner, H.E., 1981. Endotoxemia following experimental intestinal strangulation obstruction in ponies. Canadian Journal of Comparative Medicine 45, 330-332.

Nyman, G., Funkquist, B., Kvart, C., Frostell, C., Tokics, L., Strandberg, A., Lundquist, H., Lundh, B., Brismar, B., Hedenstierna, G., 1990. Atelectasis causes gas exchange impairment in the anaesthetised horse. Equine Veterinary Journal 22, 317-324.

Phillips, T.J., Walmsley, J.P., 1993. Retrospective analysis of the results of 151 exploratory laparotomies in horses with gastrointestinal disease. Equine Veterinary Journal 25, 427-431.

Proudman, C.J., Smith, J.E., Edwards, G.B., French, N.P., 2002. Long-term survival of equine surgical colic cases. Part 1: Patterns of mortality and morbidity. Equine Veterinary Journal 34, 432-437.

Qadan, M., Akca, O., Mahid, S.S., Hornung, C.A., Polk Jr, H.C., 2009. Perioperative supplemental oxygen therapy and surgical site infection, a meta-analysis of randomized controlled trials. Archives of Surgery 144, 359-366.

Smith, L.J., Mellor, D.J., Marr, C.M., Reid, S.W.J., Mair, T.S., 2007. Incisional complications following exploratory celiotomy: Does an abdominal bandage reduce the risk? Equine Veterinary Journal 39, 277-283

Tnibar, A., Grubbe, Lin K., Thuroe, Nielsen K., Christophersen, M.T., Lindegaard, C., Martinussen, T., Ekstrom, C.T., 2013. Effect of a stent bandage on the likelihood of incisional infection following exploratory coeliotomy for colic in horses: A comparative retrospective study. Equine Veterinary Journal 45, 564-569.

Torfs, S., Levet, T., Delesalle, C., Dewulf, J., Vlaminck, l., Pille, F., Lefere, L., Martens, A., 2010. Risk factors for incisional complications after exploratory celiotomy in horses: Do skin staples increase the risk? Veterinary Surgery 39, 616-620

Wilson, D.A., Baker, G.J., Boero, M.J., 1995. Complications of celiotomy incisions in horses. Veterinary Surgery 24, 506-514.

Table 1

Categorical variables associated with incisional complications at $P < 0.2$ in 278 horses undergoing general anaesthesia and coeliotomy.

	Incisional complication (n = 89)	No complication (n = 189)	P
Clinical signs of SIRS			
No	74 (83.2)	183 (96.8)	< 0.001
Yes	15 (16.8)	6 (3.2)	
Location of pathology			
Small	64 (71.9)	104 (55.0)	0.007
Large	25 (28.1)	85 (45.0)	
Enterotomy			
No	46 (51.7)	55 (29.1)	< 0.001
Yes	43 (48.3)	134 (70.9)	
Resection and anastomosis			
No	48 (53.9)	155 (82.0)	< 0.001
Yes	41 (46.1)	34 (18.0)	
Surgeon			
Surgeon 1	22 (24.7)	30 (15.8)	0.010
Surgeon 2	8 (9.0)	27 (14.3)	
Surgeon 3	3 (3.4)	28 (14.8)	
Surgeon 4	26 (29.2)	47 (24.9)	
Surgeon 5	2 (2.3)	16 (8.5)	
Surgeon 6	10 (11.8)	11 (5.8)	
Surgeon 7	9 (10.1)	18 (9.5)	
Other surgeons	9 (10.1)	12 (6.4)	
GGE for induction			
No	75 (84.3)	170 (90.0)	0.172
Yes	14 (15.7)	19 (10.0)	
Hypertonic (7.2%) saline			
No	74 (83.2)	180 (95.2)	0.001
Yes	15 (16.8)	9 (4.8)	
Antibiotics			
Procaine penicillin	68 (76.4)	131 (69.3)	0.192
Procaine penicillin + gentamicin	8 (9.0)	36 (19.0)	
Other	5 (5.6)	9 (4.8)	
None	8 (9.0)	13 (6.9)	

Data are expressed as number (%).

SIRS, systemic inflammatory response syndrome; GGE, guaiacol glycerine ether.

Table 2

Continuous variables associated with incisional complications at $P < 0.2$ in 278 horses undergoing general anaesthesia and coeliotomy.

	Incisional complication (*n* = 89)	No complication (*n* = 189)	*P*
Body mass (kg)	550 (495-614)	526 (453-581)	0.006
Initial HR (bpm)	52 (40-64)	48 (40-60)	0.196
Initial PCV (L/L)	0.39 (0.33-0.44)	0.39 (0.34-0.42)	0.131
Initial TP (g/L)	70 (64-78)	68 (62-72)	0.001
PaO_2 lowest (mmHg)	101 (65-190)	109 (70-238)	0.040
PaO_2 lowest (kPa)	13.3 (8.6-25.0)	14.3 (9.2-31.3)	0.040
Duration of anaesthesia (min)	115 (90-145)	105 (90-130)	0.117

Data are expressed as median (interquartile range).

HR, heart rate; PCV, packed cell volume; TP, total protein; $PaO_{2,}$ partial pressure of arterial oxygen; bpm, beats per min.

Table 3

Results of the final multivariable logistic regression model of risk factors associated with incisional complications in horses undergoing general anaesthesia and coeliotomy.

	OR	95% CI	*P*
Enterotomy	0.564	0.300-1.058	0.075
Resection	4.056	2.231-9.323	<0.001
Hypertonic (7.2%) saline	3.167	1.132-8.861	0.028
Initial TP (g/L)	1.061 [a]	1.021-1.102	0.002
Body mass (kg)	1.004 [a]	1.001-1.006	0.004
Antibiotics [b]			
Penicillin	4.145	1.568-10.958	0.009
Other	1.317	0.270-6.437	0.734
None	3.071	0.960-14.341	0.057

OR, odds ratio; 95% CI, 95% confidence intervals; TP, total protein.

[a] Odds ratio per unit increase in value of continuous variable.

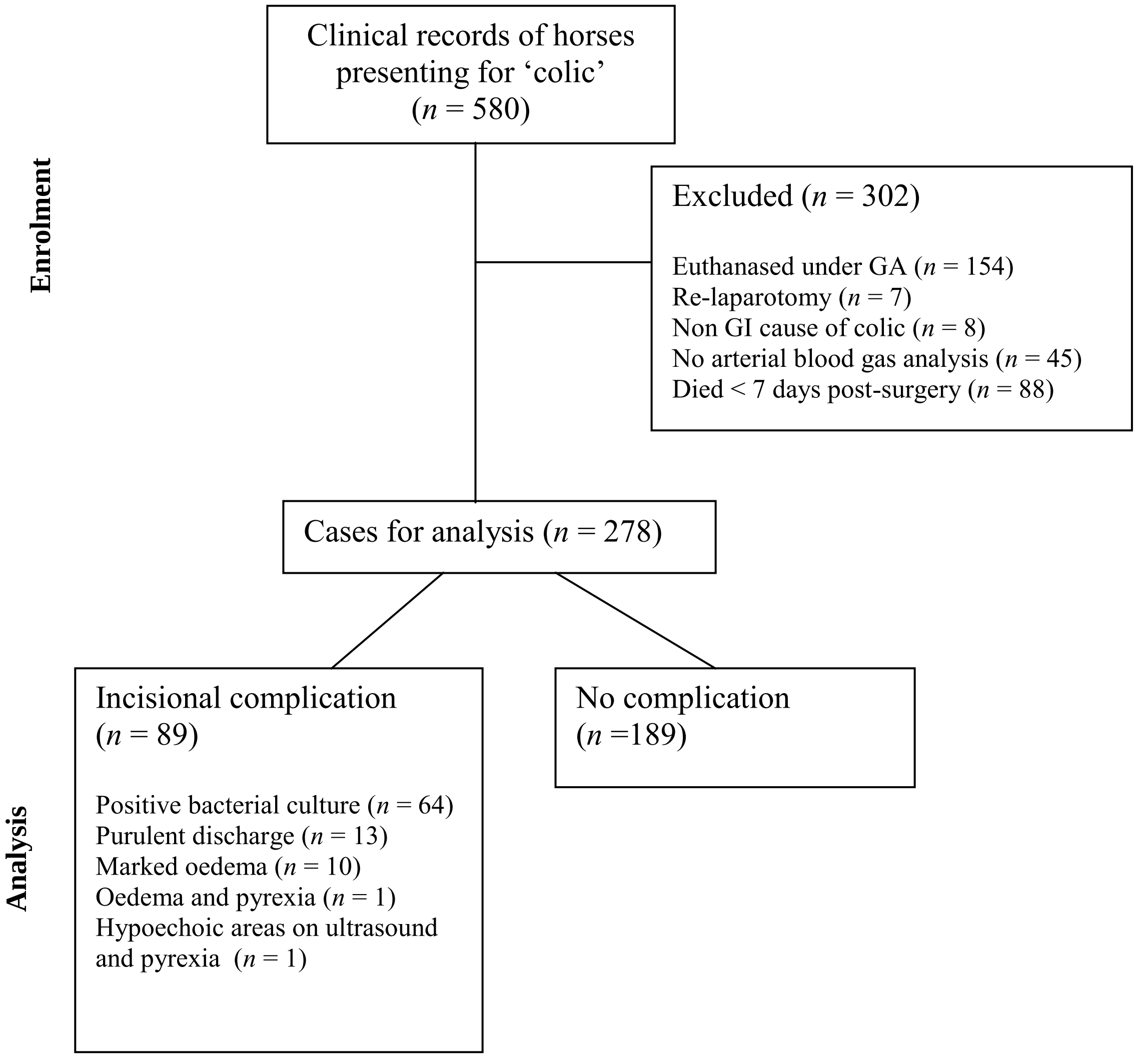
[b] Referent to penicillin and gentamicin.

Figure legend

Fig. 1. Flow diagram of case enrolment and drop out

GA, general anaesthesia; GI, gastrointestinal.

Figure 1


Clinical records of horses presenting for 'colic' (n = 580)
Enrolment
Excluded (n = 302)
Euthanased under GA (n = 154)
Re-laparotomy (n = 7)
Non GI cause of colic (n = 8)
No arterial blood gas analysis (n = 45)
Died < 7 days post-surgery (n = 88)
Cases for analysis (n = 278)
Incisional complication (n = 89)
Positive bacterial culture (n = 64)
Purulent discharge (n = 13)
Marked oedema (n = 10)
Oedema and pyrexia (n = 1)
Hypoechoic areas on ultrasound and pyrexia (n = 1)
No complication (n =189)
Analysis

Highlights

- Clinical records of horses undergoing general anaesthesia for colic were studied.
- No association was found between intra-operative PaO_2 and incisional complications in a multivariable model.
- Hypertonic saline, total protein, body mass and intestinal resections were associated with incisional complications.
- Use of penicillin was associated with more incisional complications than use of penicillin-gentamicin in combination.

***Revision Note**

I have addressed the editor's comments in the main manuscript, highlighting my changes in blue. I was copying the style of the editor's comments whereby the highlighted the areas they wanted me to address in yellow. I hope this is acceptable, if not please let me know and I can revise the manuscript differently.