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Time-related changes in post-operative equine morbidity; a single-centre study

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Suggested running title: Post-operative equine morbidity.

Acknowledgements:
We thank Dr Mark Senior for sharing the data from the original study.
Abstract

Objective

To test the hypothesis that the prevalence and type of post-operative equine morbidity (POEM) at a single centre does not change over time.

Study Design

Retrospective and prospective observational study.

Animals

The post-operative case records of 92 (of 96) horses undergoing non-abdominal procedures, and surviving to discharge, were compared with previous data from the same centre (Senior et al., 2007).

Methods

Pre-defined morbidities were recorded from horses undergoing surgery between August 2013 and July 2014. This was compared with data collected from the same institute from April 2004 to June 2005 and published in a previous study (Senior et al., 2007).

Results

The overall prevalence of morbidities increased from 13.4% to 25%. The prevalence of post-anaesthetic colic, thrombophlebitis, pyrexia, lameness, neuropathy and myopathy increased while the proportion of incidence of diarrhoea, respiratory distress and wounds sustained in recovery decreased.

Analysis - There was a statistically significant association (p = 0.045) between the duration of surgery and the prevalence of PAC (post-anaesthetic colic). Geldings were
less likely (OR 0.12, CI 0.02, 0.84) to develop swelling at the catheter site and the likelihood of thrombophlebitis increased by 1.20 (CI 1.01, 1.41) for every year of life.

Conclusions and clinical relevance

Tracking morbidities and changes in their prevalence may elucidate their possible causation and allow prophylactic measures to be taken.

Keywords: Anaesthesia; Equine; Horse; Morbidity; Post-operative
Introduction

Postoperative morbidities in horses prolong convalescence and increase hospitalisation costs (Bennett-Guerrero et al., 1999). Mild complications may resolve spontaneously and inconsequentially; severe morbidities may cause permanent lesions, precipitate natural death, or necessitate euthanasia on medical, humane or economic grounds.

Critical incident reporting and identification of factors influencing post-operative morbidities have been recognised as essential in human medicine (Bolsin et al., 2010, Smith and Mahajan, 2009, Tewari and Sinha, 2013) and the recording of postoperative morbidities is a requirement of the Royal College of Veterinary Surgeons (RCVS).

The prevalence of post-operative equine morbidities (POEMs) is sparsely described. Young and Taylor included information on anaesthetic-related problems in 19/1314 horses following general anaesthesia for non-abdominal procedures, almost all of whom suffered from myopathy (Young and Taylor, 1993). The third confidential enquiry into postoperative equine fatalities (CEPEF) described non-fatal complications but did not classify these beyond myopathies (Johnston, 2005).

A previous multicentre study (Senior et al., 2007) examined the prevalence of several morbidities affecting horses undergoing non-abdominal surgery, between April 2004 and June 2005, in four equine hospitals including the Royal (Dick) School of Veterinary Studies (R(D)SVS), which provided data from 194 anaesthetics. The principal problems identified in this study, in the first 72 hours after recovery from anaesthesia, were: post-anaesthetic colic (PAC) and prolonged recovery (7.7% and 3% respectively).
In the course of time, putative risk factors may change (e.g. yard and clinical staff, horse population characteristics) producing corresponding changes in the prevalence of morbidities. There is an expectation that morbidity rates should decrease over time with ongoing improvements in clinical practice. The purpose of the current study was to test the (null) hypothesis that the prevalence and type of morbidity at a single centre do not change over time.
Materials and Methods

After approval from the Veterinary Ethical Review Committee of the R(D)SVS (2014) the proportion of horses suffering from pre-defined morbidities (Table 1), arising between recovery from anaesthesia and hospital discharge, were recorded from horses undergoing non-abdominal surgery between August 2013 and July 2014. This data was then compared with data collected at the same institute from April 2004 and June 2005, and which had been incorporated into the multi-centre study of Senior et. al. (2007).

During both periods, animal characteristics (body weight, age, breed and sex) and pertinent case information (duration of hospitalisation, surgical categorisation e.g. orthopaedic versus soft tissue) of animals surviving surgery was entered into a database. The surgery performed was briefly noted e.g. arthroscopy, laryngoplasty. Details of POEMs were gleaned from each animal’s clinical case notes and the anaesthetic record. Further details were collected during post-operative rounds when the cases were discussed.

Two populations were defined for analysis: 2013-14 and 2004-2005 (Senior et al., 2007). Data from horses experiencing prolonged recoveries (recumbency lasting > 30 minutes per hour of anaesthesia time) were not analysed in the current study unless extraordinary interventions, e.g. slinging, were required (Senior et al., 2007).
Statistical Analysis

Statistical analyses were performed using Minitab® (version 16.0 for Windows). Comparisons were made to detect differences between groups for age, body weight, sex, elective or emergency status and anaesthesia time. Anaesthesia time was defined as the time from induction of anaesthesia until the horse was moved into the recovery box. A value of $p < 0.05$ was considered statistically significant. Each of the categories were examined for normality of distribution using a probability plot of the data. Body weight, time for hospitalisation and age were not normally distributed in comparison to anaesthesia time. A Mann-Whitney test was used to examine the non-parametric data (age and body weight) while a 2 sample t-test was used to compare anaesthesia time between groups. A $\chi^2$ test was used to analyse sex and elective-emergency status differences. Statistical analysis of changes in morbidity prevalence were carried out using a $\chi^2$ test.

The prevalence of morbidities was analysed using binary logistic regression to determine if signalment or procedure status i.e. emergency/elective, duration of surgery, age, body weight or time in the hospital, had any significant association with the individual morbidities. A two stage process was adopted. First, univariate analyses of individual variables was carried out. Second, multivariable analyses were conducted to establish if combined factors e.g. sex and age, bore significant relationships with specified morbidities. For this, those univariate terms where $p < 0.2$ were entered into initial multivariable binary logistic analyses (Hosmer and Lemeshow 2000) and terms were excluded until a final model of statistical significant terms was achieved.
Results

A total of 96 cases were recorded between 1st August 2013 and 31st July 2014. Of these 92/96 survived to discharge. Two of the anaesthetics were repeated. The previous data (Senior et al., 2007) reported a total of 194 anaesthetics for non-abdominal procedures of which full data were available for 101 cases.

The results are presented in Table 2. Information regarding age, body weight, emergency status, time in hospital and anaesthetic time only pertained to the subset of data provided by M. Senior (101 of 194 anaesthetics) while the prevalence of morbidities relate to the short communication (Senior et al., 2007).

Signalment

Horses did not differ in age (median 6.0 years in the 2004-5 and 2013-14 groups, p = 0.564). Hospitalisation time was statistically significantly longer in 2013-14 (median of 9 days vs 6 days, p < 0.01). Both data sets were incomplete with respect to sex: 2 and 4 horses were missing from the 2013-14 and 2004-2005 data sets, respectively. Geldings made up 63% of group 2013-14 compared with 49% of horses from Senior’s dataset from 2004-2005 (p<0.001). The average anaesthetic time was statistically significantly longer in procedures conducted in the most recent time period (103, compared to 87 minutes in 2004-5, p = 0.003) and the number of emergency cases was statistically significantly greater in the more recent data set (29%, compared with 21%; p <0.001).

Orthopaedic surgery was carried out in the majority of cases (54/92, 59% in 2013-14 and 58/101, 57%). The majority of the orthopaedic cases involved arthroscopy with lavage while soft tissue cases largely comprised upper airway surgery and castration.
The overall prevalence of post-operative morbidities was 13.4% when prolonged recovery was excluded in the 2004-5 data. This compares with 25% in the 2013-14 data meaning that the overall prevalence of morbidities had increased. The prevalence of PAC, thrombophlebitis, pyrexia and neuropathy, myopathy and post-operative lameness increased over time. Post-anaesthetic colic increased in prevalence from 7.7% to 18.5% (p = 0.01). In the study by Senior et al no horses experienced post-operative lameness, myopathy or neuropathy in comparison to 3% of horses in the 2013-14 data set (p = 0.06) and the proportion of horses with thrombophlebitis increased from 1% to 2% (p = 0.053). Horses classified as pyrexic increased from 0.5% in 2004-5 to 7.6% (p = 0.002). No horses had a fracture in the post-operative period in either dataset. Fewer horses suffered from diarrhoea in the 2013-14 dataset (2% vs 1%, p = 0.92). Similarly, in the 2004-5 dataset 1.5% of horses were described as being in respiratory distress compared to 0% in the 2013-14 dataset (p = 0.563). One horse (0.5%) in the 2004-5 dataset had wounds in recovery in comparison to 0% in the 2013-14 dataset (p = 0.490). Wound infections were not reported in the 2004-5 data set while one horse was reported to have a wound infection in the 2013-14 data.

**Binary Regression Analysis**

Univariate analysis revealed a statistically significant association (p = 0.045) between the duration of anaesthesia and the prevalence of PAC in horses. Duration of anaesthesia was not found to be significantly associated with the other morbidities reported. No statistically significant association was found between colic and sex (p =
0.390), time in hospital (p= 0.816), body weight (p=0.169), age (p = 0.403) or emergency status (p = 0.075). Multivariable univariate logistic regression revealed no statistically significant associations between body weight or emergency status, and PAC.

Univariate analysis of all horses revealed a statistically significant association (p= 0.036) between age and thrombophlebitis: the odd’s ratio indicated its likelihood increased by 1.20 (CI 1.01, 1.41) for every year of the horse’s life. No statistically significant relationships were found for wound infections or pyrexia.

Discussion

The purpose of the current study was to test the null hypothesis that the prevalence and type of morbidity at a single centre did not change over time. The null hypothesis was rejected as the overall prevalence of morbidities increased.

Post-anaesthetic colic, after non-abdominal surgery, increased from 7.7% (2004-5) to 18.5% (2013-14) which is statistically significant and clinically important. Additionally, there was a significant association between PAC and the duration of anaesthesia, which has not been identified previously. The prevalence of PAC was greater than that found in other studies, which ranged from 2.8% (Senior et al., 2004, Andersen et al., 2006, Mircica et al., 2003, Senior et al., 2007, Nelson et al., 2013) to 10.5% (Jago et al., 2015).
The reasons for the increase in prevalence are not known. The current study did not investigate post-anaesthetic colic with respect to administration of drugs, personnel or out-of-hours surgery. Emergency status was not associated with an increased risk. In previous studies the risk factors identified included morphine administration and out-of-hours surgery (Senior et al., 2004), decreased faecal output following surgery, the Arabian breed and increasing blood lactate (Nelson et al., 2013). Morphine was found to lead to no increased risk of colic, in contrast to the use of isoflurane and benzylpenicillin or ceftiofur (Andersen et al., 2006). Jago et al found that post-anaesthetic colic following non-abdominal surgery was significantly associated with breed, perioperative microbials and administration of butorphanol (Jago et al., 2015). Senior et al stated that the morbidities reported in the 2004-5 study were believed to be minimums and that ‘mild’ cases of colic may not have been reported (Senior et al., 2007). Senior et al also found large variations in the post-anaesthetic colic in different centres. The increase in prevalence may have been due to reporting of more ‘mild’ cases or a different population of horses. In the original data from Senior et al horses were analysed for signs of colic 72 hours following surgery whereas the most recent data included horses that displayed colic until discharge. This may go some way to explain the increase in prevalence. Given the stated risk factors in previous studies, further work investigating drugs used, faecal output and the proportion of surgeries during the out-of-hours period may be useful.

The significant association between increasing anaesthesia time and the prevalence of post-anaesthetic colic highlights the importance of minimising time spent under anaesthesia. The CEPEF study found that the likelihood of death increased as the duration of anaesthesia increased beyond 61 minutes, with the greatest risk being
operations lasting longer than 241 minutes (Johnston et al., 1995). Minimising anaesthesia time involves maximising efficiency of surgical preparation, ensuring optimal communication between anaesthesia and surgical teams and provision of sufficient personnel to reduce surgery time. The results presented reinforce the evidence that minimising the time spent by horses under anaesthesia is an important consideration for surgical intervention.

No cases of neuropathy or myopathy were recorded in horses undergoing non-abdominal procedures during the 2004-5 sampling period in contrast to 3 (out of 92) cases recorded from 2013 – 2014. Previous studies have examined the incidence of post-anaesthetic lameness. Richey at al reported an incidence of post anaesthetic lameness of 6.4%, Franci et al reported this morbidity in 0.98% of horses following surgery and Young and Taylor found that 1.2% of 575 horses developed myopathy following non-orthopaedic procedures (Young and Taylor, 1993, Richey et al., 1990, Franci et al., 2006). Richey et al found a significant association between hypotension and anaesthesia duration with respect to post-anaesthetic lameness while Young and Taylor reported no reduction of incidence when hypotension was treated but did report a decrease in severity (Young and Taylor, 1993, Richey et al., 1990). Bidwell et al reported that three cases with post-anaesthetic myopathy necessitating euthanasia were in horses that had undergone procedures lasting three or more hours (Bidwell et al., 2007). In the current study there was no significant relationship between duration of anaesthesia or body weight and the incidence of myopathy or neuropathy. The presence of hypotension during anaesthesia was not examined but this may be useful in future studies.
The prevalence of thrombophlebitis doubled in the current study from 1% to 2% and univariate analysis found a significant positive relationship between increasing age and occurrence of thrombophlebitis. Previous studies have reported thrombophlebitis in 8% to 13% horses undergoing colic surgery (Gazzerro et al., 2015, Morton and Blikslager, 2002). This may not be an appropriate comparison due to an increased incidence of coagulation abnormalities following abdominal surgery. Previous studies have examined putative risk factors: poor insertion technique, prolonged catheterisation, catheter used for induction of anaesthesia, debilitation of the horse and injection of irritants (Divers, 2003, Lankveld et al., 2001). To our knowledge, links to non-abdominal procedures have not been tested. Gazzerro et al found that geriatric horses were less likely than mature horses to have thrombophlebitis (OR 0.68) which contrasts with our findings (Gazzerro et al., 2015). However, previous studies have found increased co-existing systemic disease with increasing age in horses (Vasto et al., 2006, Fermaglich and Horohov, 2002) which may explain the greater propensity for this complication.

Wound infection was recorded in 1/92 horses in the most recent data set. This is likely to be an underestimation of the actual rate. In the current study the criteria for identification of wound infections involved a swab being taken for culture and sensitivity and a purulent or seropurulent discharge. In reality, the majority of horses were treated with antibiotics and only if the infection was non-resolving would a swab be taken. Freeman et al previously defined post-operative infection as the persistent (> 32 hours) drainage of serous, purulent or serosanguinous fluid from the incision, more than 48 hours after the post-operative period, and local or systemic treatment (Freeman et al., 2012). Further studies using less stringent criteria may yield very different results, highlighting the importance of defining morbidities.
Pyrexia may arise from inflammation or infection following surgery. In the current study, pyrexia was reported in 7/92 horses compared with 1/194 in the 2004-5 data.

The reason for this increase is unknown. No changes in the use of non-steroidal anti-inflammatory use had been implemented. No previous studies have examined the incidence of pyrexia following non-abdominal surgery in horses, but in human patients incidences vary from 9.3% to 18% (Galicier and Richet, 1985, Petretta et al., 2013, Garibaldi et al., 1985). Many of these studies failed to find a cause for the pyrexia and not all patients developed an infection. Likewise, in horses, previous studies have shown that pyrexia is not necessarily associated with infection (Freeman et al., 2012).

Further studies may aid identification of contributing factors.

Previous morbidity studies have investigated risk factors or predictors of survivability with respect to different morbidities. Common factors were; drug use, breed, procedure performed, intra-operative complications, re-laparotomy and personnel. Future studies investigating changes in morbidity with these factors may be useful. However, in order to draw firm conclusions large numbers of horses are required, necessitating a multi-centre study with similar methods of recording post-operative morbidities.

Several limitations became apparent when analysing the results of this study. In the initial study by Senior et al 194 anaesthetics were examined (Senior et al., 2007). This contrasts with the current study's data in several ways. First, the data from 2013-14 was taken over 12 months compared to 14 months in the 2004-5 data set. Ideally this data would have been matched to the exact time period and the time of year. In addition, many of the records from 2004-5 were incomplete with respect to signalment which led to the inclusion of full data for only 101/194 horses. This introduced bias as the records
of animals with significant morbidities are more likely to be complete due to the
importance of maintaining legal records when complications occur. It may also be that
other morbidities are more likely to be identified if the horse already has a complication,
owing to more frequent examination. A further concern was the binary nature of
recording, i.e. morbidity present or absent, which does not reflect the subtleties of mild,
moderate or severe clinical signs. The decision as to what is included in definitions of
morbidity is subjective and disputable (Johnston et al., 1995).

In conclusion, increases in the prevalence of morbidities were found between 2004-5
and 2013-14 following non-abdominal procedures. The expectation was that
improvements in clinical practice over time would lead to a decrease in the prevalence
of morbidities. Reasons for the overall increase in the prevalence of morbidities are
likely to be multifactorial and may include better recording practices, a change in the
population of horses or a change in clinical practice. In light of the requirement from
the RCVS to audit clinical practice, accurate identification of morbidities is essential.
Further studies would be useful to formally define each morbidity with the goal of
standardising reporting. Ideally a large scale study would be conducted to identify
influencing factors that may have been missed when analysing relatively small numbers
of cases.


Table 1. Definitions of post-operative equine morbidities identified in previous and current studies. (Tinker et al., 1997, Senior et al., 2007)

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombophlebitis</td>
<td>Inflamed vein with <em>in vivo</em> blood clot formation. Diagnosis on basis of physical signs (venous hardening, redness, warmth and/or pain), or ultrasonography.</td>
</tr>
<tr>
<td>Dyspnoea/respiratory obstruction</td>
<td>Upper airway lesion necessitating intervention e.g. tracheostomy.</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>Signs of coughing, wheezing, rales on thoracic auscultation with pink frothy fluid appearing at the nares or mouth, identified on endoscopy or at post-mortem examination.</td>
</tr>
<tr>
<td>Lameness, muscle damage, neuropathy</td>
<td>Inability to bear equal weight on all four limbs. Painful, swollen muscles, myoglobinuria, creatinine kinase values &gt;15000 iu/L. Neurological deficits causing lameness or muscle weakness.</td>
</tr>
<tr>
<td>Postoperative colic in (previously) non-colic cases</td>
<td>Any recognised sign of abdominal pain, for example, pawing the ground, kicking the abdomen, attempts to lie down (Tinker et al., 1997).</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>Rectal temperature &gt; 39 °C</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>Soft or liquid faeces with increased volume and frequency.</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>Seropurulent or purulent discharge at surgical site necessitating swabbing for culture and sensitivity.</td>
</tr>
</tbody>
</table>
Table 2. Data comparing horses undergoing non-abdominal procedures in 2013-14 and from Senior et al, 2007. *subset of data used from Senior et al.

<table>
<thead>
<tr>
<th></th>
<th>Non-abdominal 2013-14</th>
<th>Senior et al., 2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age in years (range)*</td>
<td>6 (0 - 21)</td>
<td>6 (1 - 25)</td>
</tr>
<tr>
<td>Median Body Weight in kg (range)*</td>
<td>502 (102 – 836)</td>
<td>500 (252, 690)</td>
</tr>
<tr>
<td>Median Time in Hospital in days (range)*</td>
<td>9 (0 – 145)</td>
<td>5 (1 – 36)</td>
</tr>
<tr>
<td>Mean Anaesthetic time in minutes (SD)*</td>
<td>103 (35.8)</td>
<td>87 (39.5)</td>
</tr>
<tr>
<td>Emergencies (%)*</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>Post-anaesthetic colic (%)</td>
<td>18.5 (17/92)</td>
<td>7.7</td>
</tr>
<tr>
<td>Diarrhoea (%)</td>
<td>1 (1/92)</td>
<td>2</td>
</tr>
<tr>
<td>Lameness, Myopathy, Neuropathy (%)</td>
<td>3 (3/92)</td>
<td>0</td>
</tr>
<tr>
<td>Fractures (%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Wounds in Recovery (%)</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>7.6 (7/92)</td>
<td>0.5</td>
</tr>
<tr>
<td>Thrombophlebitis (%)</td>
<td>2 (2/92)</td>
<td>1</td>
</tr>
<tr>
<td>Wound infection (%)</td>
<td>1 (7/92)</td>
<td>n/a</td>
</tr>
<tr>
<td>Respiratory Distress (%)</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>