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A comparison of two ketamine doses for field anaesthesia in horses undergoing castration

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Summary

Background: Ketamine at 2.2 mg/kg given i.v. is often used to induce anaesthesia for surgical procedures in horses under field conditions. Commonly, additional doses are needed to complete the surgery. We hypothesised that surgical conditions would be improved when 5 mg/kg of ketamine was used to induce anaesthesia, while induction and recovery qualities would not differ from those when 2.2 mg/kg ketamine was used.

Objective: To compare the anaesthetic effects of two ketamine doses (5 mg/kg and 2.2 mg/kg) during field anaesthesia for castration of horses.

Study design: Prospective, randomised, blinded, clinical study.

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Method: Seventy-seven client-owned Icelandic horses presenting for castration under field conditions were studied. Pre-anaesthetic medication was xylazine (0.7 mg/kg) butorphanol (25 µg/kg) and acepromazine (50 µg/kg) injected i.v. Anaesthesia was induced with either 2.2 mg/kg (K2.2) or 5 mg/kg (K5) i.v. of ketamine mixed with diazepam (30 µg/kg). The quality of induction, surgical conditions and recovery were compared using subjective and objective measures, and the number of additional ketamine doses recorded.

Results: Ketamine 5 mg/kg provided better surgical conditions and a more rapid induction. Recovery quality was subjectively better in K2.2. Five horses in K2.2 and two in K5 required additional ketamine doses.

Main limitations: While the pre-anaesthetic sedation and benzodiazepine doses were consistent among horses, the level of sedation and muscle relaxation achieved before induction differed.

Conclusion: A ketamine dose of 5 mg/kg can be used to improve the quality of field anaesthesia for castration in Icelandic horses. Although recovery quality is subjectively poorer with this dose, no adverse events were observed during recovery.

Introduction

Ketamine given i.v. at 2.2 mg/kg was first described by Muir *et al.* for inducing general anaesthesia in horses [1]. It remains a popular drug for providing surgical anaesthesia for castration under field conditions in equine practice. The dose of 2.2 mg/kg given after suitable pre-anaesthetic medication, is reported to provide approximately 10 - 15 minutes of surgical anaesthesia [2]. However, this may be insufficient even for brief procedures such as castrations, in which movement or other undesirable responses may occur. Movement may compromise surgical cleanliness and, if excessive, may cause injury to operators and/or the horse. Giving additional doses of ketamine (or other intravenous anaesthetics) to prolong surgical anaesthesia requires extra staff or the disruption of surgery.

In Iceland, it is common practice to use a higher dose of ketamine for field anaesthesia in horses than is recommended on the data sheet. Icelandic equine practitioners favour the use of a higher ketamine dose (5 mg/kg) claiming it provides longer periods of surgical anaesthesia and decreases the need for supplementary dosing, whilst having no adverse effects on induction and recovery quality (unpublished data from questionnaire sent to Icelandic practitioners to evaluate clinical experience of using 5.0 mg/kg ketamine induction dose for field castration in horses). Muir, Skarda and Milne [1] compared two i.v. doses of ketamine, 2.2 and 6.6 mg/kg after xylazine pre-anaesthetic medication. They concluded that the higher ketamine dose caused major side effects during recovery, i.e. muscle tremor and rigidity, mydriasis, oculogyric movement, sweating, hypertension, tachycardia and increased rectal temperature [1]. In 2011, Wise, Klöppel and Leece compared 2.2 and 3 mg/kg ketamine given i.v. with diazepam (20 µg/kg) after pre-anaesthetic medication with romifidine (100 µg/kg) and butorphanol (50 µg/kg) and found no differences between the two doses for induction, surgical or recovery quality [3].

An ideal technique for field anaesthesia would involve a single drug injection that produced a safe anaesthetic induction and recovery, with a duration and quality of anaesthesia that allowed the surgery to be completed without complication. The study objective was to compare the quality of induction, anaesthesia and recovery produced by i.v. ketamine at doses of 2.2 and 5 mg/kg for field castration in Icelandic ponies.

Materials and methods

Horses presented for field castration at Dýralæknaþjónusta Suðurlands over the period of 28 May – 3 June 2016 were studied. All were client-owned, with verbal consent given by the owner. The physical status of all horses was classified as 1 according to the criteria of the American Society of Anesthesiologists. Exclusion criteria were an inability to administer pre-anaesthetic medication i.v. and cryptorchidism. Block randomisation was used to generate numbered anaesthetic records which became the study number of each horse. The ketamine dose to be given was indicated on each record but obscured by a sticker, ensuring that the assessors (H.H. and S.O.) were unaware of the treatment group assignment.

Food, but not water, was withheld the night before surgery. On presentation, the horses were allocated a temperament score 1 - 5, modified from Donaldson *et al.* [4] (Supplementary Item 1), where 1 represented a biddable, docile animal and 5 an intractable or feral animal. Body mass was estimated using a weight tape [5] (Pony Weight Tape)[a].

Pre-anaesthetic medication for all horses was xylazine (0.7 mg/kg; Chanazine)[b], butorphanol (25 µg/kg; Alvegesic)[b], and acepromazine (50 µg/kg; Plegicil)[c] administered slowly i.v. Five minutes later, a sedation score was allocated (range, 1 – 5) modified from Klöppel and Leece [7] (Supplementary Item 1), where 1 represented an animal showing profound sedation and ataxia and 5 an animal where no sedation was apparent. No additional pre-medication was administered irrespective of the sedation score. Anaesthesia was induced with i.v. ketamine (Aniketam)[b] at either 2.2 mg/kg (K2.2) or 5 mg/kg (K5) drawn from labelled vials. These contained ketamine either diluted or not diluted with 9 mg/ml sodium chloride (Vetivex 1)[d] to ensure equal drug volumes were given to both groups. Ketamine was then combined with diazepam (30 µg/kg; Stesolid Novum)[d] and administered i.v. Additional drug doses (0.25 mg/kg xylazine and 0.5 mg/kg ketamine) were pre-calculated and made available for use. The induction of anaesthesia was video-recorded from the time of ketamine administration until the horse was recumbent.

The following events were recorded at induction: a) time at ketamine injection; b) time at full relaxation (in lateral recumbency); c) the number of steps taken from injection to recumbency; d) the number of rigid limbs when first in lateral recumbency; e) the direction of fall (during induction), described as either “backwards” (desired) or “any other direction”. Videos of the induction were subjectively assessed for: f) overall induction quality, using a 0 – 4 scale modified from Kerr *et al.* [7] (Supplementary Item 2); g) muscle tension once in lateral recumbency (using a 4-point Likert scale; 0: None; 1: slight neck tension and/or leg twitching; 2: moderate neck and/or limb tension; 3: whole body tension or rigidity, rigid non-dependent limbs parallel to casting surface).

Surgical time was taken as the interval between the first incision until emasculator removal from the second testicle. The surgical quality (1-4) was evaluated by one author (S.O.) at the time of 1) scrotal incision and testicular exposure and 2) emasculator closure, for each testicle, using a scoring system modified from Klöppel and Leece [6] (Supplementary Item 1). A score of 1 indicated no cremaster muscle retraction; no response to surgical cut, whilst a score of 4 indicated movement to surgical stimuli, additional dose of ketamine needed.

Anaesthesia monitoring consisted of observation of respiratory rate, palpation of peripheral pulses, and assessment of muscle tension, eye position and nystagmus. A veterinary Monitor Im*pact*-III[e] was used to measure expired carbon dioxide ($P_{E'}CO_2$) via a 26 cm long 6.0 Nalgene 180 PVC metric tube[f] passed into the ventral meatus of the non-dependent nares. Oxygen saturation (SpO_2) was measured using pulse oximetry. The heart rate (HR), and respiratory rate (*fr*), $P_{E'}CO_2$ and SpO_2 was recorded every 3 minutes. Depth of anaesthesia was monitored and additional drug doses administered if the depth of anaesthesia was judged to be inadequate or recovery from anaesthesia was felt to be imminent. Signs considered to indicate an inadequate depth of anaesthesia included: a rapid nystagmus, brisk palpebral reflexes, an increase in *fr*, and/or breath holding with surgical stimuli. Signs of imminent recovery were muscle tension or movement after surgical stimulation, or increased tension on the leg rope. The reasons for giving additional drug doses and the time given were recorded. When surgery was complete the gelding was left undisturbed and observed from a distance. The recovery from anaesthesia was video-recorded.

The times when a) first movement occurred after surgery and b) the horse was standing were recorded. The number of c) attempts to achieve sternal recumbency; d) attempts to stand; e) falls (i.e. the number of standing attempts resulting in the horse returning to sternal or lateral recumbency); f) falls with longitudinal rotation (i.e. an attempted movement into sternal or the standing position resulting in 180° rotation along the animal's long axis) and g) steps taken in the first 30 seconds after standing were also documented.

Video recording was used to facilitate the assessment of the overall recovery quality. This was scored using a 1 – 6 scale modified from Young and Taylor [8] (Supplementary Item 3). As this was a field anaesthesia, the environment could not be standardised. Procedures took place under a variety of conditions e.g. inside stables or in the stable corridor, outside in parking areas; in a stone, sand or gravel arena; or in grass paddocks ranging in area from 20 to >200 m^2. Surfaces in some cases were dry, wet, uneven and/or sloping. Assessors were thus also asked to comment on whether environmental factors e.g. noise, disturbance from people entering the area, or environment were felt to have adversely affected induction or recovery. This was recorded in each case with a yes/no response.

It was also noted whether a companion, i.e. a familiar horse from the same herd or having had previous contact, was present in the same area and visible during recovery. The effect of having a companion was subjectively analysed using the video recordings as: a) overall recovery quality and b) subjective attitude of the horse, assessed using a 4 point Likert scale; 0 - Normal appearance (calm and relaxed); 1 - Slightly anxious appearance, does not appear to be fearful or stressed; 2 - Moderately anxious appearance, appears fearful or stressed; 3 - Appears very anxious/fearful appearance and stressed.

Data were analysed using Microsoft Excel[g] and Minitab[h] in a three-step process; 1) all data; 2) data from horses in which environmental factors were *not* felt to have adversely affected induction or recovery quality (statistical significance reported as *P exclude*); 3) data analysis irrespective of ketamine dose used, to analyse influence of factors (including; temperament, pre-anaesthetic medication, heart rate, companion animal present) on surgery quality and recovery. Recovery analysis excluded all horses that received an additional drug dose during surgery. The video recordings of induction and recovery for each horse were edited using Windows Movie Maker (Version 6.0.6002.18273 Microsoft® Windows®)[g] and scored by two experienced equine anaesthetists (K.J.B. and P.J.M.) who were unaware of the ketamine dose used. The order of examination was randomised (Excel Randomise list)[g] for each assessor. The mean value from the two assessors was used for data analysis of the subjective video assessments. Anaesthesia recordings (HR, *f*r, $P_{E'}CO_2$ and SpO_2) for each individual horse were summarised as individual mean value and used for data analysis. Subjective and objective data were tested for normality using the Kolmogorov-Smirnov test. Mean and standard deviation (s.d.) were reported for normally distributed data and differences between means analysed using Student's *t* test. Median and interquartile range (IQR) was used to describe non-normally distributed data, and differences analysed using Mann-Whitney *U* or Kruskal – Wallis test, and Dunn's test for *post-hoc* analyses when appropriate. Correlation between non - normally distributed data were assessed using Spearman Rho. Mean values of HR, *f*r, $P_{E'}CO_2$ and SpO_2 for each horse were calculated and compared using Student's *t* tests. Fisher's exact test was used to compare the direction of fall during induction and the need to use additional drug doses during surgery. Where there was a statistically significant difference between the groups, a post-hoc analysis using Bonferroni Correction was used, when appropriate, to account for multiple comparisons ($P_{Bonferroni}$). Level of significance was set at p value of <0.05.

Results

Eighty-four horses were presented for the study (Fig 1). Seven horses were excluded: one was cryptorchid, two were feral and i.v. access was not possible; and four were associated with technical difficulties (camera did not record, camera was not set up in time for recovery). Data from 77 horses were analysed: 38 horses received K2.2 and 39 horses K5. Age ranged from 1 – 2 years, with most being yearlings. Four horses receiving K2.2 and 5 horses receiving K5 were 2-year-olds. Mean estimated body mass was 214 kg in both groups (K2.2: mean 214 ± 30.8 kg; K5: mean 214.4 ± 31.1 kg, *P* = 0.9). Temperament and pre-anaesthetic medication score were not significantly different between the two groups (*P* = 0.1 and *P* = 0.2, respectively, Table 1). However, the temperament of the horse did correlate with sedation quality (Spearman rho: 0.532, *P*<0.0001) irrespective of the ketamine dose used.

Induction

Data for induction quality are shown in Table 1. Horses receiving K5 became relaxed more rapidly after becoming laterally recumbency (K2.2: 38 ± 6.1 sec; K5: 34 ± 5.7 sec, *P* = 0.001 [95% CI 1.7 to 7 seconds]). This was also evident when data from horses that were affected by adverse environmental factors were excluded. The direction of fall was not significantly different between groups (Fisher's exact test, *P* = 0.1) nor was there any difference in the overall induction quality (*p* = 0.5). Muscle tension was analysed both subjectively and objectively when the horse was in lateral recumbency (critical $P_{Bonferroni}$ = 0.025), and there was no statistically significant finding either subjectively (*p* = 0.04) nor objectively (*p* = 0.4).

Surgery

The total surgical time (Supplementary Item 4) was similar between groups (K2.2: 05:27 ± 1.06 min:sec; K5: 05:08 ± 00:28 min:sec *P* = 0.1). Seven horses received additional drug doses during anaesthesia; 5 in K2.2 and 2 in K5 (Fisher's exact, *P* = 0.1). Six horses (K2.2: n = 4, K5: n = 2) had one additional dose administered to complete the surgery, and one horse in group K2.2 needed two additional drug doses to prolong anaesthesia. Both groups had a relatively high mean heart rate, with horses in K5 statistically significantly higher HR though the anaesthesia (K2.2: 51 ± 8 beats/min; K5: 54 ± 9 beats/min *P* = 0.05 [95% CI -7.4 to 0.1 beats/min]). No differences in other clinical variables (*f*r, $E'CO_2$, SpO_2) were detected between groups during surgery. There was a correlation between heart rate during anaesthesia and both poorer temperament score (Spearman rho: 0.432, *p*<0.0001) and poorer sedation (Spearman rho: 0.618, *p*<0.0001), irrespective of ketamine dose administered.

Surgical conditions (critical $P_{Bonferroni}$=0.0125), during second testicle at 1) surgical incision and testicular exposure (*P* = 0.003) and 2) emasculator placed (*P* = 0.005) were statistically significantly improved in the K5 group (Fig 2). Sedation quality did not have a significant effect on surgical quality, with either ketamine dose. However, poor sedation had an adverse effect on surgical quality when the emasculator was placed on the second testicle irrespective of the ketamine dose given (Kruskal-Wallis *P* = 0.03). Dunn *post hoc* analysis showed that horses with sedation 3 (Mild sedation, with head slightly lowered, easily aroused, *P* = 0.02) and score 4 (Barely sedated – easily aroused, *P* = 0.002), had a significantly worse surgical quality score when the emasculator was placed on the second testicle compared to horses that scored 2 (Moderate sedation and ataxia).

Recovery

Overall recovery quality (Table 2) was statistically significantly poorer in K5 group (*P*<0.0001) and had statistically significantly more attempts to reach sternal recumbency (*P* = 0.04). Number of falls and 'falls with longitudinal rotation' (critical $P_{Bonferroni}$ = 0.025) was assessed objectively: a greater number of ‘falls with longitudinal rotation’ were seen in group K5 (P = 0.007). Three horses in K2.2 had “falls with longitudinal rotation” (once in 2 horses and three times in one horse), and 17 horses in K5 (once in 9 horses, twice in one horse, three times in 3 horses and four times in 4 horses). However, if horses were excluded where the environment was considered to have an adverse effect on recovery there was no statistically significant difference in attempts needed to reach sternal recumbency (P = 0.3) or the incidence of “number of falls with longitudinal rotation” (P = 0.08). Horses in K2.2 had statistically significantly higher number of mean steps taken in the first 30 seconds after standing (P = 0.02).

Physical intervention was required during the recovery of 4 horses (K2.2: n = 1, K5: n = 3), two of these horses (one from each group) failed to relax after induction and throughout surgery, and for that reason both were given additional drugs to complete surgery. Environmental factors during the recovery was also judged to adversely affect the recovery of all four horses.

A statistically significant correlation was found with an attitude in recovery and a poorer recovery score (Spearman Rho: 0.376, P = 0.007) irrespective of the ketamine dose. Horses that recovered with a companion appeared better attitude in recovery (companion horse: n = 56, median 0.5, IQR: 0.0 – 1.0; alone: n = 21, median: 1, IQR: 0.875 – 1.65, P = 0.005), irrespective of the ketamine dose used.

Discussion

Induction

The adverse effects of increased muscle tension when using a high dose ketamine-based anaesthetic protocol have been previously reported [1]. In the current study, the benzodiazepine dose at induction was not increased in the K5 group in order to avoid confounding assessment of the two ketamine doses. Co-administration of muscle relaxants, such as benzodiazepines, is widely accepted when using ketamine-based anaesthesia protocols [9]. Despite this, muscle tension after induction was not statistically significant in the current study. This disagreement from previously reported studies may be due to lack of any muscle relaxant in the previous study [1], as those horses had received xylazine alone.

A brief induction time, i.e. from induction drug administration to the horse reaching lateral recumbency, is usually desirable. The time from induction to full relaxation in lateral recumbency was on average, 4 seconds more rapid in the K5.0 group compared to the K2.2 group and was not influenced by any adverse environmental factors. This may be important when a quicker induction could decrease any potential risk of harm to the horse or handlers. The clinical relevance of 4 seconds faster induction time may be questionable; however, it could be important in situations where horses need to be anaesthetised quickly in an uncontrolled environment, such as rescue procedures.

Surgery

Poor oxygenation of horses under field anaesthesia is commonly reported in the literature [7,10,11]. Partial pressures of oxygen ranging from 5.6 to over 9.3 kPa [7,10], and SpO_2 90 to 95% [10,11] have been reported when using similar protocols as the current study. There were no differences in oxygen saturation (SpO_2 89%) between the two groups, nor any adverse effects associated with the use of K5 on respiratory rate and end tidal CO_2 when compared to K2.2. Both groups had a relatively high heart rate during surgery and may have been a manifestation of anxiety or stress as poorer temperament and sedation scores were correlated with heart rate during surgery (irrespective of ketamine dose administered). Horses with a poor temperament score, had a significantly worse sedation score, when the same pre-anaesthetic medication was given; and poor sedation scores affected the surgical quality (irrespective of the ketamine dose used). This further emphasises the importance of appropriate pre-anaesthetic sedation for anxious horses and shows how confounding factors can influence the anaesthesia.

For simplicity's sake, injectable field anaesthesia for brief procedures, such as castration, should involve a single dose of anaesthetic drug to produce adequate conditions for surgery. This would preclude the need for additional staff to be available to give drugs during surgery or interrupting the procedure to attend to inadequate anaesthesia. Surgical conditions were significantly better in horses in group K5, although two horses did require an additional anaesthetic drug dose. The surgical score during removal of the second testicle was significantly improved when using the high dose of ketamine, indicating a more adequate depth of anaesthesia. However, two horses (one in each group) did not become fully relaxed after induction, and although neither grossly reacted to surgical stimulation, the lack of relaxation meant an additional drug dose was required, which proved to be ineffective. Hall and Taylor [12] reported similar findings, where surgical relaxation was incomplete in 4 (out of 30) horses using 1.1 mg/kg xylazine, and then 2.2 mg/kg ketamine, and they described no obvious adverse responses to surgery. This lack of muscle relaxation may be attributed to the dissociative effect of ketamine-based techniques, and may not indicate an inappropriate depth of anaesthesia.

Recovery

Muir *et al.* [1] reported that a high dose of ketamine (6.6 mg/kg) prolonged the time from induction of anaesthesia to standing (93 min ± 13 min). This contrasts with the current study in which recovery times were similar between groups. Muir also reported that horses receiving 6.6 mg/kg ketamine after xylazine had poorer quality recoveries characterised by muscle twitching, spasm, rapid rotary nystagmus, extreme incoordination, oculogyric movement and excitement. These descriptions may have discouraged the use of higher doses of ketamine in horses. However, it should be noted that only 3 horses were studied with this dose, benzodiazepines were not given and surgery was not performed. In the current study, none of these reported adverse effects were noted. However, the K5 group of horses had worse recoveries (K2.2: *"Good recovery"*, K5: *"Fair recovery"*), and experienced a significantly higher number of falls with longitudinal rotation during recovery. There was no statistically significant difference, however, when horses in poor environments were removed from data analysis. This may indicate a need for appropriate case selection when using a higher dose of ketamine or where environmental conditions are suboptimal.

Intervention was required during recovery in one and 3 horses from groups K2.2 and K5 respectively. All 4 horses were considered to be very excitable or dominant/aggressive, all had low sedation scores, and all recovered in less than ideal environments. These factors complicate the assessment of dosage effects. Environmental factors could not be standardised in the current study because it was conducted under field conditions. Additional sedation was not administered before induction even when the effects of pre-anaesthetic medication were poor. These results possibly indicate that horses receiving K5, may have an increased residual plasma concentration of ketamine when they recover and may be more sensitive to adverse environmental conditions. It is possible that recoveries in horses receiving K5 may have benefited from the administration of longer-acting sedatives during pre-anaesthetic medication, or from additional sedation administered before recovery. Horses receiving the higher dose of ketamine were less active in the first 30 seconds after standing, assessed by step count, however clinically relevance could not be assessed.

Horses recovering from anaesthesia incur a high risk of injuries. This has been associated with the individual characteristics of the horse. In the current study, horses had a statistically significantly improved attitude in recovery if there was a companion horse present, which may reflect herd instincts. Environmental enrichment with a companion animal has not been studied in horses recovering from anaesthesia, although a beneficial effect of a companion animal has been demonstrated during transit of horses [13].

Limitations

The study was conducted under field conditions, so it was not possible to standardise the environment. An attempt was made to account for these factors by awarding a pre-induction sedation score and by asking the assessors to indicate whether they felt external factors adversely affected induction or recovery quality. Additionally, field settings preclude accurate weight measurement using a weighbridge. The accuracy of weight tapes and other measurements have been previously reported: however, none have been assessed in Icelandic horses. Ellis and Hollands (2002) reported that the Dodson and Horrell – pony weight tape, provided the most accurate measurement for horses up to 14.2 hands high (mean: 100.5 %, StDev 6.2, R^2 0.90), and was used in this study to standardise the weight estimation [5].

Sedation was sub-optimal in many horses, as no additional sedation was administered if the horses were scored as barely or not sedated. Although this does not follow usual clinical practice, it permitted a better comparison of the two ketamine doses.

Conclusion

High dose ketamine, 5 mg/kg has some advantages over the more commonly used 2.2 mg/kg dose, i.e. a more rapid onset of anaesthesia and improved surgical anaesthesia. The recovery time was not prolonged as previously reported by Muir *et al.* [1]: however, recoveries were subjectively better with low dose ketamine. Having a companion animal present during recovery improved overall attitude in recovery, irrespective of the ketamine dose used.

Authors' declaration of interests

No competing interests have been declared.

Ethical animal research

Ethical approval was granted by the Veterinary Ethical Review Committee of the Royal (Dick) School of Veterinary Studies, University of Edinburgh prior to the study taking place. Owners gave consent for their animals' inclusion in the study.

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Authorship

H. Hardardottir designed and executed the study, analysed and interpreted the data, and prepared the manuscript. P. Murison and K. Blissitt assisted with study design and writing of the manuscript. S. Olasson assisted with execution of the study and assisted with analysis. E. Clutton assisted with study design and writing of the manuscript. All authors gave their final approval of the manuscript.

Manufacturers' addresses

[a] Dodson and Horrell Limited, Kettering, Northamptonshire, UK.

[b] Parlogis, Reykjavík, Iceland.

[c] Distica, Garðabæ, Iceland.

[d] Vistor, Garðabæ, Iceland.

[e] Vetronic Services Ltd, Newton Abbot, Devon, UK.

[f] ACE Veterinary Supplies Ltd, Checkendon, Oxfordshire, UK.

[g] Microsoft Corporation, Redmond, Washington, USA.

[h] Minitab, Coventry, Warwickshire, UK.

Figure Legends

Fig 1: Flowchart illustrating case recruitment. Inclusion criteria: all horses presented to Dýralæknaþjónusta Suðurlands over the period of 28 May – 3 June 2016, with physical status classified as 1 according to the criteria of the American Society of Anaesthesiologists. Total of 7 horses were excluded from the study. Data from 77 horses were analysed. 1) Horses receiving either 2.2 mg/kg (K2.2) or 5 mg/kg (K5) ketamine induction dose; 2) data from horses in which environmental factors were *not* felt to have adversely affected induction or recovery quality; 3) data analysis irrespective of ketamine dose used, to analyse influence of factors (including; temperament, pre-anaesthetic medication, heart rate, companion animal present) on surgery quality and recovery.

Fig 2: Box and whisker plot showing surgical quality resulting from two ketamine doses (2.2 and 5 mg/kg). Dot indicated median, box the interquartile range with whisker the maximum. Surgical conditions were assessed at 2-time points during surgery on each testicle: 1) scrotal incision and testicular exposure; 2) emasculator application. The surgeon awarded a score between 1 (No cremaster muscle retraction; no response to surgical cut) – 4 (Movement to surgical stimuli, additional dose of ketamine needed). Critical statistical significance after Bonferroni adjustment for multiple comparisons $p = 0.0125$ (*).

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Supporting Information

Supplementary Item 1: Temperament, sedation and surgical quality scores.

Supplementary Item 2: Induction quality score.

Supplementary Item 3: Recovery quality score.

Supplementary Item 4: Cardiorespiratory variables and surgical time.

Table 1: **Induction quality in 77 Icelandic horses receiving either ketamine at 2.2 (K2.2) or 5 (K5) mg/kg.** Data are presented as median (interquartile range) or mean ± s.d. if normally distributed. *P* value obtained from comparisons between groups using Mann-Whitney U or t-tests (including difference between means of K2.2 and K5 (95% CI of *P* value) as appropriate). *P exclude*: *P* values obtained for comparisons between groups where data from horses in which the environment was considered to have had a negative influence on induction were removed from analysis (K2.2: n = 24, K5 n = 30). Statistical significance $p<0.05$ (*) and Bonferroni correction (critical $P_{\text{Bonferroni}} = 0.025$) when as assessing muscle rigidity†.

	K2.2	**K5**	***P* – 95% CI**	***P***	***P* exclude**
Temperament score	2 (2 – 3)	2 (1 – 3)	-	0.6	-
Premedication score	2 (2 – 3)	2 (2 – 3)	-	0.2	-
Subjective video assessment					
Overall induction quality (score)	1 (0.5 – 2)	1 (0.5 – 1.5)	-	0.5	0.7
Muscle rigidity of the horse in lateral recumbency (score)†	1.5 (0.375 – 1.5)	2 (1 – 3)	-	0.04	0.3
External factors	0 (0 – 0.5)	0 (0 – 0)	-	0.4	-
Objective assessment					
Number of rigid limbs (count)†	1 (0 – 2)	1 (0 – 2)	-	0.4	0.6
Steps taken after injection of induction dose (count)	0 (0 – 1)	0 (0 – 0)	-	0.1	0.2
Time to full relaxation (seconds)	38 (± 6.1)	34 (± 5.7)	4 (1.7 to 7)	0.001 *	0.003 *

Table 2: **Recovery quality in 70 Icelandic horses receiving either ketamine at 2.2 (K2.2) or 5 (K5) mg/kg.** Recovery analysis excluded all horses that received additional anaesthesia dose during surgery (K2.2 n = 33, K5 n = 37). Data are presented as median (interquartile range) or mean ± s.d. if normally distributed. *P* value obtained from comparison between groups using Mann-Whitney U or t-tests (including difference between means of K2.2 and K5 (95% CI of *P* value) as appropriate. *P* exclude: *P* values obtained for comparisons between groups where data from horses in which the environment was considered to have had a negative influence on recovery were removed from analysis (K2.2. n = 26, K5 n = 24). Statistical significance $p<0.05$ (*) and Bonferroni correction (critical $P_{Bonferroni} = 0.025$) when assessing number of falls†.

	K2.2	K5	*P* – 95% CI	*P*	*P exclude*
Subjective video assessment					
Overall Recovery Score (score)	**2.0** **(1.5 – 2.5)**	**3.0** **(2.25 – 4.5)**	-	**<0.0001 ***	**0.002 ***
Adverse environment factors effecting recovery	**0** **(0 – 0)**	**0** **(0 – 1)**	-	**0.3**	-
Objective assessment					
Time from induction – 1st movement (minutes:second)	**26:28** **(21:42 – 27:34)**	**25:31** **(20:31 – 31:37)**	-	**0.2**	**0.9**
Number of attempts to sternal (count)	**1** **(1 - 1)**	**1** **(1 - 2)**	-	**0.04***	**0.3**
Number of attempt to stand (count)	**1** **(1 - 2)**	**2** **(1 - 3)**	-	**0.08**	**0.2**
Number of falls (count)†	**0** **(0 - 1)**	**1** **(0 - 2)**	-	**0.03**	**0.2**
Number of "fall with rotation" (count)†	**0** **(0 - 0)**	**0** **(0 - 1)**	-	**0.007 ***	**0.08**
Time from 1st movement – standing (minutes:second)	**03:00** **(00:36 – 05:45)**	**03:43** **(01:57 - 07:47)**	-	**0.2**	**0.9**
Number of steps taken in 30 sec after standing (count)	**21.8 ± 14**	**14.5 ± 12.1**	**0.97 to 13.52**	**0.02***	**0.04***

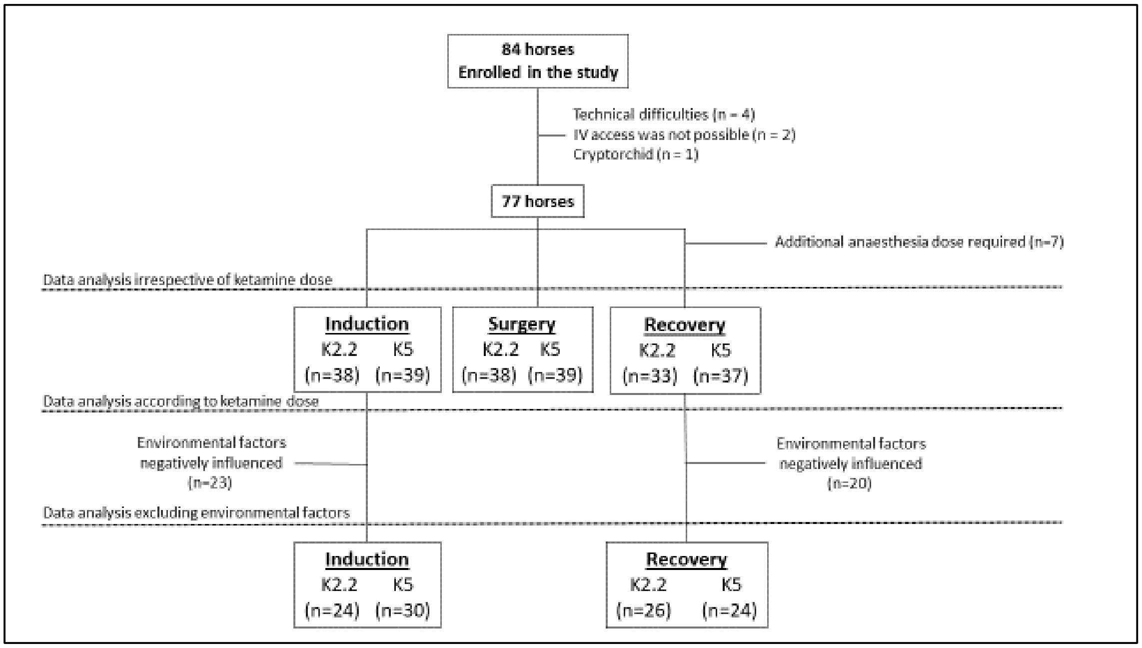

Figure 1. Flowchart illustrating case recruitment. Inclusion criteria: all horses presented to Dýralæknaþjónusta Suðurlands over the period of 28th May – 3rd June 2016, with physical status classified as 1 according to the criteria of the American Society of Anaesthesiologists. Total of 7 horses were excluded from the study. Data from 77 horses were analysed. 1) Horses receiving either 2.2 mg kg^{-1} (K2.2) or 5 mg kg $^{-1}$ (K5) ketamine induction dose; 2) data from horses in which environmental factors were *not* felt to have adversely affected induction or recovery quality; 3) data analysis irrespective of ketamine dose used, to analyse influence of factors (including; temperament, pre-anaesthetic medication, heart rate, companion animal present) on surgery quality and recovery.

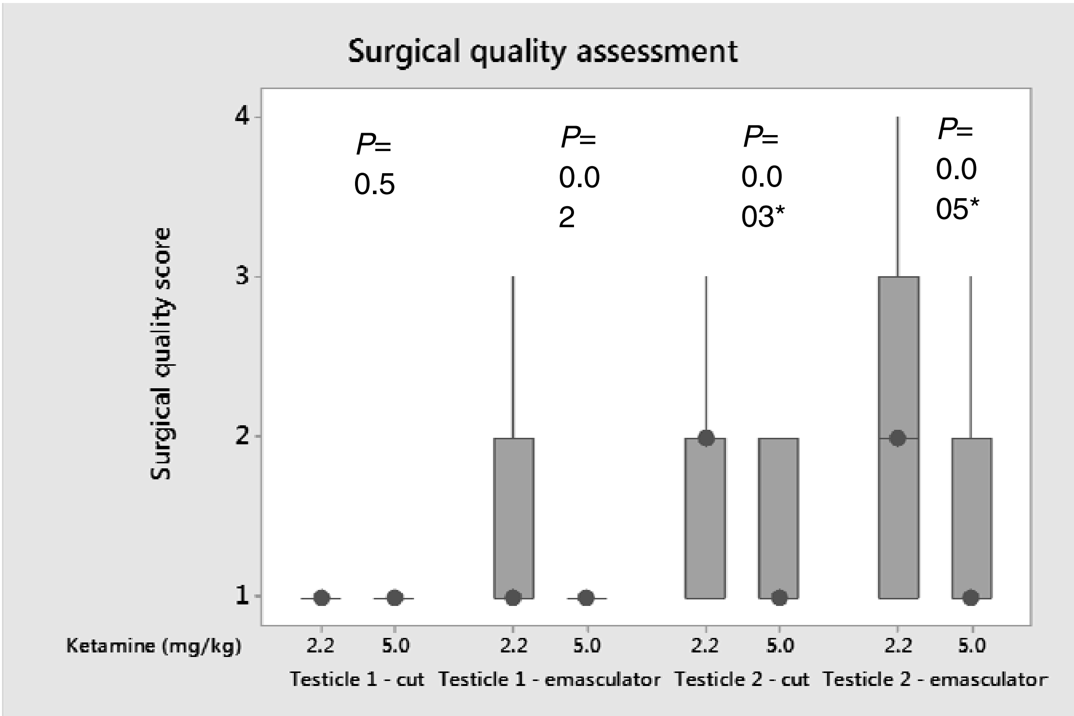

Figure 2. Box and whisker plot showing surgical quality resulting from two ketamine doses (2.2 and 5 mg kg^{-1}). Dot indicated median, box the interquartile range with whisker the maximum. Surgical conditions were assessed at 2-time points during surgery on each testicle: 1) scrotal incision and testicular exposure; 2) emasculator application. The surgeon awarded a score between 1 (No cremaster muscle retraction; no response to surgical cut) – 4 (Movement to surgical stimuli, additional dose of ketamine needed) Critical statistical significance after Bonferroni adjustment for multiple comparisons p=0.0125 (*).