Introduction

The equipment required for equine anesthesia ranges from the simple syringe used in short-term field interventions to the complex anesthesia machine used for more complicated surgery in the operating theater. Anesthesia should last no longer than one hour when the availability of supplementary oxygen is limited [5, 18].

Numerous studies have addressed the combined anesthetic action of detomidine followed by a dissociative anesthetic such as tiletamine and a benzodiazepine such as zolazepam, a regime that has been proved to be highly effective in horses and ponies [6, 8, 19]. Response to the tiletamine-zolazepam (T-Z) combination, classed as a general anesthetic, is governed by its dissociative component: the patient’s eyes remain open, even during deeper planes of anesthesia; the corneal and palpebral reflexes, and often the laryngeal, pharyngeal and pedal reflexes, are maintained; salivation is common [15]. Anesthesia induction is smooth and swift, as is recovery in many species. Muscle relaxation and general absence of

SUMMARY

The aim of this study was to assess the efficacy of tiletamine-zolazepam anesthesia by continuous infusion in horses, and the influence of oxygen supplementation. Five horses were preanesthetized with detomidine and butorphanol and anesthetized using tiletamine-zolazepam both for induction and maintenance, according to three different regimes, with a 15-day minimum interval between Regimes: Regime I: 2 mg/kg for induction and 1 mg/kg for maintenance, with no oxygen; Regime II: as Regime I, but administering oxygen at 8 liters/minute; Regime III: 1 mg/kg for induction and 2 mg/kg (0.033 mg/kg/min) via infusion, with 8 liters/minute oxygen. The following parameters were assessed: induction times, intubation quality, degree of analgesia, nystagmus, temperature, heart rate and respiratory rate, % oxygen saturation of arterial hemoglobin and recovery time and quality. Results indicated a good response to both induction doses. All maintenance parameters displayed greater stability in Regime III, although Regime I may represent a valid alternative where no oxygen source is available. Recovery, though relatively poor in all three Regimes, was better with continuous infusion and oxygen supplementation.

KEY-WORDS : Tiletamine-zolazepam - equids - continuous infusion - oxygen.

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response to external stimuli have increased clinical use of T-Z [7]. In 1992, LIN published a comparative study in which ponies received 2 or 3 mg T-Z/kg intravenously (IV), combined with detomidine at doses of 0.02, 0.04, or 0.06 mg/kg IV. All combinations provided rapid induction, deep analgesia and good muscle relaxation. At higher doses, anesthesia lasted longer but recovery was more violent: a dosing schedule of T-Z 2 mg/kg IV and detomidine 0.04 mg/kg IV ensured swift induction, good analgesia and smooth recovery; the poorer quality of recovery at higher doses of T-Z/detomidine was ascribed more to the increased T-Z dose than to the detomidine component [6]. An equally significant study by MUIR et al. in 2000 compared six compounds: diazepam, xylazine, ketamine, tiletamine/zolazepam, guaifenesin and thiopental, in four combinations for anesthesia of horses undergoing abdominal surgery. Quality of recovery with the only combination containing tiletamine/zolazepam was significantly worse, with a greater number of attempts to stand, than with all the other combinations [13].

The present study sought to evaluate the anesthesia induction efficacy and the cardiovascular support provided by tiletamine-zolazepam, simply repeating the dose when the induction dose wore off, in order to achieve 60-minutes anesthesia. The combination of tiletamine-zolazepam used for anesthesia induction varied according to regimes, thus enabling assessment of any differences between regimes [6, 10, 14]: for regimes I and II, anesthesia was induced with 2 mg/kg IV, and maintained by a continuous infusion of T-Z. The influence of oxygen supplementation during anesthesia was also assessed.

Material and methods

Five adult horses of both sexes (age 3-13 years, mean weight 392 kg), crossbred, healthy, received three different anesthetic regimes (Table I), with a minimum interval of 15 days between regimes. Their food regimen was grazing. The horses have been included in the same order in the different protocols. All regimes used the same preanesthetic medication, delivered via jugular catheter: the alpha-2-adrenergic agonist detomidine (0.02 mg/kg) and the opiate agonist-antagonist butorphanol (0.044 mg/kg). The dose of tiletamine-zolazepam used for anesthesia induction varied according to regimes, thus enabling assessment of any difference between doses [6, 10, 14]: for regimes I and II, anesthesia was induced with 2 mg/kg IV, and maintained by a repeat dose of 1 mg/kg IV when a loss of the recorded degree of analgesia was seen. For regime III, the induction dose was 1 mg/kg IV; the remaining 2 mg/kg were administered via continuous infusion; all animals thus received the same overall dose at each regime. Since the minimum plasma T-Z concentration in horses is unknown, the infusion rate was calculated by dividing the 2 mg/kg dose by the 60 minutes of intended anesthesia, giving a rate of 0.033 mg/kg/min. In regimes II and III, 100% oxygen was delivered at 8 liters/minute.

Prior to preanesthesia, the following baseline values were measured: temperature (Tm), heart rate (HR), respiratory rate (RR), color of mucous membranes and capillary refill time (CRT). Duration of preanesthesia was recorded from administration to induction, together with the degree of sedation achieved, subjectively classified as light, moderate or marked. The following induction parameters were determined: induction time, i.e. time from administration of the induction dose to lateral recumbency (seconds), endotracheal intubation quality (Table II), knockdown quality and presence of post-induction apnea. Thereafter, total anesthesia time was measured in minutes, taking administration of the induction dose as the start of anesthesia, and in regimes I and II the time of application of the repeat dose was recorded; the following qualitative parameters (Table II) were assessed on a scale from 1 to 3, to enable statistical analysis: degree of analgesia, degree of muscle relaxation, and nystagmus (presence and frequency). In regimes I and II, initial loss of the recorded degree of analgesia was taken as the signal for the repeat dose, while subsequent loss marked the end of anesthesia. The end of anesthesia in regime III was marked by exhaustion of the infusion drip. The remaining parameters were quantitative, and were determined directly: percentage oxygen saturation of arterial hemoglobin (SpO2) by a finger probe placed on the tongue (Pulse Oximeter 515A, Wallingford USA) temperature (Tm), heart rate (HR), and respiratory rate (RR). The following parameters were assessed during recovery: time to first movement, time to extubation, time to sternal recumbency, time to standing, time to leaving recovery stall and number of attempts to stand. All times were measured from the start of anesthesia and expressed in minutes. Recovery quality was assessed in terms of the degree of muscle twitching and ataxia.

All variables were expressed as mean ± standard deviation; since all values displayed normal distribution, an analysis of variance was performed to identify potential statistically-significant differences due to regime or anesthesia time.

Results

PREANESTHESIA

Baseline values for Tm, HR, RR and CRT were normal for all three regimes, with no statistically-significant differences (Table III). Preanesthesia time was 132 ± 26.8 seconds for regime I, 134 ± 27.9 seconds for regime II and 109 ± 8.9 seconds for regime III; there were no statistically-significant differences. The mean value between the injection of the alpha-2 and the induction was 125 ± 24.2 seconds. The degree of sedation achieved was moderate in most animals.

INDUCTION

- Regime I: Mean time to knockdown was 96 ± 25.1 seconds. Intubation was complication-free. Four animals displayed apnea lasting around 30 seconds following administration of the induction dose, though with no adverse consequences.
- Regime II: Induction time was 81 ± 29.2 seconds. Intubation was complication-free. Post-induction apnea of 30 seconds was observed in two horses.
- Regime III: Induction time was 68 ± 21.6 seconds. Time from induction to the start of infusion ranged from 4 to 10 seconds. Two animals displayed post-induction apnea lasting a few seconds, and one exhibited moderate stiffness on intubation and a slightly more marked swallowing reflex.
Comparison between Regimes: Induction times were suitable in all Regimes. Overall mean time to knockdown for the three Regimes was 81.7 ± 26.4 seconds, with no significant differences between Regimes.

MAINTENANCE

Mean values for all parameters and regimes are shown in Tables III and IV.

- Regime I: Mean duration of maintenance was 61.6 ± 17.5 minutes (Table V). The second dose of T-Z was administered after a mean interval of 41.6 ± 6.8 minutes. Analgesia declined significantly at minute 40, reaching a mean value of 1.6 (Graph 1); muscle relaxation, however, remained stable throughout anesthesia time; nystagmus increased significantly over time, recording a peak value of 2.4 at minute 40. SpO₂ values remained low throughout anesthesia (Graph 2).
Tm dropped at minute 20, and continued to decline throughout anesthesia, reaching 37.3°C by minute 60; this value represented a statistically significant decline with regard to baseline (Graph 3). HR and RR remained virtually unchanged; recorded variations showed no significant effect for anesthesia time (Graphs 4 and 5).

- Regime II: total anesthesia time was 68.4 ± 11.2 minutes (Table V); the second dose was administered after a mean interval of 37.8 ± 4.8 minutes. The degree of analgesia also declined towards minute 40, though the decline was not significant with regard to anesthesia time (Graph 1). A good level of muscle relaxation was recorded throughout mainte-

### Data are expressed as mean ± SD
- Regime I significantly lower than regimes II and III
- * Significant changes from baseline in each regimen (p<0.05)
- + Regime I significantly higher than regimes III

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Analgesia</th>
<th>SpO₂ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>2.4±0.8</td>
<td>3.6±0.4</td>
</tr>
<tr>
<td>20</td>
<td>3.6±0.6</td>
<td>3.4±0.6</td>
</tr>
<tr>
<td>40</td>
<td>1.6±0.3</td>
<td>2.4±0.4</td>
</tr>
<tr>
<td>60</td>
<td>1.2±0.1</td>
<td>1.8±0.6</td>
</tr>
</tbody>
</table>

### TABLE IV. — Analgesia and percentage oxygen saturation of arterial hemoglobin (SpO₂).

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Regime I</th>
<th>Regime II</th>
<th>Regime III</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>61.50 ± 17.9</td>
<td>62.40 ± 11.2</td>
<td>64.20 ± 8.0</td>
</tr>
<tr>
<td>20</td>
<td>67.30 ± 14.1</td>
<td>72.60 ± 10.2</td>
<td>77.70 ± 5.6</td>
</tr>
<tr>
<td>40</td>
<td>79.60 ± 13.2</td>
<td>79.90 ± 9.6</td>
<td>79.30 ± 8.4</td>
</tr>
<tr>
<td>60</td>
<td>80.70 ± 15.6</td>
<td>79.50 ± 6.5</td>
<td>79.20 ± 8.6</td>
</tr>
</tbody>
</table>

**N.D.** Not determined
- All data are expressed as mean ± standard deviation
- Time are expressed as minutes from the start of anesthesia

### TABLE V. — Total anesthesia time and mean values for recovery parameters, for the three regimes.

- Regime I significantly lower than regimes II and III
- * Significant changes from baseline in regime I (p<0.05)
- + Regime I significantly higher than regime III

**GRAPH 1. — Mean analgesia values at different times.**

**GRAPH 2. — Mean SpO₂ values at different times.**
nance, diminishing only at minute 60. However, incidence of nystagmus varied significantly, increasing at minute 40 and thereafter remaining at that level until the end of anesthesia. Percentage SpO₂ declined from minute 20, and continued to fall until minute 40; thereafter, values rose again towards minute 60, though failing to regain baseline levels. These variations were not significant (Graph 2). Temperature started to drop around minute 20, differences becoming significant with respect to baseline at minutes 40 and 60, with values of 37.1 and 37.0 °C, respectively (Graph 3). HR did not vary significantly as a function of anesthesia time, although it fell at minute 20 and thereafter recorded a progressive recovery (Graph 4); in contrast, RR recorded a significant drop with respect to resting values at minute 5, and again at minute 20, remaining around these lower levels until the end of anesthesia (Graph 5).

- **Regime II**: Total anesthesia time was 64.2 ± 8.0 minutes (Table V). The degree of analgesia registered a very slight decline around minute 40, to a non-significant value of 2.8 (Graph 1); muscle relaxation remained constant around desired values throughout anesthesia; nystagmus values displayed no significant differences with respect to baseline, recording a slight increase at minute 20 and thereafter remaining stable throughout anesthesia. Percentage SpO₂ declined at minute 20 but rose again at minute 40; there were no interim variations, and changes were not significant (Graph 2). Temperature remained around baseline values (38.3°C) throughout anesthesia; the lowest value (38.0°C) was recorded at minute 60 of anesthesia, and did not represent a significant variation (Graph 3). The only significant variations were found for HR (Graph 4), which fell significantly at minute 5, rose slightly at minute 20 and thereafter continued to rise until minute 60, by which time it was no longer significantly different to resting values. RR values fell at minutes 20 and 40 and recovered slightly by minute 60; baseline rates were not regained, but changes were not significant (Graph 5).

- **Comparison between regimes**: Overall mean total anesthesia time for three regimes was 64.7 ± 12.2 minutes; Regime II was the longest and regime I the shortest, though differences were not significant (Table V). Interval to administration of the repeat dose did not differ significantly between regimes I and II. The degree of analgesia achieved in regime I differed significantly at minute 40 to that recorded in regime III (Graph 1). Neither muscle relaxation nor nystagmus varied significantly as a function of regime. Percentage SpO₂ displayed significant variations between regimes: from minute 5 onwards, values in regime I were significantly lower than those recorded for the other two regimes, which were not significantly different from each other. At minute 40, significant differences in percentage SpO₂ were noted between regimes I and III. The behavior of this parameter was most stable in regime III (Graph 2). Mean temperature values declined progressively in all regimes from minute 5 onwards. Significant differences in mean temperature were recorded between regimes II and III at minutes 40 and 60 (Graph 3). Mean HR values were significantly lower in regimes II and III than in regime I, though not significantly different from each other; the most marked diffe-
rence were recorded at minute 60. The greatest stability for heart rate values was recorded in regime III (Graph 4). RR displayed behavior similar to that of HR: Regime I values were significantly higher than those of regimes II and III. At minute 20, a significant difference was noted between regimes I and II; at minutes 40 and 60, regime I differed significantly from both II and III. The greatest stability for respiratory rate was also recorded for regime III (Graph 5).

**RECOVERY**

Mean times for all parameters and regimes are shown in Table V.

- **Regime I**: Recovery was acceptable in three of the five horses, which stood up at the first attempt; ataxia was observed in all except one, and muscle twitching in all except two. Recovery in the other two was poor; time to sternal recumbency was prolonged, with various falls and two attempts required to stand; ataxia and muscle twitching were observed.

- **Regime II**: Recovery was acceptable in four animals, which stood at the first attempt, displayed little or no evidence of ataxia, and in only one case mild muscle twitching. Recovery in the fifth animal, however, was very poor; numerous attempts were made to stand; sternal recumbency was not achieved until 70 minutes after the end of anesthesia; on achieving «seated dog» posture, the horse displayed marked hindlimb ataxia. Time to standing was 2 hours and 47 minutes, and although the horse was able to walk from the recovery stall, left gluteal myositis was observed the following day.

- **Regime III**: Recovery was again acceptable in four of the five animals; the other made various attempts to stand and fell on several occasions; although such falls can be dangerous, the horse was not hurt, and once standing displayed no signs of ataxia or muscle tremor, and only mild lack of hindlimb coordination. The other animals stood at the first attempt and showed no ataxia or notable muscle tremor.

- **Comparison between regimes**: Overall, recovery in the three regimes can be considered as poor; two animals had difficulties in regime I, and one animal in each of the other regimes.

**Discussion**

**PREANESTHESIA**

Baseline physiological values were totally normal. The highest baseline temperature was recorded in regime III, while the highest values for baseline HR and RR were found in regimes II and I, respectively. Following premedication, animals displayed moderate sedation; the detomidine dose was sufficient to reduce the dose of induction anesthetic required, provide a satisfactory degree of analgesia for 60 minutes and at the same time allow the animal to remain standing until induction [16]. Studies of combined use of detomidine with opiates report that butorphanol provides an additive analgesic effect prior to the induction of general anesthesia, clearly increases sedation and decreases the response to external stimuli; the most effective combination for cardiopulmonary side-effects appears to be detomidine 10 to 20 μg/kg and butorphanol 0.04 to 0.05 mg/kg [1]. None of the animals in the present study displayed adverse reactions to preanesthesia.

**INDUCTION**

Induction time with T-Z was lowest for Regime III; the dose was lower, albeit not significantly, than in the other Regimes. However, one animal presented a certain stiffness at intubation together with a marked swallowing reflex; these symptoms were not observed in the other two Regimes. The number of post-induction apnea episodes was proportionately greater in Regimes I and II than in III. Knockdown quality was good in all cases. A study by SHORT et al. (1989) in horses, comparing a range of T-Z induction doses (1.1, 1.65, and 2.2 mg/kg IV) following administration of xylazine 1.1 mg/kg, with an interval of between 5 and 11 minutes between xylazine and T-Z, reported times to recumbency ranging from 45 seconds to 2 minutes; increasing the T-Z dose did not shorten induction time [17].

**MAINTENANCE**

In the present study, anesthesia was successfully maintained for roughly 60 minutes, with a mean total anesthesia time of 64.73 for the three regimes. Administration of the repeat dose in regimes I and II took place around minute 40, with no significant difference between regimes. A lower degree of analgesia was achieved with regime I; the difference with respect to the other regimes attained statistical significance at minute 40, when a less marked decline in analgesia was also recorded for regimes II and III. This appears to coincide with the loss of analgesia noted immediately prior to administration of the repeat anesthetic dose, which was recorded at around minute 41.60 in this regime. Loss of analgesia at this stage was less marked in regime II. Regime I was the least stable for this parameter. WILSON et al. recommend that T-Z analgesia should be supplemented by other drugs [20]. Muscle relaxation and nystagmus were stable in all three regimes, with no significant inter-regime differences. Percentage oxygen saturation of arterial hemoglobin was lower, throughout anesthesia, in regime I; differences with respect to the other regimes were already apparent in the brief interval between intubation and the start of monitoring. Significant differences with respect to regime III were recorded at minute 40 of anesthesia, and were ascribed to the lack of oxygen supplementation in regime I, where mean values were below 85 % (83 % at minute 40), compared with around 90 % for regimes II and III. Measurement of SpO2 enables assessment of the degree of hypoxemia occurring during anesthesia; although the method used - placing of a pulsemeter on the tongue - usually gives an underestimation, the same method was employed in all regimes [12]. A number of authors suggest that, while there is no linear relationship between percentage oxygen saturation and arterial partial pressure of oxygen, SpO2 values of around 90 % correspond to roughly 60 mmHg. Below these values hypoxemia can be
expected; when the animal is obliged to breathe ambient air, PaO₂ often falls to 50 mmHg [4]. Oxygen administration may thus be considered of major importance in equine intravenous anesthesia, particularly if it exceeds 40 minutes.

Temperature declined significantly in all regimes, but was higher in regime III, due - as indicated earlier - to higher baseline values. Variations were more marked in regimes I and II, perhaps reflecting greater variations in the plane of anesthesia. The fall was significant in the final minutes (40 and 60), since temperature declines with anesthesia time; additionally, T-Z is reported to prompt a drop in temperature due to the deep muscle relaxation it causes [7].

A significant difference was recorded for heart rate between Regime I and Regimes II/III at minute 60. This finding is not in itself remarkable, since Regime I had the shortest anesthesia time (61.6 min), suggesting that most animals were probably coming round by that stage; more interesting is the fact that HR values were consistently higher throughout this Regime. The most stable results for HR were recorded for Regime III. Similarly, respiratory rate was highest in Regime I, which differed significantly from both II and III at minutes 20, 40 and 60, and was most stable in Regime III. The behavior of HR and RR would suggest greater cardiopulmonary instability in Regime I, attributable to lack of oxygen supplementation. Anesthesia prompts a fall in cardiac output, but tissue uptake of oxygen remains constant, leading to an increase in heart rate and respiratory rate to maintain oxygen supply to tissues [2]. A comparison of three combinations in miniature donkeys found that T-Z caused greater respiratory depression, with a decline in respiratory rate and pH and an increase in PaCO₂ due to the joint effects of sedation and recumbency (11). There was also a decline in PaO₂, as found in the present study and also reported by HUBBEL et al. in 1989 [3].

### RECOVERY

There is some doubt as to the recovery to be expected with this anesthetic; it is widely reported that zolazeapm, whose half-life is longer than that of tiletamine, continues to prompt muscle relaxation after the anesthetic has worn off, leading to ataxia (6,9). In horses, ataxia may give rise to a greater number of attempts to stand, and thus to poor recovery. In regime I, none of the parameters attained maximum values, even though tissue perfusion was presumably worse; however, animals displayed ataxia and muscle tremor which were not evaluated statistically. One animal in regime II developed myositis in the gluteal region, and thus recorded the longest times to extubation, first movement and sternal recumbency; one animal took a long time to wake, but once standing presented no further problems and in fact recorded the shortest time to standing and the lowest number of attempts to stand. Taking all recovery parameters together, regime I animals took less time to come round and recorded the shortest time to first movement. However, it should be noted that times were measured from the start of anesthesia, and regime I had the shortest anesthesia time; animals awoke earlier, but attempts to stand were premature and caused excitation, leading to greater ataxia and instability. By contrast, in regime III animals took longer to come round, but stood earlier, more safely and at fewer attempts; once standing, stability was good. Under continuous infusion, anesthesia was administered until around minute 60, whilst in regimes I and II the last dose was administered at roughly minute 40. The smoothest and most stable recovery was achieved with regime III, although this is a subjective assessment, since no significant inter-regime differences were noted for any recovery parameter.

### Conclusion

The following conclusions can be drawn:

1. Administration of detomidine 20 μg/kg and butorphanol 0.044 mg/kg as preanesthetic medication achieved moderate sedation, sufficient to enable induction and maintenance of anesthesia using tiletamine-zolazeapm.

2. T-Z provided a good level of induction at both doses. Induction was better with 2 mg/kg, although 1 mg/kg also proved sufficient.

3. Continuous infusion at 0.033 mg/kg/min with oxygen supplementation provided greater stability of all parameters during maintenance anesthesia.

4. The most notable complication in equine anesthesia using intravenous tiletamine-zolazeapm, with or without oxygen supplementation, was the poor quality of recovery in all regimes, although recovery was smoother following continuous infusion with supplementary oxygen.

Thus, for minor surgery up to 45–60 minutes duration, continuous infusion T-Z anesthesia with oxygen supplementation is recommended.

### References


