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PHYSIOLOGICAL AND BEHAVIORAL RESPONSES OF GRAY WOLVES (*CANIS LUPUS*) TO IMMOBILIZATION WITH TILETAMINE AND ZOLAZEPAM

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ABSTRACT: We conducted a series of experiments to examine the efficacy of Telazol® (TEL) for immobilization of captive gray wolves (*Canis lupus*). Ten wolves were immobilized with either 5 or 10 mg/kg TEL. There was no difference in induction time (6.5 ± 0.8 versus 5.8 ± 1.2 min; $P = 0.63$) between the two doses, but the time to initial arousal was longer for the higher dose ($P = 0.0008$). Wolves were again immobilized with 10 mg/kg TEL and upon initial arousal were given additional doses of either 5.0 mg/kg TEL or 2.5 mg/kg ketamine (KET) to maintain immobilization. Wolves given boosters of TEL had longer second recovery times than wolves given KET ($P = 0.01$). There were no differences in induction times or arousal times for wolves immobilized with TEL that had been reconstituted with sterile water and stored at 20 C for 30 days ($P \geq 0.11$) or 60 days ($P \geq 0.27$) when compared to immobilization times using fresh solution. Induction times for wolves given TEL reconstituted with water and propylene glycol and stored for 60 days at −9 C were longer ($P < 0.05$) than such times for wolves given standard TEL, but time to initial arousal was unchanged ($P \geq 0.44$). There were no differences in heart rates ($P = 0.36$), blood pressures ($P = 0.32$), respiratory rates ($P = 0.91$), and rectal temperatures ($P = 0.62$) between the two TEL doses. Telazol® was shown to be an effective and safe immobilizing agent for gray wolves.

Key words: Gray wolf, *Canis lupus*, Telazol®, tiletamine, zolazepam, ketamine, chemical immobilization, physiology.

INTRODUCTION

Telazol® (TEL) is an injectable anesthetic comprised of equal weights of the arylcycloalkylamine, tiletamine hydrochloride (HCL), and of the pyrazolodiazepinone, zolazepam HCL. When used alone, tiletamine produces convulsive seizures and clonic muscular reactions while zolazepam alone causes aggressive behavior in domestic cats (Massopust et al., 1973). Combining these two drugs results in fewer convulsions, good muscle relaxation and smoother recoveries (Massopust et al., 1973). Telazol® is currently only approved for use in dogs and cats, but during its development over the past 15 yr TEL (previously identified as CI-744) was used on over 200 non-domestic vertebrate species (Gray et al., 1974; Boever et al., 1977; Schobert, 1987). Controlled clinical evaluations, however, have only been conducted on dogs, cats, primates and rodents.

Gray wolves (*Canis lupus*) have been immobilized with a variety of drugs or drug combinations (Seal and Kreeger, 1987) including TEL (Gray et al., 1974; Boever et al., 1977). Previous reports on use of TEL on wolves were limited by small sample sizes and use on injured or otherwise compromised animals. This study examines the physiological and behavioral responses of healthy gray wolves immobilized with TEL under controlled conditions.

MATERIALS AND METHODS

These studies were conducted from July 1988 through February 1989 in east central Minnesota. Sixteen (8 male, 8 female), adult wolves were used with some wolves used for more than one experiment. The locality and husbandry of these animals has been previously described and some of these wolves have been used for other immobilization studies (Kreeger et al., 1987, 1988). Wolves were immobilized with tiletamine plus zolazepam (Telazol®, A. H. Robins Co., Richmond, Virginia 23220, USA) given intramuscularly (i.m.) via pole syringe. Telazol® was

TABLE 1. Induction and recovery times for wolves immobilized with different doses of Telazol® (TEL) that was reconstituted and stored under different conditions. Values reported as mean (±SEM).

Drug dose (mg/kg)	Solution	*n*	Induction time (min)	Initial arousal time (min)	Second arousal time (min)
5 TEL	Fresh	10	6.5 ± 0.8	43.3 ± 5.6	
10 TEL	Fresh	10	5.8 ± 1.2	82.1 ± 8.0[a]	
10 TEL + 5 TEL[b]	Fresh	10	5.1 ± 0.5	93.8 ± 10.5	104.9 ± 21.9[a]
10 TEL + 2.5 KET[b]	Fresh	10	5.1 ± 1.1	80.8 ± 7.8	37.0 ± 4.1
5 TEL	30 day	5	8.2 ± 0.2	42.0 ± 8.6	
5 TEL	60 day	5	5.2 ± 0.7	40.4 ± 8.0	
5 TEL	60 day[c]	5	13.4 ± 3.0[a]	36.2 ± 5.4	

[a] Value significantly different from other values in column between dividing lines ($P < 0.05$).
[b] Wolves were given additional doses of either TEL or ketamine (KET) upon initial arousal.
[c] TEL reconstituted with a 1:1 mixture of sterile water and propylene glycol.

reconstituted with sterile water to a concentration of 50 mg/ml each of tiletamine and zolazepam. Fresh TEL was made for every test except Experiment three. Experiments and trials within an experiment were conducted at the same time of day at least 7 days apart. Statistical analyses were by one-way ANOVA or ANOVA for repeated measures at a significance level of $P < 0.05$. Means are reported with standard errors (SE).

Experiment one

Ten wolves (six male, four female) were immobilized with either 5 or 10 mg/kg TEL and induction and arousal times were compared. In a second trial, these wolves were immobilized with 10 mg/kg TEL and upon initial signs of arousal were given booster doses of either 5 mg/kg TEL or 2.5 mg/kg ketamine HCL (Ketaset®, Bristol Laboratories, Syracuse, New York 13221, USA). The purpose of the second trial was to compare arousal times between booster doses of TEL or KET when KET was given on a comparable weight basis to tiletamine (i.e., 5.0 mg/kg TEL contains 2.5 mg/kg tiletamine). Induction time (IT) was defined as the time from injection of TEL until the animal was unconscious. Arousal times included the time from loss of consciousness until the animal first raised its head (HUT1) and the second head up time (HUT2) which was time from HUT1 until the animal raised its head a second time. Additional drug was administered at HUT1 in the second trial.

Experiment two

To test the effects of storage time on drug efficacy, five wolves (three male, two female) were immobilized with 5 mg/kg TEL which was reconstituted and held at room temperature (20 C) for 30 and 60 days. Since much wildlife immobilization occurs during winter, TEL was reconstituted with a 1:1 mixture of sterile water and propylene glycol, stored at −9 C for 60 days, then used to immobilize five other wolves (4 male, 1 female) at 5 mg/kg. Induction times and HUT1 were compared with times recorded for the same dose in Experiment one.

Experiment three

To examine physiological responses of wolves to TEL anesthesia, five wolves (three male, two female) were immobilized with either 5 or 10 mg/kg TEL as before. All wolves received both doses in a randomized crossover design conducted 14 days apart. They were brought indoors immediately after induction and attached to a vital signs monitor (Propaq® 102, Protocol® Systems, Inc., Beaverton, Oregon 97006, USA) which simultaneously measured electrocardiogram, blood pressure and rectal temperature. Respiratory rates were counted visually. Data were recorded at 1, 5, 10, 20 and 30 min after attachment of the monitor.

RESULTS

Experiment one

There was no difference in IT ($P = 0.63$) between wolves immobilized with 5 or 10 mg/kg TEL (Table 1). However, it took longer for wolves given 10 mg/kg TEL to initially raise their heads ($P = 0.0008$). Wolves given 5 mg/kg booster doses of TEL took significantly longer ($P = 0.01$) to raise their heads a second time compared to wolves given boosters of KET (Table 1).

Inductions and recoveries for both doses of TEL were generally smooth. Salivation

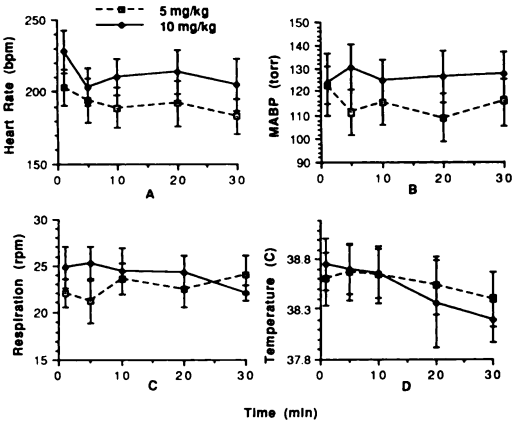

FIGURE 1. Mean heart rate (A), mean arterial blood pressure (MABP; B), respiratory rate (C), and rectal temperature (D) of five wolves immobilized with either 5 or 10 mg/kg Telazol®.

tended to be more copious at the higher dose. One male wolf, regardless of TEL dose, had extremely rough recoveries characterized by ataxia, peddling, falling backwards, and severe (i.e., requiring medical treatment) self mutilation. Each time this animal began mutilation, he was sedated with 2.2 mg/kg xylazine hydrochloride (Rompun®, Miles Laboratory Inc., Shawnee, Kansas 66201, USA) which kept the animal calm for several hours after which recoveries were uneventful.

Experiment two

There were no differences in IT or HUT1 between wolves given 30- ($P \geq 0.11$) or 60-day-old TEL ($P \geq 0.27$) and those given fresh solution (Table 1). Wolves immobilized with 60-day-old TEL reconstituted with propylene glycol had a longer IT than any other group of wolves immobilized with 5 mg/kg TEL ($P < 0.05$). There was no difference in HUT1 between wolves given TEL mixed with propylene glycol and any other group ($P \geq 0.44$).

Experiment three

There were no differences in heart rates ($P = 0.36$), mean arterial blood pressures ($P = 0.32$), respiratory rates ($P = 0.91$), and rectal temperatures ($P = 0.62$) between the two TEL doses (Fig. 1). All these indices remained relatively stable throughout the test period.

DISCUSSION

Experiment one

Doubling the TEL dose did not achieve quicker induction times but it did lengthen time to initial arousal. We did not measure total recovery time because judging complete recovery is subjective with TEL. It appeared that the longer initial arousal time noted at the 10 mg/kg dose resulted in a longer total recovery time.

The second part of this experiment was to determine if booster doses of TEL lengthened recovery times, which appeared to be the case. Tiletamine is an analog of both phencyclidine and ketamine and has a relative potency of one-half that of phencyclidine and 2.5 times that of ketamine (Beck, 1972). In this experiment, KET was administered at an equal weight (2.5 mg/kg) to that of tiletamine. The longer time to HUT2 when KET was used as the booster drug could be a function of tiletamine's greater relative potency; however, it is more likely a combination of potency plus synergistic effects of additional zolazepam. In situations where the initial TEL dose would be inadequate to maintain immobilization, but quicker recoveries are desired, we recommend maintaining anesthesia with additional boosters of KET only.

The rough recoveries noted in one male were felt to be an exceptional individual response to TEL as this animal had relatively rough inductions and recoveries when given KET as well. However, thrashing was much more violent with TEL and self mutilation had never been observed in this animal with other drugs. This reaction may be a function of the greater potency of tiletamine exacerbating a tendency for abnormal recoveries in this animal. However, it suggests another inter-

esting hypothesis. It is well known that benzodiazepine tranquilizers can induce hyperphagia in animals (Hunt et al., 1988). Self-mutilation may have been an aberrant manifestation of hyperphagia induced by the zolazepam component of TEL. During the self mutilation there appeared to be little analgesic effect from TEL as the animal whined and yelped while biting itself.

The copious salivation noted was bothersome, but not considered a problem. Excess salivation might be controlled with parasympatholytic agents, such as atropine, although this was not tested. The positive chronotropic effects of atropine (Adams, 1982) should be considered given that TEL already increased heart rate.

Experiment two

Due to drug testing requirements, the manufacturer currently limits shelf life of reconstituted TEL to 4 days when stored at room temperature or 14 days refrigerated. The drug did not appear to lose clinical effectiveness over longer times when used on wolves. Since these studies were undertaken, we have also immobilized two female wolves with 5 mg/kg TEL kept at room temperature for 90 days. Induction time for each was about 5 min and HUT1 averaged 32 min. This 90-day solution was colored a pale yellow and the manufacturer warns that, "only clear solutions should be administered." Based on these results, we see no reason to discard TEL that has been reconstituted for less than 60 days.

Reconstituting TEL in a mixture of water and propylene glycol increased induction times, but did not alter other anesthetic properties of TEL. This is important for immobilizations conducted in cold weather where the normal aqueous preparation of TEL could quickly freeze in needles, syringes, or darts. The stability of this preparation for 60 days under freezing temperatures could make it useful for applications such as recapture collars (Mech et al., 1984).

Experiment three

Cardiovascular effects of TEL were consistent with those reported for dogs given tiletamine only (Chen et al., 1969). Heart rates recorded during TEL anesthesia appeared to be higher than in wolves given either KET plus xylazine (Kreeger et al., 1987), butorphanol plus xylazine (Kreeger et al., 1988), or the resting heart rate of unanesthetized wolves as measured by radiotelemetry (84 ± 4 bpm; Kreeger et al., 1989). The heart rates were similar to wolves immobilized with KET and promazine (Kreeger et al., 1989). There were no effects on respiratory rate or body temperature regulation during the time monitored.

Results of these studies indicate that TEL is a safe and effective anesthetic for gray wolves. The abnormal reaction in the one wolf was considered an exceptional response since it occurred in only one of 16 wolves, but recoveries should be monitored in case intervention is necessary. Also, TEL reconstituted either with sterile water or a 1:1 mixture of water and propylene glycol can be stored for 60 days without decreasing its clinical effectiveness in wolves.

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