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Source: Journal of Wildlife Diseases, 39(3) : 665-674

Published By: Wildlife Disease Association

URL: https://doi.org/10.7589/0090-3558-39.3.665

Journal of Wildlife Diseases, 39(3), 2003, pp. 665–674

EVALUATION OF THREE COMBINATIONS OF ANESTHETICS FOR USE IN FREE-RANGING ALPINE MARMOTS (*MARMOTA MARMOTA*)

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ABSTRACT: From April 1998 to September 2000, 241 free-ranging alpine marmots (*Marmota marmota*) were anesthetized in the course of a field project using either xylazine plus ketamine (XK), medetomidine plus ketamine (MK), or xylazine plus a 1:1 mixture of zolazepam and tiletamine (XZT). For each of the combinations, the respective doses for short term and long-term surgery were established and seasonal variations in the amount of drugs needed were assessed. No fatalities occurred, and doses for efficient and safe anesthesia in spring were as follows (XK, MK, and XZT, respectively, in mg/kg body mass): short term surgery 3+40, 0.25+35, and 3+15; long term surgery 20+80, 0.5+70, and 10+20. In late summer/autumn, higher doses (20+60, 0.2+60, and 10+15 for short term surgery) had to be administered, probably due to increase of marmots' body fat content. Heart rate, respiratory rate, rectal temperature, palpebral reflex, muscle relaxation, and analgesia were monitored to evaluate the animals' responses to each of the drug combinations. Hypothermia was induced by all combinations and heart rate significantly decreased during anesthesia, especially in marmots receiving MK. Respiratory rate was highly variable and no significant differences between the drugs were found. Muscle relaxation was rather poor in marmots anesthetized with XK. The XZT combination tended to have a longer induction period but was found to subsequently depress the palpebral reflex and induce muscle relaxation and analgesia very efficiently. We conclude that, regardless of the anesthetics used, doses should always be adjusted to the planned manipulations, the marmots' nutritional state, and to the time of year. Furthermore, close monitoring of physiologic parameters, especially body temperature, should be guaranteed. On the basis of physiologic and behavioral responses, XZT is the most effective drug combination for anesthetizing alpine marmots, especially for long term, potentially painful procedures.

Key words: Alpine marmot, anesthesia, ketamine, *Marmota marmota,* medetomidine, tiletamine, xylazine, zolazepam.

INTRODUCTION

Marmots are large, herbivorous sciurids within the order Rodentia. They comprise 14 species found in the northern hemisphere of Eurasia and North America. Only the alpine marmot (*Marmota marmota*) is common in Europe where it occurs on alpine meadows from 900 m to 3,200 m above sea level (Bibikow, 1996).

Various species of the genus marmota have been extensively used in scientific studies during the past decades, both in field studies as well as under laboratory conditions. Marmots represent an optimal model for studying the mechanisms of hibernation (e.g., Arnold, 1992). Furthermore, the discovery of woodchuck hepatitis virus (WHV, family: *Hepadnaviridae*) in the woodchuck (*Marmota monax*) has prompted numerous studies on this species in recent years because WHV is closely related to hepatitis B virus (HBV), a dangerous human pathogen (Tennant and Gerin, 2001).

Despite extensive use of marmots in studies which often require immobilization, sedation, or anesthesia of the animals, only limited data on suitability of injectable anesthetic agents in marmots is available. Various drugs and drug combinations have been applied in marmots, including various barbiturates (Armour et al., 1974; Noyes and Siekierski, 1975; Young and Sims, 1979; Eagles et al., 1988; Zatzman and Thornhill, 1988), phencyclidine (Armour et al., 1974), ketamine (Noyes and Siekierski, 1975; Frase and van Vuren, 1989), droperidol plus fentanyl (Noyes and Siekierski, 1975), and xylazine plus ketamine (Concannon et al., 1983, 1997; Mrozek et al., 1995; Wiesner, 1998). However,

most of these studies did not evaluate physiologic responses of animals to treatment, and judgment of the anesthetics' suitability was based mainly on observation, experience, and anecdotal evidence.

In this study we present data on the use of three combinations of anesthetics: xylazine plus ketamine (XK), medetomidine plus ketamine (MK), and xylazine plus zolazepam and tiletamine (XZT) in free-ranging alpine marmots. Our objectives were 1) to establish an effective and safe dose for each of the combinations for short-term (biopsy) and long-term (intraabdominal implantation of transmitters plus biopsy) surgery, 2) to assess seasonal variations in the dose necessary to produce anesthesia in light of the change in fat content of the marmots during their active season, and 3) to compare physiologic responses of the animals to the drug-combinations.

MATERIALS AND METHODS

We conducted the study in an alpine area of the Avers-Bregalga Valley (46°26′N, 9°33′E, 2,100 m elevation) in Grisons, Switzerland. It was carried out within an ecophysiological project on the influence of fatty acids on hibernation of alpine marmots. This involved intraabdominal implantation of temperature-sensitive radio transmitters and biopsy of inguinal fat depots. All procedures of this study conformed with the current laws regulating animal welfare in Switzerland (approval No. 5/1997 of the Cantonal Veterinary Authority, Grisons). Alpine marmots were trapped with single-door life traps (Tomahawk Live Trap, Tomahawk, Wisconsin, USA) in spring (April/May) and late summer/autumn (August/September) during 1998 to 2000. Trapped marmots were then brought to a field laboratory located in a mountain hut. Ambient temperatures in the field lab were around 10–15 C.

After a brief visual examination of the animals' nutritional and health state, they were weighed to the closest 50 g with a spring balance and transferred to a wooden box where the marmots remained until further manipulation. We used three combinations of anesthetic agents for anesthesia: xylazine (Rompun® 20 mg/ml, Bayer, Leverkusen, Germany) plus ketamine (Ketamidor® 100 mg/ml, Richter Pharma, Wels, Austria), medetomidine (Domitor® 1 mg/ml, Orion, Espoo, Finland) plus ketamine and xylazine plus Zoletil® (Virbac, Carros, France), the latter being a mixture of 50 mg/ml tiletamine and 50 mg/ml zolazepam. For anesthesia, the marmots were taken out of the boxes, the anesthetics were administered into the musculature of the upper hind leg and the animals were returned into the boxes immediately afterwards. An induction time of 10 min was allowed during which the animals were left undisturbed. Thereafter, the marmots were taken out of the boxes and depth of anesthesia was evaluated. This was done by assessing muscular tone and palpebral and corneal reflex responses and by determination of pupillary size, capillary refilling, and reaction to pain. If depth of anesthesia was considered unsatisfactory according to stages of general anesthesia, i.e., the level of anesthesia was judged stage II or lower (which sometimes was the case at the beginning of the study while establishing effective doses for each of the combinations), half of the initial dose was injected again and a further 10 min induction time was allowed.

Initial doses (in mg/kg body mass) for implantations were 10+50 (XK), 0.2+20 (MK), and 2+10 (XZT). Since time course of the field project didn't allow pilot studies, these doses were based on recommendations in the literature for wild mammals of comparable size. If doses were found ineffective in the marmots before or during surgery, doses were raised by approximately half of the initial dose in subsequent animals until safe and effective anesthesia was achieved during all manipulations. For short-term surgery (biopsies) alone, half of the doses producing satisfactory anesthesia for implantation were initially given and titrated accordingly. In case of decreasing anesthetic effects during surgery, an isoflurane (Isofluran "Rhodia", Torrex Pharma, Vienna, Austria)—oxygen mixture was delivered via a face mask to deepen anesthesia.

When depth of anesthesia was considered satisfactory, we clipped the hair at the abdominal and/or the inguinal region and the skin was scrubbed with a polyvidone-iodine-solution 1% (Betaisodona®, Mundipharma, Vienna, Austria). An ophthalmic ointment (Oleovit Augensalbe, Laevosan, Linz, Austria) was applied to the animals' eyes to prevent corneal drying. The marmots were then fixed to an operation table in dorsal recumbency, covered by surgical drapes, and the first skin incision was made in the ventral midline, approximately 3 cm caudal of the caudal end of the sternum. Length of this incision was about 8 cm. After blunt dissection of the subcutaneous tissue, the abdominal cavity was opened by a longitudinal incision of the musculus rectus abdominis and the peritoneum. The transmitter (48×29×21 mm)

was inserted into the peritoneal cavity where it floated freely. Muscles and skin were each closed with interrupted horizontal mattress sutures spaced approximately 4 mm apart. Subcutaneous tissue was sutured with a continuous suture. All sutures were made with absorbable Polysorb® 2/0 or Polysorb® 0 (United States Surgical, Norwalk, Connecticut, USA), and skin sutures were coated with an oxytetracyclin HCL spray (Terramycin® Aerosol-Spray für Tiere, Pfizer Corporation, Vienna, Austria). For biopsies, a 2 cm diagonal skin incision was made in the inguinal region. After removal of approximately 2 g of inguinal fat, the incision was closed with a continuous subcutaneous suture and an interrupted horizontal mattress skin suture.

Enrofloxacine (Baytril®, Bayer, Leverkusen, Germany) was administered subcutaneously as a prophylactic antibiotic in those animals that had transmitters implanted. Antagonists (Atipamezole [Antisedan®, Orion, Espoo, Finland], tolazoline [Tolazolin, Gräub, Berne, Switzerland], and sarmazenil [Sarmasol®, Gräub, Berne, Switzerland], according to the anesthetics used) were given in about a third of the animals. Effects of antagonists on recovery will be presented in a future paper.

After surgery, animals were placed on a mat in dorsal recumbency to avoid the risk of wound contamination (e.g., by the animal urinating or defecating and subsequent contamination of the abdominal and/or inguinal wound) and observed visually during the initial phase of recovery until they were able to turn themselves into sternal recumbency. Marmots were then transferred to wooden boxes where they were left undisturbed during full recovery, except for brief visual observations approximately every 2 hr. After 24 hr, they were released at the capture site after final examination by a veterinarian.

Physiologic parameters were recorded every 10 min during manipulation and surgery, starting 10 min after administration of anesthetics. We measured respiratory rate by direct observation, heart rate by cardiac auscultation, and rectal temperature using a thermometer with a measuring range of 20–40 C and an accuracy of 0.1 C (Labor—Feinthermometer, K. Hecht, Altnau, Switzerland). Further, we determined palpebral reflex, tone of the neck muscles, and analgesia (by direct observation during surgery and by pinching the inter-digital skin at a hind limb). These parameters were graded 0 (absent) to 4 (intense).

Effective and safe dose (mg/kg body mass) for each anesthetic-combination was defined as the dose at which depth of anesthesia was sufficient for biopsy and implantation plus biopsy, respectively, without the need of additional inhalation anesthesia. A dose was regarded effective when at least four marmots were successfully anesthetized with the respective dose and no adverse effects were observed in any of the animals, both during manipulation and during recovery even if no antagonists were used.

In order to assess variations in the effective doses due to the animals' body fat reserves, this procedure was carried out both in spring (shortly after hibernation when marmots had almost depleted their fat reserves) and in late summer/autumn, when the animals had regained substantial amounts of fat for subsequent hibernation.

For evaluation of the three drug combinations used, we analyzed only data from individuals in which the initial dose was found to be effective, i.e., no additional doses were administered and no deepening of anesthesia by isoflurane was necessary. In order to prevent any bias by age, only results from adult alpine marmots were used for the statistical analysis. All data were analyzed using SPSS software (SPSS, Chicago, Illinois, USA). We used a two-way analysis of variance (ANOVA) for repeated measures to compare the effects of the anesthetics combinations and time on rectal temperature, heart rate, and respiratory rate. For the ordinal variables (palpebral reflex, tone of neck muscles, and reaction to pain), the Friedman test was used to test the influence of time on these parameters for each combination. Where significant differences occurred, the Wilcoxon test was applied to compare among time points. Comparison among drug combinations at specific time points was done using the Kruskal-Wallis test and, where significant differences were detected, the Mann-Whitney *U*-test for pairwise comparison to distinct between specific drug combinations. Times for initial recovery were compared using a one-way ANOVA and the Tukey post-hoc test. In all statistical analyses, a value of $P<0.05$ was accepted as significant.

RESULTS

In total, 241 alpine marmots (121 females, 120 males) were captured and anesthetized. We performed biopsy of inguinal fat tissue in 176 animals (123 in April/May; 53 in August/September) and abdominal implantation of transmitters plus biopsy in 65 animals (August/September only). Mean duration of surgical procedure (defined as time from first skin incision to placing of last suture) was 14 min±5 (bi-

TABLE 1. Doses (mg/kg body mass) of three combinations of anesthetics (Xyl = xylazine, Ket = ketamine, Med = medetomidine, ZT = 1:1 mixture of zolazepam and tiletamine) found effective and save for short-term (biopsy) and long-term (intraabdominal implantation of transmitter plus biopsy) surgery in alpine marmots.

Procedure	Season	Xyl + Ket	*n*	Med + Ket	*n*	Xyl + ZT	*n*
Biopsy	April/May	3 + 40	16	0.25 + 35	27	3 + 15	49
	August/September	20 + 60	9	0.2 + 60	10	10 + 15	5
Implantation	Autumn only	20 + 80	4	0.5 + 70	5	10 + 20	4

opsies) and 45 min±14 (implantations+biopsy). No fatalities occurred during anesthesia and surgical procedures and no adverse effects were noted in the marmots after being released in the field. Age of the animals ranged from 3.5 mo to approximately 6 yr and the body mass from 850 to 4,800 g (mean values and standard deviation: juveniles 1100 g±150 [n=9]; yearlings 1,760 g±930 [n=23]; 2 yr and older 3130 g±740 [n=209]).

We used XK in 78 marmots (20 implantations, 58 biopsies), MK in 61 marmots (14 implantations, 47 biopsies), and XZT in 102 marmots (31 implantations, 71 biopsies). In 12 animals (seven anesthetized with XK, three with MK, and two with XZT, respectively), anesthesia was found to be insufficient after 10 min induction time and half of the initial dose was given in addition. Inhalation anesthesia with isoflurane had to be given to deepen anesthesia in the course of 40 implantations (62%) and 30 biopsies (17%). The necessity of administration of additional doses as well as use of inhalation anesthesia mostly occurred during the initial phase of this study while we were establishing effective doses of the injectible anesthetics. Furthermore, doses found to be sufficient for biopsies in spring did not produce satisfactory anesthesia in late summer/autumn. We therefore had to reevaluate the respective doses for use during that time of year. Doses found effective and safe for the use in alpine marmots in respect to time of year and surgical manipulation are presented in Table 1.

The physiologic responses of marmots to the three combinations are shown in Figures 1 and 2. All three combinations had a consistent and significant effect on body temperature which decreased remarkably in course of anesthesia ($P<0.001$ for each of the combinations). Values after 40 min were approximately 2 C lower than 10 min after induction. Regarding their effect on body temperature, no significant difference was found between the three combinations.

Heart rate also decreased significantly during the initial phase of anesthesia in all combinations used ($P<0.001$ for each of the combinations) and tended to increase again after 30 min. However, this trend was not statistically significant in any of the combinations. The MK combination had the most pronounced effect on lowering of heart rate throughout anesthesia, values differed significantly from XK ($P=0.003$) and from XZT ($P=0.011$). Marmots anesthetized with the XK combination tended to exhibit the highest heart rates though there was no statistically significant difference compared to XZT.

Respiratory rate showed a large variation throughout anesthesia in all combinations used. Thus, there was neither a statistically significant difference between the combinations, nor an influence of time on respiratory rate within each drug combination.

The palpebral reflex remained sluggish throughout 40 min of anesthesia in animals anesthetized with MK or XK and no effect of time was observed (Fig. 2). The XZT combination produced a longer induction period with respective animals exhibiting a significantly more prominent palpebral reflex after 10 min compared to

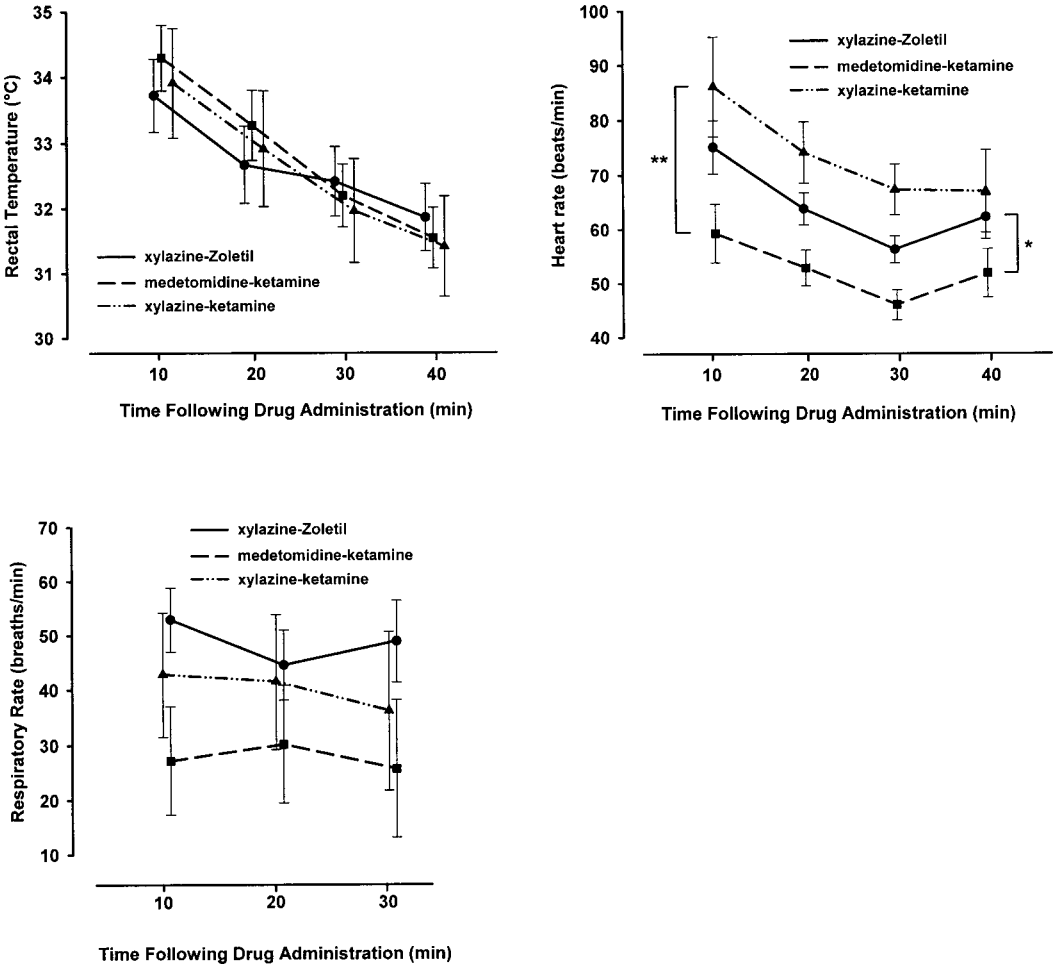

FIGURE 1. Physiologic responses of alpine marmots during anesthesia with xylazine-zolazepam/tiletamine (Zoletil®), medetomidine-ketamine, and xylazine-ketamine. Means and standard error bars are presented. Significant differences between drug treatments are indicated by asterisks (* $P<0.05$, ** $P<0.01$).

animals anesthetized with MK or XK ($P=0.004$). After 20 min, however, the palpebral reflex became depressed in the XZT-anesthetized marmots and remained at a similar sluggish level as in the other drug combinations. We detected no significant differences between drug combinations at minutes 20, 30, and 40 after induction of anesthesia.

Muscular relaxation was well developed after 10 min in all combinations used although MK and XK produced a better relaxation compared to XZT ($P<0.001$). In the marmots anesthetized with MK or XK, muscle tone continuously increased until 40 min after induction of anesthesia (influence of time: $P<0.001$ for both mixtures). This was especially prominent with the XK combination and significant differences were observed between drug combinations at minutes 20, 30, and 40 due to this effect ($P=0.015$, $P=0.011$, and $P=0.049$, respectively). As observed in the palpebral reflex, the XZT combination exhibited a longer induction time and muscular relaxation with this combination was developed best 20 min after drug administration (difference between minute 10 and minute 20: $P=0.003$). Muscle tone then progressively increased again (difference between mi-

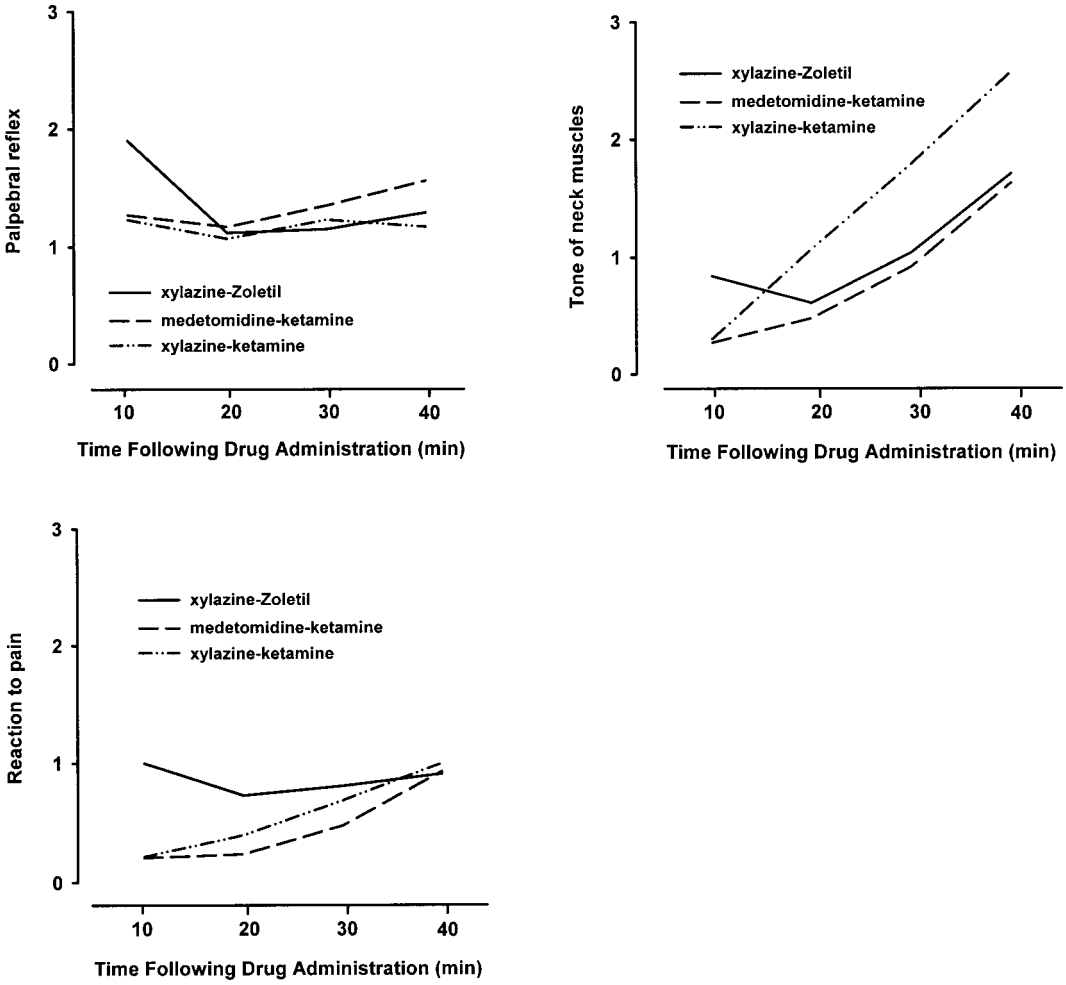

FIGURE 2. Time course of palpebral reflex, tone of neck muscles, and reaction to pain in alpine marmots during anesthesia with xylazine-zolazepam/tiletamine (Zoletil®), medetomidine-ketamine, and xylazine-ketamine. Means of scores are presented.

nute 20 and minute 40: $P<0.001$), closely following the pattern of MK.

Surgical analgesia was sufficient for 40 min with all combinations used. Marmots anesthetized with MK or XK exhibited a slight but not significant trend towards minimal reaction to pain in course of anesthesia. During the initial phase of anesthesia, XZT produced lighter (but still sufficient) analgesia compared to the other combinations (10 min: $P=0.005$, 20 min: $P=0.001$). Again, this drug combination showed a tendency towards a longer induction period with maximum analgesia reached after 20 min. However, this trend was not significant.

Regardless of the application of antagonists, recovery was smooth with each of the combinations used and all animals had regained full locomotor ability and consciousness <8 hr after induction of anesthesia. Times (in min) for initial recovery of marmots not receiving antagonists, i.e., time from immobilization to the point when animals turned themselves in sternal recumbency, were as follows (XK, MK, and XZT, respectively; mean values and standard deviation): implantation plus bi-

opsy 92±20, 78±50, and 102±32 (no significant differences); biopsy spring 47±9, 79±26, and 66±15 (no significant differences); biopsy late summer 51±11, 101±35, and 109±34 (XK vs. MK P=0.012; XK vs. XZT P=0.002). No significant differences existed between autumn recoveries and spring recoveries for each specific drug combination.

DISCUSSION

Few data exist on anesthesia in marmots. In hoary marmots (*Marmota caligata*), Noyes and Siekierski (1975) used sodium pentobarbital, ketamine hydrochloride, and a combination of droperidol and fentanyl and found the latter combination to give the best results. Young and Sims (1979) and Eagles et al. (1988) recommended use of sodium pentobarbital injected intraperitoneally in woodchucks. Ketamine was found to be effective for short-term immobilization of yellow-bellied marmots (*Marmota flaviventris*) by Frase and van Vuren (1989). Armour et al. (1974) used sodium thiopental and phencyclidine for anesthesia. However, even at low doses, barbiturates (pentobarbital and thiopental) and opioids (fentanyl) are potent toxic substances in both animals and humans, and the use of barbiturates in wild animals is often difficult due to the necessity of intravenous or intraperitoneal administration. Phencyclidine has been taken off the market due to its hallucinogenic property and cases of human abuse (Nielsen, 1999). On the other hand, ketamine has no muscle relaxation properties and may induce various side effects and rough recovery. It is therefore regarded unsuitable for anesthesia in many mammals when used alone (Lin, 1996). A XK combination was recommended by Mrozek et al. (1995) for anesthetizing woodchucks and by Wiesner (1998) for immobilization of marmots. Concannon et al. (1983, 1997) used this combination for short-term anesthesia in woodchucks.

All three combinations of anesthetic agents evaluated in this study produced satisfactory anesthesia in alpine marmots. We were able to establish the doses for each of the combinations generating effective and reliable anesthesia for both short term and long-term surgery. As expected, higher doses were needed for intraabdominal implantation of transmitters. Because this made necessary the opening of the abdominal cavity, it was a more painful procedure compared to biopsies of inguinal fat depots and required deep surgical anesthesia for up to 1 hr. However, doses for long-term surgery were only slightly higher than respective doses for biopsies in late summer/autumn.

Furthermore, we observed seasonal variations in the amount of drugs needed. In all combinations used, higher doses were necessary to produce equivalent anesthesia for biopsies in autumn compared to spring. This was especially the case with XK, where six times more xylazine per kg body mass had to be administered. We assume that the substantial increase of body fat content of marmots towards hibernation accounted for that observation, although animals with large quantities of fat are reported to have a lower basal metabolic rate per unit of body weight and require less anesthetics (Thurmon et al., 1996a). During summer, marmots typically build up large fat depots for subsequent hibernation, leading to an increase of body fat (Bibikow, 1996). This increase may result in a higher percent of lipophilic anesthetics being taken up by fat depots and thus lower levels in the nervous system during the initial phase of anesthesia. However, because we found no significant difference between times for initial recovery in spring and in autumn this remains elusive. Noyes and Siekierski (1975) also concluded the dose rate in marmots should be adjusted to the nutritional state of the animal as well as to the absolute weight.

Of the combinations used, XK was the only combination that had been documented before for use in marmots. The doses found effective for biopsy in this

study were comparable to those used by Concannon et al. (1983, 1987) for blood sampling and intubation (4+40 and 5+50). Mrozek et al. (1995) used higher doses (7.5+75) for subcutaneous injection of microchip implants, while Wiesner (1998) recommended up to 12 times more xylazine (about 37.5 mg/kg body mass) and less ketamine (about 30 mg/kg body mass) for immobilization of marmots. Considering the relatively distinct side effects of xylazine at higher doses, especially its depressing effects on the respiratory and circulatory system (Thurmon et al., 1996b), we recommend use of the XK doses found to be effective in this study.

No information regarding their use in marmots was found in the literature for the MK and the XZT combinations. However, doses producing effective anesthesia in marmots compared well with those recommended for general anesthesia in rabbits. Nevalainen et al. (1989) found 0.5 mg/kg medetomidine +25–60 mg/kg ketamine to be effective, while Popilskis et al. (1991) reported 5 mg/kg xylazine plus 15 mg/kg zolazepam/tiletamine to produce satisfactory surgical anesthesia in this species.

Hypothermia was induced in marmots by each of the three combinations used. Forty minutes after drug administration, rectal temperatures had decreased approximately 2 C. This effect was highly consistent and we never observed any signs of hyperthermia. In several animals, rectal temperature had dropped well below 30 C several hours after induction of anesthesia (data not shown). This was also observed by van Vuren (1989) in course of intraperitoneal transmitter implantation in yellow-bellied marmots (*Marmota flaviventris*) using ketamine as the sole anesthetic agent. Consequences of this response in alpine marmots remain unclear. Although marmots, like other hibernators, are capable of adjusting their body temperature over a wide range, several studies in humans indicate a negative effect of hypothermia during surgery on the immune system (Wenisch et al., 1996), wound healing (De Jong and Kemp, 1984), blood clotting (Kurz, 1997), and general recovery (Lenhardt et al., 1997).

All combinations induced bradycardia. This effect was most profound in anesthesia with MK which lowered heart rate to about a third of that seen in active, nonanesthetized marmots (132–160 beats per min in yellow-bellied marmots; Zatzman and Thornhill, 1987). Bradycardia as the result of applying MK has been reported before in various species, e.g., otters (Fernandez-Moran et al., 2001). Although this depressive effect is typical for most alpha-2 agonists (Klein and Klide, 1989), XK and XZT combinations had significantly less bradycardiac potency in marmots. Thus we conclude that lowering of heart rate was mainly caused by medetomidine. Respiratory rate was highly variable and no statistically significant difference between the combinations was found. Because respiratory rate of alpine marmots varies depending on ambient temperature (around 30–100 breaths per min between 20 and 30 C; Ortmann, 1989), we were unable to distinguish between pharmacologic and external effects on respiration. Regarding the low levels of heart rate and respiratory rate in marmots anesthetized with medetomidine, we recommend xylazine as the preferable alpha-2 agonist in marmots.

Marmots anesthetized with XZT exhibited a longer induction period compared to the other combinations. Depth of anesthesia on basis of palpebral reflex, muscle tone, and analgesia was developed best after 20 min. Although muscle relaxation decreased thereafter, we observed continuous and good analgesia and a decreased palpebral reflex, indicating persisting surgical anesthesia. This is in accordance with former studies in rabbits (e.g., Popilskis et al., 1991), where XZT was found to induce prolonged surgical anesthesia compared to XK. Possible causes for this observation are greater potency and longer duration of action of tiletamine compared to ketamine (Lin, 1996). In the doses used in this

study, both MK and XK had sufficient analgesic potency after 40 min although there was a trend in both towards slight reaction to pain. Still, muscle relaxation became weak in course of anesthesia in the marmots anesthetized with XK. Therefore the use of XZT may be advantageous if potentially long and painful procedures are carried out in marmots.

Recovery was smooth with each of the combinations used. Although XZT tended to have the longest initial recovery time which is in accordance with its long anesthetic effects, antagonism of the zolazepam and the xylazine components of this combination can offer a solution if swift recovery is required after anesthesia under field conditions. Effects of various antagonists for the combinations used in this study will be presented in a future paper.

We conclude that several aspects should be considered when anesthetizing marmots. Although inhalation anesthesia may be the best choice if working with laboratory marmots, injectible anesthetics are advantageous under field conditions because only limited equipment is necessary. However, duration and severity of manipulations planned as well as the time of year (and hence the animals' fat reserves) and absolute body mass should be carefully taken into consideration to ensure animal welfare and avoid fatalities. Doses of drugs used should be adjusted accordingly. In this study, we established the respective doses for three combinations of injectible anesthetics. Each of them generated safe and effective anesthesia, although rectal temperature should be closely monitored because hypothermia in course of anesthesia seems to be a common response in marmots. However, on the basis of physiologic and behavioral responses, we recommend use of XZT in marmots, especially for long term, painful procedures. This combination had minimal adverse cardiopulmonary effect, induced good muscle relaxation, and showed good analgesic properties of long duration.

ACKNOWLEDGMENTS

The authors want to thank the many people who assisted in collecting field data, especially U. Bruns, F. Frey-Roos, A. Fuerst, M. Gmeiner, M. Janovsky, and P. Kerschbaumer. We appreciate the helpful comments of T. Ruf on the manuscript. This study was supported in part by the Austrian Science Fund (FWF project P12430-BIO), the Swiss Union Bank (UBS), and the Gesellschaft zur Förderung des Forschungsinstitutes für Wildtierkunde und Ökologie.

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Received for publication 24 September 2002.