"FENTAZIN" AND XYLAZINE IN DEER

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Xylazine has achieved widespread use as a tranquillizer, sedative or chemical immobilisation agent in farmed deer worldwide (Hunter, 1981, Mackintosh and van Reenen, 1984, Keep, 1984; Zomborsky and Sugar, 1990) However, veterinary practitioners report variation in responses of red deer to given doses of xylazine (Hunter, 1981) and there is considerable variation in dose responsiveness between species. Some species require high dose rates, hence decreasing the safety margin. As a result there has been an evaluation of a wide range of alternative chemical immobilising agents and tranquillizers, either alone or in various combinations for use in a variety of deer species (Keep, 1984)

In New Zealand the development of the drug combination "Fentaz" comprising fentanyl citrate (10 mg/ml) and azaperone (80 mg/ml) overcame some of the short-comings of xylazine alone for deer capture and immobilisation However, it was an expensive drug and at dosages used was dangerous to the user and is now no longer commercially available The combination of "Fentaz" with xylazine achieved widespread use in clinical veterinary practice in New Zealand and Australia during the 1970s and 1980s (Hunter, 1981, English, 1991, Keep, 1984) The combination was prepared by practitioners and various ratios of drugs were used Recently a commercially available mixture "Fentazin" (Parnell Laboratories [NZ] Ltd) comprising xylazine as a 5% solution, also containing 0 4 mg fentanyl citrate and 3 2 mg azaperone per ml has become available

This paper presents research results of an evaluation of a range of dose rates of xylazine (Xy) alone or "Fentazin" (F) at different dose rates and to evaluate the relative merits of Xy or F for velvet removal without local anaesthetic and the reversal responses to yohimbine alone or a mixture of yohimbine and naloxone

EXPERIMENT 1 - DOSE COMPARISON

This experiment set out to examine the sedative and analgesic properties of different dose rates of Xy and F Full detail of experimental method and results are published elsewhere (Wilson *et al* 1993). This presentation provides a summary of the method and results.

1.1 Method

Six one-year-old female red deer were used for this study from October 1992 to January 1993 Deer were managed at pasture on the Massey University deer research unit

Each deer was randomly assigned to one of six treatments of either xylazine alone as a 5% solution ("Xylaze Forte injection", Parnell Laboratories (NZ)) or "Fentazin" (Parnell Laboratories NZ)), such that xylazine alone was given at 0 4 and 0 6 mg/kg and "Fentazin" was given at doses which delivered 0 2, 0 4 and 0 6 mg/kg xylazine A sixth treatment was a sterile water control. Treatments days were at least 9 days apart

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Table 1. DESCRIPTION OF SCORING SYSTEM FOR EACH OBSERVATION OR RESPONSE TO STIMULUS USED TO MONITOR THE EFFECTS OF "XYLAZE" AND "FENTAZIN"

Observation	Score			
	0 (normal)	1	2	3 (Nil response)
Angle of neck	Head up at approx 45° above horizontal.	Head above horizontal but below normal.	Head below horizontal but above 45°.	Head down approx 45° below horizontal. Head on or near ground.
Body Stance	Upright, legs in normal position. Normal movement	Slow or no movement, legs slightly splayed.	Unsteady or staggering legs in "saw-horse" stance.	Recumbent.
Degree of eye closure	Wide open	Partly but less than half closed.	Partly but more than half closed.	Almost fully closed
Palpebral/Head withdrawal reflex (Response to sharp movement of the hand toward the eye)	Rapid eye blink and vigorous avoidance head movement	Slower response to move head. Eye blink	No head movement Slow blink of eye.	No response
Resistance to head movement	Strong resistance when head is held and moved sideways or up and down.	Modest resistance to forced movement.	Little resistance to forced movement	No resistance to movement
Response to noise (shrill whistle).	Alert eye, ear or head movement.	Modest eye, ear or head movement.	Very sluggish eye, ear or head movement.	No response.
Response to ear touch The ear border was gently touched with a pair of Allis tissue forceps	Rapid avoidance by vigorous head movement and/or ear flinching after touch	Modest head movement and ear flick	Sluggish head movement and ear flick.	No response.
Response to ear pinch. The tip of the ear was pinched once with Allis tissue forceps	Rapid avoidance by vigorous head withdrawal and ear flicking.	Modest head movement and/or ear flick.	Sluggish head movement and/or ear flick	No response.
Response to needle prick. A 15G x 1" needle was used to gently prick the skin in the gluteal region	Leg or body movement, twitching of skin and flinch	Modest movement flinch or skin twitch	Sluggish movement flinch or skin twitch	No response.

On each day of treatment syringes were loaded with the appropriate treatments by a third party, such that the administration and observations were undertaken without knowledge of treatment or dose Administration was by rapid intramuscular injection into the anterior neck Observations were taken immediately prior to injection and then 5, 14, 25, 35, 60, 90, 120, 150, 180, 210, 240 and 300 minutes thereafter Heart and respiration rates were counted and a range of postural changes and responses to painful stimuli were scored and recorded according to the description in Table 1

Time from injection to recumbency was recorded for each animal as was the time that the deer returned to a standing posture

Heart and respiration rate data and time to recumbency and duration of recumbency (after log transformation) were subject to two-way analyses of variance Median individual behavioural responses were examined graphically and to present overall response patterns a "sedation score" was computed by adding median scores for angle of the neck, body stance, eye closure, palpebral reflex, resistance to head movement and response to noise, and an "analgesia score" was computed by adding the median scores for response to ear touch, ear pinch and needle prick at each observation time

1.2 Results and Discussion

Five of the six deer showed no sign of aversion to repeated experimental procedures, but the sixth occasionally became recumbent before injection of drug and became recumbent even after administration of sterile water Time to and duration of recumbency for that animal was not used in statistical analyses

Mean heart and respiration rates and overall sedation and analgesia scores are presented in Figures 1 and 2

Changes in posture, responses to stimuli, and heart and respiration rates were observed within 5 minutes following injection of either Xy or F and many responses had not returned to normal even 5 hours after administration, particularly at the higher dose rates There was considerable variation between animals for all observations Both Xy and F at all dose rates produced a significant reduction in heart and respiration rates (P <0 001) and that reduction was persistent throughout the period of observation, particularly at higher dose rates

The sedation score shows a rapid onset of sedation for all treatments with peak responses 14-35 minutes after administration of drug There were only minor differences in the degree of sedation at each dose rate, but the higher doses of both Xy and F produced a more persistent response The analgesia score shows a rapid reduction in response to touch and painful stimuli for all doses of Xy and F, with a slight delay to peak response and slightly lower response following the lower doses of Xy and F There were no significant differences in sedative and analgesic responses between drugs and dose rates

The mean times to and duration of recumbency are presented in Table 2

Table 2 TIME TO RECUMBENCY AND DURATION OF RECUMBENCY OF DEER AFTER INJECTION OF VARIOUS DOSES OF "FENTAZIN" AND "XYLAZE"

Dose (mg/kg xylazine)	No Treated	No Recumbent	Mean Minutes to Recumbency (range)+	Mean duration (min)of Recumbency (range)+
0 2 "Fentazin"	5	6	12 2 (8 0 - 20 6)	81 6 (42 6 - 134 5)
0 4 "Fentazin"	6	6	7 3 (4 1 - 12 3)	136 4 (64 6 - 301 8)
0 6 "Fentazin"	6	6	6 9 (4 0 - 13 3)	174 9 (102 6 - 247 8)
0 4 "Xylaze"	6	6	13 4 (2 5 - 29 8)	136 1 (73 8 - 171 8)
0 6 "Xylaze"	6	6	8 0 (3 2 - 16 1)	189 6 (79 6 - 265 1)
Control	6	3	101 9* (205- 233 2)	44 3 (10 4 - 92 5**)

+ Data from 1 deer which repeatedly stood and sat throughout the 5 h period of observation and which repeated that pattern after sterile water injection have been deleted from these calculations

* Data only for the 3 deer recumbent

** Data for this deer includes 4 periods of recumbency

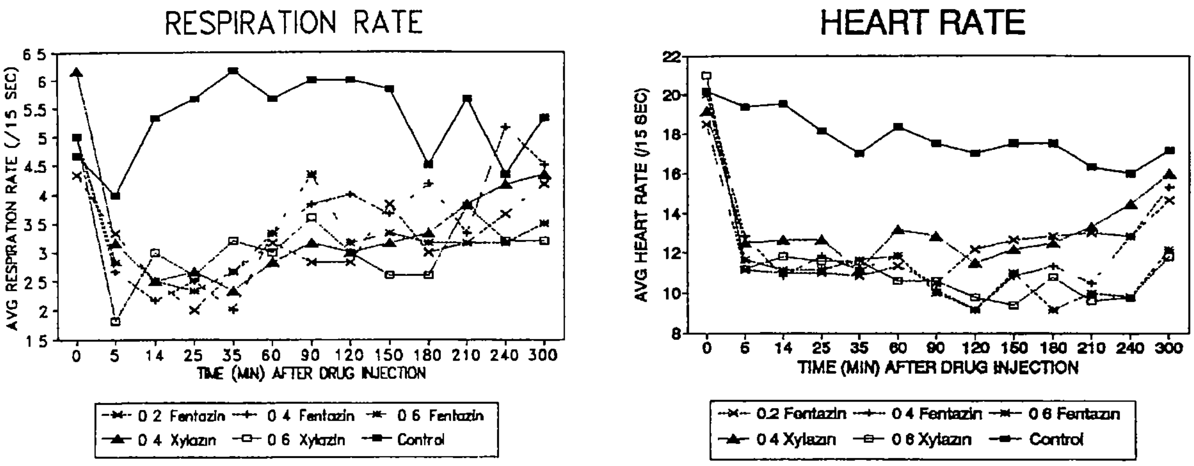

Figure 1 Mean heart rate and respiration rate (per 15 secs) for 6 deer given each treatment of xylazine and "Fentazin"

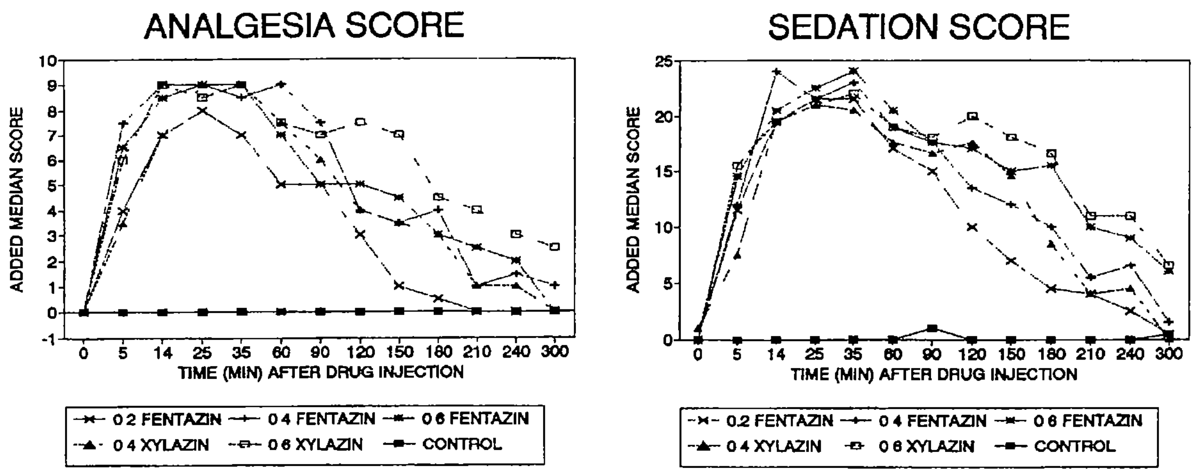

Figure 2 Sedation and analgesia scores for 6 deer given each dose rate of "Fentazin" and xylazine

All deer given each dose of Xy and F became recumbent Some deer took up to 30 minutes to become recumbent at the lower dose rates of Xy, whereas there was less variation of time to recumbency following a similar dose of F or at higher dose rates of Xy and F. While the time taken for deer to become recumbent was lower at higher dose rates, this effect was not statistically significant There was a significant treatment effect on duration of recumbency ($P < 0.001$) but that is related to dose rate rather than drug type

This experiment has shown no statistically significant differences in behavioural and physiological responses to Xy when compared with F at the range of doses used Veterinary practitioners report that F produces a more reliable knock-down effect and maintenance of recumbency That trend was observed in this study, more so at the mid-dose range than at the higher dose rates.

The quantity of fentanyl citrate and azaperone in "Fentazin" is not great and the dose rates used in this study, while covering a range 0.2-0.6 ml/kg fall within the ranges reported elsewhere (Keep, 1984)

Part 2 of this paper presents more data to substantiate these effects.

EXPERIMENT 2

2. Xylazine and "Fentazin" for Velvet Removal

This study evaluated the properties of xylazine and "Fentazin" at one dose rate for chemical immobilisation for velvet harvesting of stags

2.1 Method

Twenty four one-year-old and six two-year-old red and red x 25% wapiti stags averaging 91kg raised on pasture at the Massey University deer research unit were used Stags were randomly assigned to receive either a 5% solution of xylazine alone at 0 5 mg/kg or "Fentazin" to deliver xylazine at 0 5 mg/kg. Administration was by rapid intramuscular injection into the neck region using syringes which were coded so observers were unaware of the drug or combination used on each deer. Physiological and behavioural observations and responses to stimuli were recorded in Table 1, with the additional observation of the animal's response to pinching of the antler tip with an Allis-tissue forcep Observations were undertaken immediately prior to injection and at 5, 14, 25 and 30 minutes after administration

Upon completion of observations 14 minutes after immobilising agent injection, 8-10ml of local anaesthetic was infused as a ring block about each antler pedicle, a tourniquet applied and after approximately 6 minutes the antler was removed using a medium tooth saw. Approximately 15 minutes later the tourniquet was removed and reversal agent appropriate to the immobilising agent yohimbine ("Reverzine", Parnell Laboratories Ltd) for xylazine and yohimbine plus naloxone ("Contran -H", Parnell Laboratories Ltd for "Fentazin") was given by jugular intravenous injection to those deer still recumbent Time taken for signs of reversal were recorded Table 3. Time to recumbency and duration of recumbency were also recorded

Statistical analyses of immobilising drug effect on heart and respiration rates were undertaken by two-way analysis of variance Time taken to recumbency and observations of recovery after reversal were analysed by analysis of variance after logarithmic transformation. Sedative and analgesia scores were computed as for part 1. The "analgesia score" for this study included the response to squeezing of the antler tip.

2.2 Results

All deer became recumbent with the 0 5mg/kg dose of Xy or F. The mean time to recumbency after F was 9min 42sec, significantly shorter than time to recumbency of 12min 52sec after xylazine alone (P <0 05) Heart and respiration rates and sedative and analgesia scores are presented in Figures 3 and 4. Heart rate and respiration rates were reduced by similar amounts after either Xy or F The sedation and analgesia scores indicate very similar responses to either Xy and F

Four of the 14 deer treated with Xy alone stood spontaneously within 15 minutes of velvet antler removal, whereas only one of 16 sedated with F stood spontaneously during that time. Times taken to regain movements and to return to a standing posture after injection of reversal agent were extremely variable between animals and between doses, and while deer treated with F stood on average 30secs earlier than those with Xy alone after appropriate reversal, this difference was not statistically significant (see Table 3)

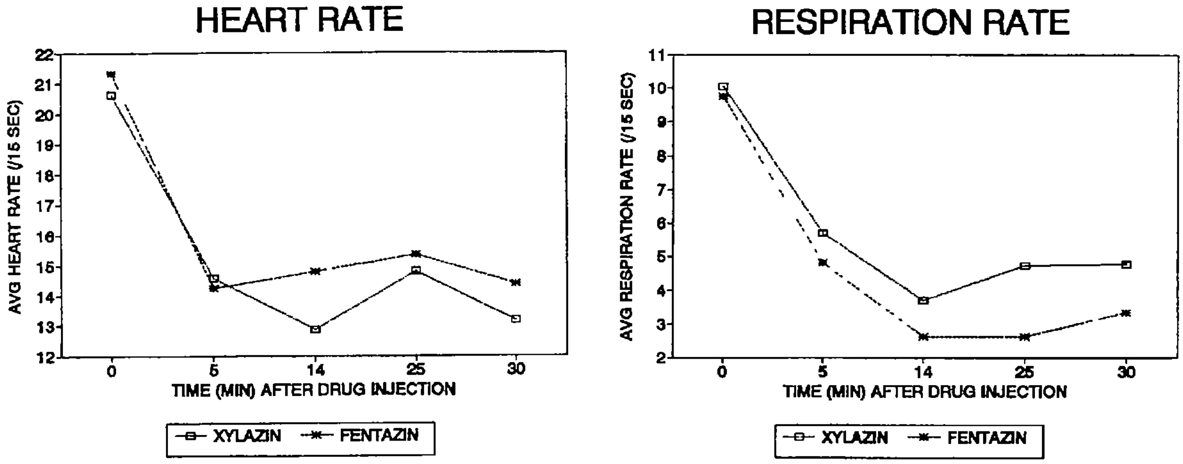

Figure 3 Mean heart and respiration rates (per 15 sec) for deer given Xy (n = 14) or F (n = 16) at 0.5 mg/kg for velvet removal

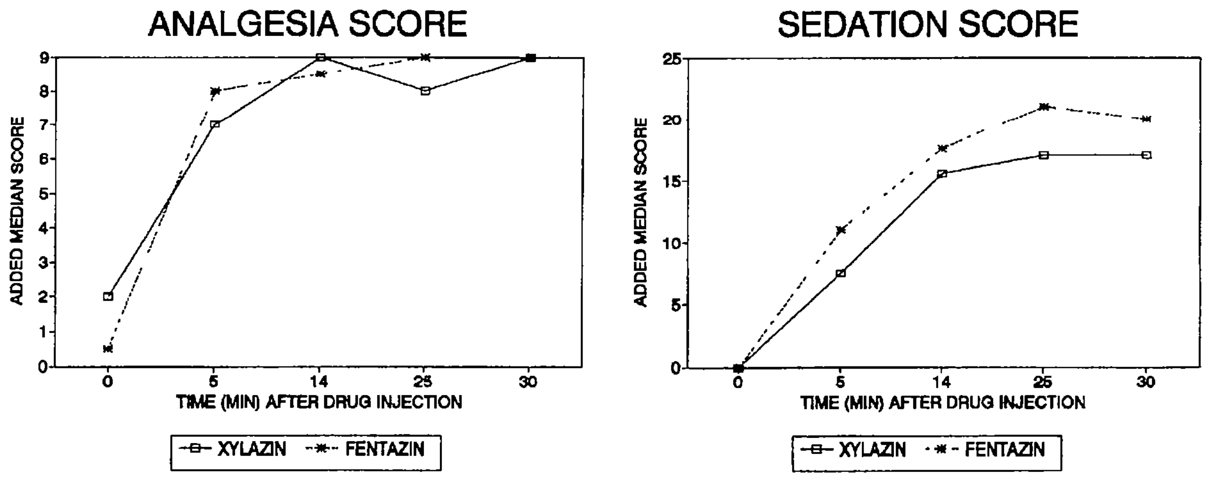

Figure 4 Sedation and analgesia scores for deer given Xy (n = 14) or F (n = 16) at 0 5 mg/kg for velvet removal

Table 3. **Mean (and range) of times to observations of responses following reversal of Xy and F with either Yohimbine or Yohimbine + Naloxone respectively (Seconds)**

Sedative Treatment	Xy	Xy + FA
Reversal Treatment	Yohimbine	Yohimbine + Naloxone
No observations	10	15
First Ear movement	63.2 (11-214)	66 (23-259)
First Eye movement	62 1 (35-122)	60.8 (7 - 210)
Elevation of head	63 5 (27-207)	79 8 (23-195)
Standing	136 3 (60-318)	106.3 (40-290)

This experiment has shown that one and two-year-old stags responded to Xy and F in a manner similar to one-year-old hinds studied in part 1 The major significant effect was the that time to recumbency in this trial after F was significantly shorter than following Xy alone Further, those treated with F remained recumbent more persistently than those treated with Xy alone. The dose rate used here was a modest dose and these differences may not be observed at higher dose rates, as was reported in experiment 1

The response to pinch of the antler indicated that not all deer responded vigorously to this stimulus prior to immobilising agent injection and there was little sensitivity to this test after 5 minutes. However, responses to pinching of the ear persisted for longer and in some cases responses were observed throughout the duration of observations Thus, it would seem the sensitivity of the ear may exceed the sensitivity of the other organs tested.

EXPERIMENT 3

3. Reversal of "Fentazin"

3.1 Method

Forty three three-year-old red deer stags averaging 158kg liveweight were chemically immobilised for velvet harvesting in batches over a three week period using "Fentazin" at a dose rate to generally deliver 0.7 mg xylazine per kg Stags which failed to become recumbent were given an additional 0.5ml "Fentazin" intravenously Once the stags became recumbent they were given a nerve block local anaesthesia, a tourniquet applied and antlers removed as for section 2 1 Stags were randomly allocated such that 22 received yohimbine hydrochloride reversal, while the remainder received a combination of yohimbine and naloxone ("Contran-H") at a standard dose rate approximately 15 minutes after velvet antler removal. Time to first observation of recovery parameters including ear and head movements and return to standing posture were recorded.

3.2 Results

Mean data are presented in Table 4

The average time to regain a standing posture after yohimbine administration was 67 5 secs (range 35-163 secs) whereas the time to regain standing posture after yohimbine + "Naloxon" was 73.3 secs (range 45-148 secs) The difference was not statistically significant

Table 4 **Mean (and range) of times to observations of responses following reversal of "Fentazin" with either Yohimbine or Yohimbine + Naloxone (Seconds)**

Reversal agent	Yohimbine	Yohimbine + Naloxone
No observations	22	18
First Ear movement	38 1 (14-121)	45 6 (25-90)
First Eye movement	40 1 (10-105)	36 2 (9-71)
Elevation of head	46 7 (18-157)	47.5 (11-100)
Standing	67.5 (35-163)	73.3 (45-148)

Thus, it would appear that the small amount of fentanyl citrate and azaperone in the drug combination is insufficient to influence the recovery time if yohimbine alone is administered.

4. VELVET HARVESTING WITHOUT LOCAL ANAESTHETIC

Fentanyl citrate is considered to be a potent analgesic drug (Sackman, 1991) It is considered by some that addition of fentanyl citrate to xylazine may provide sufficient systemic analgesia to permit the removal of velvet antler without application of local anaesthetic This experiment set out to evaluate physical responses by the animal following a range of dose rates of Xy and F used for chemical immobilisation for velvet harvesting without local anaesthetic

4.1 Method

Fourteen red and red x wapiti one-year-old stags averaging 106kg were chosen for this study For the first animal a dose rate of F at 0 5 mg/kg Xy was given That animal responded when the antler was cut. Subsequent doses of 0 7 and 0 75 mg/kg Xy were given according to the schedule in Table 4

Fifteen to 20 minutes after recumbency a saw cut was made on the lateral side of one antler and the animal observed closely for signs of eye and/or head movement i e withdrawal reflex. If no reflex was observed a second and subsequent cuts were made If any reflex was observed, sawing ceased immediately and the animal was given local anaesthetic by ring block around the pedicle. The antler was removed after four minutes. Ten of 14 animals responded after between 1 and 3 saw cuts, even at the higher dose rate of Xy and F (Table 5)

Table 5. Actions after commencement of sawing of velvet antler on stags given various doses of Xy or Xy + FA without local anaesthetic

Deer No.	Sedative Drug	Dose (mg/Xy/kg)	Action
42	Xy + FA	0 5	LA after 1 cut
41	Xy + FA	0 7	LA after 1 cut
44	Xy + FA	0 7	Velvet removed, no local
48	Xy + FA	0 7	Velvet removed, no local
28	Xy + FA	0 75	LA after 1 cut
36	Xy + FA	0 75	Velvet removed, no local
38	Xy + FA	0 75	LA after 1 cut
40	Xy + FA	0 75	LA after 3 cuts
47	Xy + FA	0 75	LA after 3 cuts
30	Xy	0 75	LA after 1 cut
35	Xy	0 75	LA after 1 cut
49	Xy	0 75	LA after 1 cut
50	Xy	0 75	Velvet removed, no local
51	Xy	0 75	LA after 1 cut

LA = Local anaesthetic (Mepivicaine hydrochloride) given as a ring block.

The clear conclusion from this study was that insufficient analgesia is provided by Xy or F even at dose rates that produce rapid, profound and persistent recumbency. Local anaesthetic must therefore be applied during all instances of velvet antler removal using Xy or F. Further evaluation of systemic analgesic properties of a combination of systemic analgesic drugs with xylazine will be needed before other combinations are accepted for velvet harvesting in the absence of local anaesthetic

The national code of conduct for the removal of velvet antlers stipulates only forms of analgesia approved by the Chief Veterinary Officer are permitted for velvet harvesting Currently the CVO permits only the use of local anaesthetic or full general anaesthesia

5. CONCLUSION

These studies have shown that the major differences between xylazine and "Fentazin" are that "Fentazin" produces a more rapid knock-down effect and animals remain recumbent more predictably and persistently when equivalent doses of xylazine in each drug is used. Both of these factors are advantageous to the practitioner, given that the addition of fentanyl citrate and azaperone to xylazine did not produce significantly greater sedative responses which may place the animal at greater risk.

Reversal of "Fentazin" can be achieved adequately by the use of yohimbine alone Field evaluation of stags after administration of yohimbine alone for reversal of F have been undertaken to evaluate whether persistent effects of F may modify post-velvetting behaviour These results will be reported elsewhere

The addition of doses of fentanyl citrate found in "Fentazin" provide insufficient analgesia to permit the removal of velvet antler without administration of local anaesthetic Therefore local anaesthetic must be applied to all animals for the purpose of velvet antler removal with currently available systemically acting immobilizing/narcotic combinations

Full detail of the methods and results presented here are to be published in the New Zealand Veterinary Journal, (Wilson et al 1993a,b,c)

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