IMMOBILON/REVIVON IN RED DEER

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Introduction

In the mid 1970s etorphine was scheduled as a Class A Controlled Drug and its use as an animal remedy was prohibited. This was largely as a result of the fatal accidental self-injection of Immobilon (which contains etorphine) by a veterinarian in the UK. This accident caused the temporary withdrawal of Immobilon the drug from the UK market. However, there was such demand for the drug that it was made available again, but with revised warnings of its dangers and with a recommendation that all users have the human antidote, naloxone, on hand at all times. I was in the UK at the time of the accident and found the drug very useful in horses. On my return to NZ I was surprised to find that Immobilon was banned here, yet a similar narcotic, Fentaz was licenced. Since working at Invermay I feel that there are good reasons why Immobilon should be available in NZ especially for deer:

(i) Only a small volume is needed to immobilise an animal. This is particularly important when using darts and pole-syringes. The blow darts used at Invermay (Corson *et al.* 1984) only hold 1.0-1.5 ml and published reports suggest that this volume of Immobilon should be sufficient to immobilise adult red deer which previously required 2 or 3 darts containing Fentaz.

(ii) Revivon, the antagonist for Immobilon is better than Lethidrone, the antagonist for Fentaz, because it more completely reverses narcotic sedation and produces less respiratory depression (Booth, 1982).

(iii) Immobilon is used extensively in deer overseas.

For the endocrinological studies at Invermay only narcotic drugs could be used for restraint and Fentaz, which was the only one licenced, was becoming prohibitively expensive.

Consequently I applied to the Minister of Health and obtained a special licence to use Immobilon in deer at Invermay. Unfortunately the safe which contained all my drugs, including Rompun, Fentaz and Immobilon, was stolen and this loss temporarily curtailed my use of Immobilon and reduced the amount of data available for presentation in this paper.

Pharmacology: Large Animal Immobilon/Revivon is presented as two 10.5 ml bottles in a polystyrene box containing directions for their use. On the back of the box is a note on "Accident Procedure" and "Reversing Agents" detailing how to deal with accidental self-injection, spillage on the skin or splashing into eyes, mouth or nose. Immobilon (in this paper refers to Large Animal Immobilon) contains etorphine hydrochloride 2.45 mg/ml and acepromazine maleate 10 mg/ml with chlorocresol BP 0.1% w/v as preservative. Revivon (Large Animal Revivon) contains diprenorphine hydrochloride 3.0 mg/ml with chlorocresol preservative.

Etorphine (see Fig.1) has a very similar structure to morphine but has up to 10,000 times its analgesic potency (Booth, 1982). Etorphine binds to the opiate receptors in a number of regions within the CNS and its use for immobilising game animals results largely from its ability to cause catatonia at very low dose levels.

Diprenorphine (see Fig.1) is a potent morphine antagonist with a potency up to 35 times greater than that of lethidrone and a duration of action 2 to 3 times greater (Bentley *et al.* 1965). The recommended Revivon dose is ml for ml of Immobilon i.e. 3 mg diprenorphine to reverse 2.45 mg etorphine.

Immobilon also contains acepromazine which improves etorphine's action in most species and produces better muscle relaxation. However, Revivon does not reverse acepromazine's action and residual tranquillisation remains for some hours.

Action: The effects of Immobilon are very similar to those of Fentaz. Within 3 to 4 minutes there is a change in posture and gait. The fore limbs are lifted high at each step and the steps are shorter. Visual accommodation is lost. Animals will approach a stationary person but movement and noise may cause them to jump and try to flee. They usually become recumbent in 5 to 7 minutes with maximum sedation in 10-15 minutes. With heavy doses immobilisation may last for over 2 hours if Revivon is not used. It is advisable to reverse the anaesthesia as soon as possible. Regurgitation and bloating are potential hazards and animals should be positioned in sternal recumbancy, if possible. If laterally recumbent then a bolster should be placed beneath the neck so that any regurgitated material drains out of the mouth. Booth (1982) also warns against Immobilons use when ambient temperatures are over 30°C.

Etorphine/Immobilon use overseas: Etorphine may be used alone or in combination with acepromazine, xylazine or other drugs (Booth, 1982). Table I presents a summary of reported dose rates in red deer, sika and elk. Immobilon has been used safely at dose rates up to 4 ml/100 kg for capturing wild deer. Dose rates of 0.8 to 1.2 ml/100 kg have been used routinely in farmed deer in the U.K.

The addition of xylazine to Immobilon reduces the dose rate required for the latter; 0.5 ml Immobilon plus 0.5 ml 10% Rompun per 100 kg is effective in farmed red deer.

Immobilon has been used successfully in Pere David's deer (*Elaphurus davidianus*) and the dose rate is lower than for red deer; 0.7 ml Immobilon/100 kg (Anon). An etorphine/xylazine combination has also been used successfully with Pere David's at a dose rate of 0.008 mg/kg etorphine plus 0.1 mg/kg xylazine (Bush, 1983).

Immobilon and etorphine have been used extensively in North America for immobilising white-tailed, black-tailed and mule deer, caribou and moose, (Thorne, 1982; Bubenik, 1982; Nielsen, 1982; Lange, 1982; Patenaude, 1982;

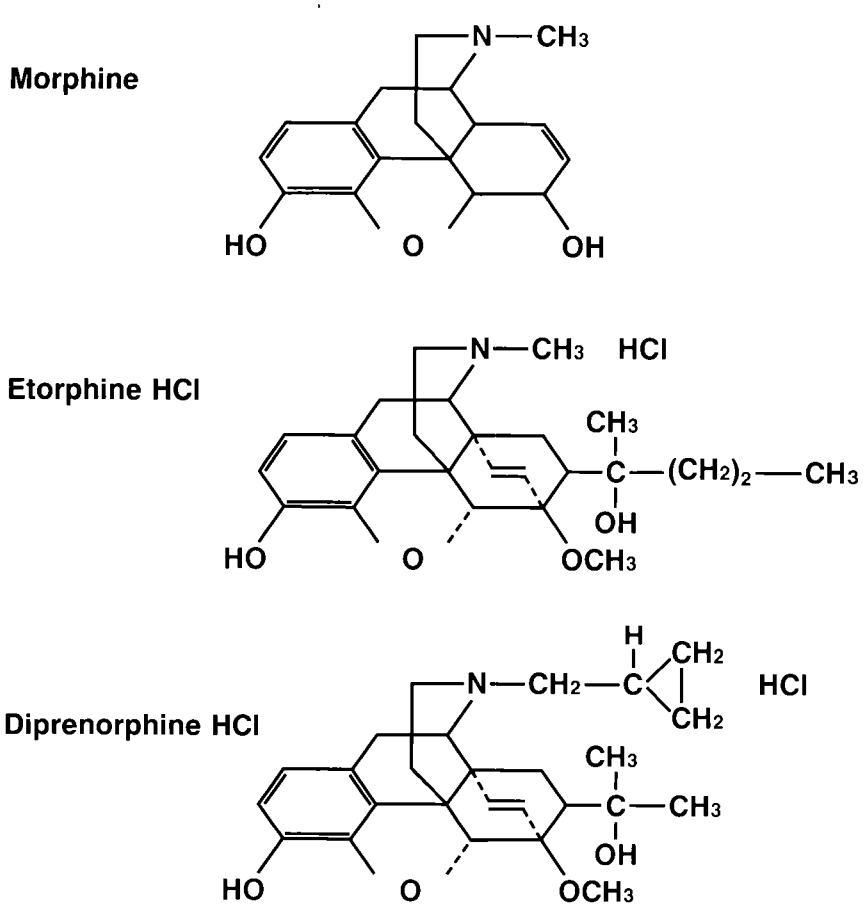

Fig. 1. : Chemical structures of morphine, etorphine and diprenorphine.

TABLE I: Dose rates of etorphine alone and in combination with acepromazine (Immobilon L.A.) and/or xylazine (Rompun) in deer of the genus *Cervus*

Drug	Deer type	Body weight (kg)	Dose rate	Vol.Immobilon L.A./100 kg (ml)	Ref. No.
ETORPHINE	*C.elaphus nannodes* (Tule Elk)	90-125	0.033	N.A.	15
	C. elaphus (Scottish red deer)	35	0.025	N.A.	24
			Etorphine + Acepromazine		
ETORPHINE + ACEPROMAZINE or IMMOBILON	*C. elaphus* (Park red deer)	N.S.	0.04 + 0.16	1.6	1
	C. nippon) (Park sika)	N.S.	0.025 + 0.1	1.0	1
	C. elaphus (farmed red stags)	100-200	0.024 + 0.1	1.0	4
	C. elaphus (farmed red pregnant hinds)	70-90	0.017 + 0.07	0.7	4
	C. elaphus canadensis (elk)	180	0.022 + 0.09	0.9	9
	C. elaphus canadensis	220-364	0.022 + 0.09	0.9	18
	C. elaphus and *C. nippon* (red and sika deer)				13
	Wild - young	N.S.	0.1 + 0.4	4.0	
	mature	N.S.	0.1 + 0.4	4.0	
	old	N.S.	0.07 + 0.28	2.8	
	Tame/semi-tame - young	N.S.	0.03 + 0.12	1.2	
	mature	N.S.	0.02 + 0.08	0.8	
	old	N.S.	0.02 + 0.08	0.8	
	C. elaphus nelsoni (Rocky mountain elk)	150-200	0.02-0.03 + 0.1	0.8-1.2	25
	C. elaphus roosevelti (Roosevelt elk)	150-200	0.02-0.03 + 0.1	0.8-1.2	25
	C. elaphus nannodes (Tule elk)	90-125	0.03-0.035 + 0.1-0.15	1.2-1.4	25
	C. elaphus (farmed red deer)	35	0.025 + 0.1	1.0	24
	C. elaphus (farmed red deer)		(J. Burdge - pers.comm.)		
	Quiet hinds	90	0.02 + 0.08	0.8	
	Large nervous hinds	115	0.036 + 0.14	1.4	
	Stage	190-220	0.026 + 0.11	1.1	

		Dose rate (mg/kg) Etorphine+Acepromazine+Xylazxine	Dose (ml/100 kg) Immobilon LA+Rompun 10%	Ref
IMMOBILON + ROMPUN	*C. elaphus* (farmed red deer)	0.012 + 0.05 + 0.5	0.5 + 0.5	22
	C. elaphus (red deer)	0.02-0.06 + 0.1 + 0.2-0.8	0.8-2.5 + 0.2-0.8	23

Franzmann, 1982) generally with dose rates of 0.02-0.05 mg/kg. Xylazine/etorphine combinations were particularly effective and allow lower doses of etorphine.

The use of Immobilon is contra-indicated in fallow deer due to this species' sensitivity to acepromazine (Anon; Harrington, 1982). However, etorphine/xylazine combinations have been used successfully at dose rates of 0.015-0.03 mg/kg etorphine plus 0.3-0.6 mg/kg xylazine (Anon; Harrington, 1982).

Immobilon use at Invermay: (see Table II) Immobilon was used to restrain stags for 1-2 hour periods of blood sampling during the course of endocrine studies. All the stags had been kept in pens and fed only nuts. This diet provided all their nutritional requirements but lacked fibre. Consequently their rumen contents were always very liquid. Unfortunately due to the constraints of the trial the animals could not be fasted prior to immobilisation and the animals were therefore at risk from regurgitation. Animals were positioned with polystyrene blocks under their necks to allow any regurgitated fluid and saliva to flow out of their mouths. To add to the risks the animals had to remain anaesthetised for 1-2 hours before being given Revivon. Under these circumstances 2 animals died during 28 anaesthetic procedures with Immobilon. The first died from inhalation of regurgitated rumen contents. The second died of pulmonary oedema and froth in the airways and was subsequently found to have extensive pulmonary abscessation and consolidation in the apical lobes. This may have been the consequence of inhalation of rumen contents on a previous occasion.

The stags were all quite tame and were injected with a pole syringe. The dose rates ranged from 0.01-0.03 mg/kg (0.4-1.25 ml/100 kg). The stags all became recumbent in 4-7 minutes. Relaxation was usually adequate although some deer had slight muscle rigidity and tended to jerk when touched. After an equal volume of Revivon was injected intravenously all stags stood up in 1-2 minutes. They remained somewhat tranquillised for some time but no evidence of "enterohepatic recycling" (Anon) of etorphine was seen.

The relatively small dose rates required for restraint may reflect the quietness of the stags.

Fentaz/Rompun and Immobilon/Rompun combinations: Rompun is the most frequently used drug for restraint at Invermay. However, for procedures such as laparoscopy, egg transfer and ultrasonic scanning the addition of 1 ml Fentaz (10 mg fentanyl plus 80 mg azaperone) to 25 ml 2% Rompun produces much better relaxation and minimises limb movement. The dose is 2.5-3.0 ml of the mixture per hind (approximately 0.5-0.6 mg/kg Rompun plus 1 mg/kg fentanyl plus 8 mg/kg azaperone) by intravenous injection. Intramuscular injection requires a 50% greater dose rate. Yohimbine (Mackintosh and van Reenen, 1984) (0.25 mg/kg) alone reverses most of the sedation produced by this combination because of the small Fentaz component. However, 0.1 ml Lethidrone (0.02 mg/kg) can also be administered simultaneously with the yohimbine to improve the reversal effect.

TABLE II: Immobilon use in red stags at Invermay.

Date	Liveweight (kg)	Dose (ml)	Dose rate (mg/kg)	Dose/100 kg (ml)	Comments
24/8	165	1.5	0.022	0.9	Slight muscle rigidity - tended to jerk when touched - down 24 min before reversed
30/8	135	1.5	0.027	1.1	Good relaxation - recumbant 1 hr 30 min before reversed
17/9	154	1.5	0.023	1.0	OK. Recumbant 2 hr 13 min before reversed.
	152	1.5	0.024	1.0	OK. Recumbant 1 hr 34 min before reversed.
	137	1.5	0.027	1.1	OK. Stood up 1 hr 50 min after injection - given Revivon while standing.
20/9	120	1.5	0.03	1.25	OK. Recumbant 1 hr 10 min before reversed.
2/10	134	1.2	0.022	0.9	Poor relaxation- regurgitated but apparently drained from mouth. OK for 60 min, but found dead 70 min after injection.
20/2	182	1.0	0.013	0.55	OK.
	155	1.0	0.016	0.65	OK.
21/3	3 animals 200-250	1.0	0.01-0.012	0.4-0.5	OK.
	7 animals 145-200	1.0	0.01-0.016	0.5-0.7	OK.
30/4	6 animals 150-200	1.0	0.012-0.016	0.5-0.7	OK.
	2 animals 200-250	1.2	0.012-0.015	0.5-0.6	OK.
	1 <150	0.8	0.013	0.53	Stag in poor condition - found dead after 10 min.

On the basis that Immobilon has 2-3 times the potency of Fentaz, 0.5 ml Immobilon was added to 500 mg Rompun and used at the same dose rate as before. However, despite a very rapid knockdown the animals were not as relaxed; 25% kicked or twitched and the uterus was not as relaxed as with the Fentaz/Rompun mixture. Also 0.1 ml Revivon was required in addition to yohimbine to reverse the anaesthesia. It was therefore concluded that this Immobilon/Rompun mixture was not as good as the Fentaz/Rompun mixture for these procedures.

Cost of Immobilon: Last year the landed cost of Immobilon/Revivon was $40 per packet (10.5 ml of each) i.e. at a dose rate of 1 ml/100 kg this equates to $4/100 kg. Fentaz at $120/20 ml and at 2 ml/100 kg costs $15/100 kg plus Lethidrone at $12/5 ml costs $4.50/100 kg; i.e. a combined cost of nearly $20/100 kg. Thus Immobilon/Revivon is one quarter the cost of Fentaz/Lethidrone.

Safety: Although etorphine has approximately 10 times the potency per mg of fentanyl, Immobilon (etorphine 2.45 mg/ml) has only 2-3 times the potency per ml of Fentaz (fentanyl 10 mg/ml) in deer. Nevertheless it has been estimated that as little as 0.1 ml Immobilon could be fatal in man. Therefore, great care should be taken when handling both of these drugs. There have been a number of accidents involving Immobilon reported overseas (Firn, 1973; Goodrich, 1977; Orr, 1977) and at least one of these was fatal (Anon, 1976). This fatality may have been prevented if the veterinarian had carried with him the antidote plus instructions for its administration. Immobilon comes packed with Revivon and in an emergency Revivon may be used in humans. However, the recommended human antidote is Narcan (naloxone) and at least 20 ampoules should be readily to hand whenever Immobilon is used. The same precautions also apply to the use of Fentaz which is almost as dangerous. A full emergency kit for all these drugs is described by van Reenen (1981) and the recommended "Accident Procedure" is printed on the back of the Immobilon/Revivon packet as well as in the enclosure.

The potential dangers of using Immobilon were put into perspective by Harthoorn (1976) when he stated that since 1962 over 100,000 doses had been used in Africa with only one case of accidental self-injection. In that case Lethidrone was injected immediately and the ranger involved survived.

Immobilon is currently used in North America, Europe, Africa and Australia. I believe that its prohibition in NZ is an over-reaction to mishaps which have occurred in the UK. Let us hope that Fentaz and Rompun will not be withdrawn from the NZ market because of a similar accident which occurred recently in the North Island (Veterinary Cervus, Issue 7, 1984).

Conclusions

In situations where a narcotic is preferred to Rompun/Yohimbine sedation and reversal, Immobilon/Revivon appears to be a cheap potent alternative to Fentaz/Lethidrone for use in deer. It does not produce quite the same degree of relaxation as Fentaz but it is adequate for most procedures such

as blood-sampling or velvet removal. Revivon is a very effective reversal agent. As with any narcotic it is important to guard against the inhalation of regurgitated rumen contents by recumbent deer and to reverse the anaesthesia as soon as possible.

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