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Effects of R51163 on Intake and Metabolism in Moose

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ABSTRACT: R51163, a newly synthesized purine alkyl piperidine that produces reliable sedation in cattle, was tested in five adult bull moose (*Alces alces*). Compared with controls, all animals dosed with 0.4 mg/kg BW ate significantly ($P < 0.05$) less dry matter for at least 1 wk after treatment. Median estimates of resting metabolism, measured the day of injection. did not differ between treatment and control groups, although the coefficient of variation was almost two times larger for drugged (15%) versus control (8%) individuals. Dose response was allometric, with larger animals exhibiting longer effects.

Key words: R51163, anesthesia, tranquilizer, moose, *Alces alces*, heat production, dry-matter intake.

Long-term physiological studies of wild animals often necessitate repeated sampling of blood which requires sedation. In the past, moose have been immobilized with synthetic opiates like etorphine or carfentanil (Franzmann and Arneson, 1974; Gasaway et al., 1978; Franzmann et al., 1984). Synthetic opiates are potentially lethal to humans and animals (Haigh et al., 1977; Gasaway et al., 1978; Thorne, 1982; Parker and Haigh, 1982; Franzmann et al., 1984). At the Moose Research Center (MRC: Alaska Department of Fish and Game, 34828 Kalifornsky Beach Road, Suite B, Soldotna, Alaska, 99669) we evaluated a new compound that may have potential use for moose.

R51163 is a newly synthesized purine alkyl piperidine that produces reliable sedation in cattle after intravenous and intramuscular (IM) injections at doses of 0.05 and 0.10 to 0.15 mg/kg body weight (BW), respectively (Degryse and Ooms, 1986). The purpose of this study was to test R51163 as a possible tranquilizer for moose. We wanted a drug that would calm the animals sufficiently for bleeding yet be of short duration (<24 hr) in its overall effect on the animal's physiology.

Five healthy adult (age >3-yr-old) bull moose were used to test R51163. All animals were reared at the MRC and maintained on a formulated ration (Schwartz et al., 1985). Animals were tractable to varying degrees and were accustomed to holding facilities, feeding pens and respiration chamber. All animals had been previously trained to walk onto a counterbalance scale for weighing.

We tested the effects of R51163 on resting metabolism, feed intake and sedation of animals. The experimental design was a two-period crossover (Fleiss, 1986). Animals were randomly divided equally into two groups: treatment and control. Treatment animals were given intramuscular (IM) injections of R51163; controls were not drugged. Intake trials lasted 14 days, metabolism trials lasted ≤24 hr. Two wk following injection, treatment and control animals were reversed, and the process was repeated. Separate trials were conducted to test effects of the drug on resting metabolism and intake. Animals were hand injected while standing on a weighing scale. Control animals were weighed but not injected. An animal injected with 0.2 mg/kg body weight (BW), was insufficiently tranquilized, and was capable of violent and rapid kicking when handled, consequently we conducted our tests with 0.4 mg/kg BW.

Dry-matter intake was measured daily for each moose over a 2-wk period. Animals were maintained in separate 3.1 × 15.2 m pens; water and trace mineral salt were available ad libitum. The protocol followed that of Schwartz et al. (1984). Heat production was measured using an indirect respiration chamber (Regelin et

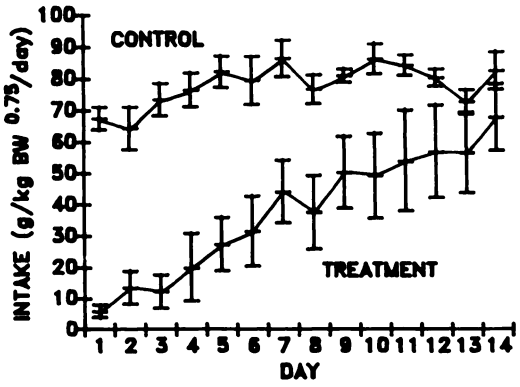

FIGURE 1. Daily intake of dry matter of five adult moose treated with R51163 (day 1), compared to five untreated moose.

al., 1981) following the recommendations and protocol described by Hubbert (1987). Heat production was measured at 15 min intervals in fed animals lying calmly in the respiration chamber.

Statistical testing of differences between treatment and control groups during metabolic trials was determined by the t-test for a 2-period crossover design (Fleiss, 1986). Linear regression and analysis of covariance were used to describe variation within and among individual animals' responses during the intake trial. Statistical significance was determined at $P = 0.05$: means were reported ±SE.

R51163 had a profound effect on intake of dry matter for at least 1 wk post injection (Fig. 1). Treated animals were anorexic the day of injection, but then generally increased food intake to pretreatment levels over the 2-wk measurement period. Regression lines of intake over time for pooled control and pooled treatment groups (Table 1) differed significantly in slope ($F = 15.81$) and elevation ($F = 141.98$).

Weight change in animals treated with R51163 (−3.5 ± 1.4 kg/d) differed significantly ($t = 2.33$) from that of control group (+1.2 ± 0.5 kg/d) during the first week following injection. Mean weight change during the second week was not different ($t = 0.89$): 0.6 ± 0.8 kg/d, and 1.8 ± 0.3 kg/d for the treatment and control groups, respectively.

Effects of R51163 on resting metabolism following injection varied among individuals. Median observations were tested in lieu of means because of the wide variation

TABLE 1. Responses of five adult moose to R51163, as measured by food intake (g/kg $BW^{0.75}$/d) over a 2-wk period following injection.

Week number	Treatment	Animal	Weight (kg) at beginning of week	I = a + b (days) Regression parameters		
				Slope (b)	Elevation ($\bar{x}$)	Intercept (a)
1	Drug	1	346	12.29[a]	48.05[a]	11.17
		2	374	9.03[b]	36.47[a]	9.37
		3	479	8.17[b]	20.13[b]	−4.38
		4	539	6.48[b]	14.24[b]	−5.19
		5	603	3.39[c]	10.94[b]	0.78
	Control	All	—	3.87	74.99	59.49
2	Drug	1	333	3.99[a]	87.09[a,e]	75.12
		2	372	2.33[a]	70.07[b,f]	63.07
		3	471	2.31[a]	67.75[b,f]	60.83
		4	499	0.71[a]	36.76[c,f]	34.63
		5	542	4.64[a]	15.13[d,f]	1.0
	Control	All	—	1.17	83.33	70.42
1 + 2	Drug	All	—	4.48[a]	40.66[a]	7.08
1 + 2	Control	All	—	1.52[b]	79.16[b]	67.76

[a,b,c,d] Values within the same week and column with the same superscripts are not significantly different.
[e] This value is not significantly different from the control.
[f] These values are significantly different from the control.

observed in some animals during treatment. Median estimates of resting heat production did not differ significantly ($t = -0.072$, $P = 0.948$) between the control (117 kcal/kg $BW^{0.75}$/day) and treatment (119 kcal/kg $BW^{0.75}$/day) groups.

Resting metabolism represented the production of CO_2 and the consumption of O_2 associated with digestion and metabolism. Theoretically, in an animal at rest, the output of CO_2 and the uptake of O_2 would be relatively constant; this was the case with control individuals. Treated animals tended to cycle between very high and low heat production readings at approximately 1-hr intervals (peak to trough); however, mean readings were approximately equal to control values. This response varied among individuals; some showed extreme variation between peak and trough measurements (>100 kcal), while others showed only slight variation (50 kcal). The coefficient of variation for drugged animals was 15%. Variation between high and low measurements in control animals seldom exceeded 30 kcal; the coefficient of variation was only 8.2%. Although we were unsure why heat production measurements cycled in treated animals, it was evident effects of R51163 were not constant over time. Animals appeared to cycle in and out of the drug's effect. This apparent cycling partially explained the varied response observed between individuals.

Dosage response of R51163 was allometric. For these studies, two bulls weighed <375 kg and two bulls >450 kg; one bull weighed >600 kg. The largest bull was unable to stand when dosed at 0.4 mg/kg BW of R51163. He attempted to stand several times by pushing his nose into the ground but could only get up on the carpal joints of his front legs. He tried "walking" on his hind feet and carpel joints, which caused injury that ultimately resulted in secondary infection of the joint area. Conversely, one small male (BW = 346 kg) dosed at 0.4 mg/kg BW was capable of standing when approached and violent kicking when touched.

Intake rates in large males (>450 kg BW) were depressed longer than small males (<450 kg BW). Regression lines of intake (Table 1) for drugged animals the first week following dosing differed significantly among slopes ($F = 3.97$) and elevations ($F = 16.17$). Paired comparisons (Newman-Keuls test: Zar, 1974) among slopes and elevations demonstrated that differences existed between animals of different weights; smaller animals generally exhibited greater slopes and elevations (i.e., faster recovery times). Differences during the second week were observed in elevations ($F = 96.62$) but not slopes ($F = 1.14$), indicating that all animals were recovering at approximately the same rate during this period; however, their level of recovery was dependent upon their response during the first week.

The significant reduction in intake for drugged animals must be considered if R51163 is to be used on wild moose, especially in spring when animals are in poor body condition. This imposed reduction in energy intake could potentially increase mortality or indirectly affect vulnerability to predation.

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