The Effect of Furosemide on Arterial Blood Gases and Performance in Quarter Horses Performing a Fatigue Test on a Treadmill

Debra M. Sime*, Richard L. Engen, PhD** and Peggy A. Miller-Graber, PhD***

Department of Veterinary Physiology and Pharmacology
College of Veterinary Medicine
Iowa State University
Ames 50010

Abstract

Four Quarter Horses (1 filly age 2, 1 mare age 5 and 2 geldings ages 3 and 4; average weight 539 kg) were used in a 2 x 2 crossover design. The effects of furosemide (Lasix(Rx)) on arterial blood packed cell volume (PCV), hemoglobin (Hb), pH, pO2, pCO2, HCO-3 and base excess (BE) were measured. Plasma lactate, heart rate, and fatigue time were determined as indicators of performance while the horses performed a fatigue test on a high-speed treadmill. The left carotid artery was surgically elevated subcutaneously to facilitate collection of arterial blood samples. Horses were conditioned for 13 weeks with increasing intensity then randomly assigned furosemide (F) or physiological saline (C) as treatments. Treatments were administered 4 hours prior to the fatigue test in accordance with racing regulations. Arterial blood samples were collected prior to treatment dose, prior to exercise, at the 2nd, 4th, and 6th minute during the fatigue test, at fatigue, and at the 5th, 15th, 30th, and 45th minute post-exercise. Arterial blood samples were analyzed for blood gases, Hb, PCV, and plasma lactate. Heart rate and fatigue time were recorded. No difference between treatments ($P > 0.05$) was observed for blood gases except for pCO2 at rest, and HCO-3 and BE at the 2 minute collection period. No difference between treatments ($P > 0.05$) was observed for Hb, PCV, lactate and heart rate except at 15 minutes post-exercise for Hb and PCV, and 45 minutes post-exercise for Hb. Fatigue times were 11 min 56 sec $\pm$ 5 min 30 sec for F horses and 11 min 35 sec $\pm$ 2 min 6 sec for C horses. No difference ($P > 0.05$) was observed in fatigue time. Based on our data, the trend indicated that all parameters measured returned to pre-exercise levels more rapidly for furosemide treated horses. However, furosemide did not enhance performance.

Key Words: Quarter Horses, Furosemide, Arterial Blood Gases, Fatigue, Treadmill

Introduction

Exercise Induced Pulmonary Hemorrhage (EIPH) is a respiratory disorder that occurs in 50 - 70% of horses subjected to strenuous exercise. It is characterized by bleeding from the respiratory tract originating beyond the trachea, usually from the lung. The etiology of EIPH is still not known[14].

*Debra M. Sime is a second year student in the College of Veterinary Medicine at Iowa State University.
**Dr. Engen is the Chairperson and a professor in the Dept. of Veterinary Physiology and Pharmacology at the Iowa State College of Veterinary Medicine.
***Dr. Miller-Graber is a Professor in the Dept. of Animal Science at Iowa State University.

In a recent workshop on EIPH, several areas of needed research were discussed including the development of effective prophylactic and therapeutic approaches to treating and preventing EIPH[15]. Currently, the drug Furosemide (Lasix®)) is routinely used as a prophylactic for EIPH. Furosemide is a diuretic and produces its effect within minutes of injection[6]. Due to the diluting effect furosemide has on the detection of other drugs in the urine, it must be administered four hours prior to racing and the dose (250 mg) is regulated by state racing commissions[1]. Since most of the physiological effects of the drug occur within the first hour of administration, why it is thought to improve the performance of EIPH horses four hours later during exercise is unclear. It has been shown that 60% or more of furosemide treated racehorses will still bleed after a race[16]. The mechanism of action for

furosemide's prevention or reduction in severity of EIPH is not known and there is no clear evidence that it is effective in preventing or reducing the severity of an EIPH episode[14]. Studies have shown conflicting results on whether furosemide improves the racing performance of EIPH horses or healthy racehorses[16].

In humans, furosemide increases arterial oxygen tension suggesting an improvement in gas exchange within the lung. It is believed that the improvement in gas exchange is due to a reduction in intrapulmonary shunting of blood[6]. In horses, when furosemide is administered 4 hours prior to exercise, it has been shown to reduce right atrial and pulmonary arterial pressures and the reduction in pressure is dose dependent[11]. The effect of furosemide on arterial blood gases when administered at the racing regulated dose of 250 mg 4 hours prior to exercise has not been investigated. The objective of this study was to determine the effect of a 250 mg dose of furosemide administered 4 hours prior to exercise on arterial blood gases and performance while horses were exercised to fatigue on a treadmill.

Materials and Methods

Four Quarter Horses were used in a 2x2 crossover design to evaluate the effect of furosemide on arterial blood packed cell volume (PCV), hemoglobin (Hb), pH, pO_2, pCO_2, bicarbonate (HCO_3), base excess (BE), and performance, using plasma lactate, heart rate and fatigue time as indicators of fitness. The left carotid artery was surgically elevated to form a subcutaneous loop in each horse[2]. Horses were housed in outdoor paddocks and fed a diet of grain mix and grass hay. Each horse was conditioned with increasing intensity 5 days a week for 13 weeks on a high speed treadmill (Sato II)[13]. Horses were randomly assigned one of two treatments, furosemide (F) or a physiological saline placebo (C). A 5 cc treatment dose of either 250 mg of furosemide or 5 cc of physiological saline was administered intravenously four hours prior to performing the fatigue test (dose and time of furosemide administration in accordance with Iowa State Racing Commission regulations[9]). Horses were not allowed access to food or water following administration of either treatment. Four hours post-treatment, the horses were warmed up 4 minutes at 3.35 m/s at an incline of 00 and then immediately tested at 6.71 m/s at an incline of 100 until fatigued. Fatigue was determined to be the point when the horse could no longer be encouraged off the tail chain.

Arterial blood samples were collected prior to dosing, at rest (before being tested on the treadmill), 2, 4, and 6 minutes into the fatigue test, fatigue (the point at which the horse was stopped), and 5, 15, 30, and 45 minutes recovery. The recovery period was passive. The arterial sample taken at dose was collected via arterial puncture. All other arterial blood samples were taken after insertion of a 16 gauge 2 inch arterial catheter into the elevated left carotid artery with an extension and three-way stopcock attached. This setup enabled freedom in collection of arterial blood samples while the horses were exercising on the treadmill. Approximately 10 cc of blood was drawn and discarded before samples were collected and each sample collection was followed by approximately 20 cc of saline warmed to 380°C to flush the apparatus.

Arterial blood samples intended for blood gas analyses were collected in heparinized glass syringes and kept on ice until analysis. Arterial blood samples for Hb and PCV analyses were collected in potassium oxalate vaccutainers and kept on ice until analysis. Arterial blood samples for lactate analyses were collected in sodium fluoride/potassium oxalate vaccutainers, centrifuged at 4000 g for 5 minutes, plasma extracted and frozen in microcentrifuge tubes until analysis.

Heart rates were recorded by a Hippocard[7] heart rate monitor at dose, rest, 2, 4, and 6 minutes of fatigue test, and 5, 15, 30 and 45 minutes recovery. The amount of time taken for each horse to reach fatigue was also recorded in minutes and seconds.

Arterial blood samples were analyzed for pH, pO_2, pCO_2, HCO_3, and BE using an IL Blood Gas Analyzer[8]. Hemoglobin was determined by the cyanmethemoglobin method. Packed cell volume was determined by microhematocrit centrifugation. Plasma lactate levels were determined by Lactate Autoanalyzer[17].

All data were analyzed for treatment effects using GLM procedures of SAS (1989)[12]. Differences due to treatment were analyzed using Least Square Means at ($P < 0.05$).

Results and Discussion

Arterial blood parameters and heart rates resulting from this study are listed in Table 1. The pO_2 level of F treated horses decreased from a resting level of 126 to 82.17 mm Hg at 6 minutes of testing and returned to resting levels within 5 minutes of recovery. Control pO_2 level exhibited a similar pattern with values slightly lower, however the difference between treatments was not significant. The pCO_2 level of F and C treated horses closely followed each other with lowest levels at fatigue and 5 minutes recovery. These results agree with studies conducted by Bayly et al[3] and Littlejohn and Snow[10] with Thoroughbred horses exercising at 7 m/sec and 10 m/sec, respectively. Arterial blood pH of F treated horses increased slightly from the dose pH of 7.415 to 7.438 when sampled at rest. This agreed with a study conducted by Freestone et al[4] where horses were dosed with 1 mg/kg. The pH then maintained a higher level for F treated horses compared to C horses throughout testing, fatigue and recovery. A significant difference due to treatment was found for pH at 30 minutes recovery ($P < 0.05$). The pH values are lower, however, than the pH values reported for Thoroughbred horses exercising at similar speeds by Freestone et al[4] and Littlejohn and Snow[10]. Bicarbonate (HCO_3) concentration and BE of arterial blood exhibited a similar pattern to pH, with a significant difference between treatments at 2 minutes for $HCO-_3$ and for BE ($P < 0.05$). Packed cell volume and Hb levels exhibited typical exercise patterns however, values were lower than those reported by Harris and Snow[5] and Littlejohn and Snow[10]. A large increase in PCV from resting levels was maintained throughout testing and a near return to resting levels was reached at 45 minutes recovery. Plasma lactate levels also exhibited an increase during exercise, however F treated horses had lower lactate concentrations throughout recovery. Heart rate showed a marked increase from rest to 6 minutes of testing, and returned to near resting levels at 45 minutes recovery. The heart rates agreed with the values reported by Bayly et al[3], Harris and Snow[5], and Littlejohn and Snow[10]. The fatigue time of F treated horses was 11 minutes and 56 seconds compared to 11 minutes and 35 seconds for C horses. The difference was not significant due to treatment.

Conclusion

No difference between fatigue time of F treated horses and C horses was observed suggesting furosemide did not enhance performance of healthy horses. Furosemide did not appear to enhance ventilation/perfusion during exercise as reflected by the similar response observed between experimental groups for arterial blood gases. A trend towards less acid/base balance disturbance was seen for the F treated horses, however this trend was not significant. A similar study needs to be performed on clinically diagnosed EIPH horses that experience frequent EIPH episodes to determine whether furosemide produces results similar to those found in this study.

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Table 1. Arterial blood parameters and heart rates[1].

Time (min)	pH	pO2 (mmHg)	pCO2 (mmHg)	mHCO-3 (mEq/L)	BE (mEq/L)
Control					
Dose	7.42 ± .026	122 ± 10.2	51 ± 1.7	32.1 ± 1.9	6.5 ± 2.0
Rest	7.42 ± .010	103 ± 10.9	51[a] ± 1.6	32.1 ± 0.8	6.7 ± 0.6
2	7.35 ± .015	90 ± 6.8	45 ± 1.9	24.5[b] ± 0.8	-0.9[c] ± 0.9
4	7.32 ± .039	82 ± 0.7	44 ± 2.0	22.1 ± 2.3	-3.5 ± 2.5
6	7.29 ± .031	77 ± 2.7	42 ± 1.8	20.2 ± 2.3	-5.5 ± 2.6
Fatigue	7.24 ± .088	95 ± 21.1	30 ± 9.9	13.0 ± 6.1	-12.7 ± 6.9
5	7.27 ± .096	114 ± 7.5	26 ± 9.0	12.6 ± 6.8	-12.7 ± 7.9
15	7.28 ± .090	105 ± 6.8	35 ± 6.2	17.1 ± 6.4	-8.5 ± 7.3
30	7.35 ± .059[g]	105 ± 7.1	43 ± 5.3	23.7 ± 6.0	-1.5 ± 6.2
45	7.38 ± .052	103 ± 2.8	46 ± 5.1	26.9 ± 5.2	1.8 ± 5.4
Furosemide					
Dose	7.41 ± .009	126 ± 3.4	50 ± 2.2	31.7 ± 1.3	6.1 ± 1.2
Rest	7.44 ± .011	108 ± 5.6	50[a] ± 1.1	32.8 ± 1.5	7.7 ± 1.6
2	7.37 ± .003	88 ± 1.3	46 ± 2.4	25.9[b] ± 1.2	0.9[c] ± 0.8
4	7.37 ± .009	84 ± 1.8	43 ± 1.9	22.9 ± 1.0	-2.4 ± 0.9
6	7.30 ± .032	82 ± 2.9	41 ± 2.3	20.1 ± 2.3	-5.5 ± 2.4
Fatigue	7.30 ± .070	107 ± 10.2	31 ± 8.4	14.9 ± 4.1	-9.7 ± 4.3
5	7.35 ± .136	117 ± 6.7	24 ± 8.4	13.1 ± 3.6	-9.7 ± 5.5
15	7.36 ± .048	107 ± 6.2	38 ± 6.0	21.1 ± 4.0	-3.4 ± 4.1
30	7.39 ± .033[g]	102 ± 6.2	44 ± 3.1	26.5 ± 3.0	1.7 ± 3.1
45	7.41 ± .031	100 ± 5.5	46 ± 3.3	28.7 ± 3.4	3.9 ± 3.4

	PCV (%)	Hb (g/100ml)	Lactate (mmol/L)	Heart Rate (beats/min)
Control				
Dose	32.1 ± 3.0	13.4 ± 1.1	0.4 ± 0.1	35 ± 3.8
Rest	31.1 ± 2.7	12.5 ± 1.1	0.5 ± 0.1	35 ± 3.0
2	47.0 ± 1.7	19.2 ± 1.0	8.5 ± 1.5	196 ± 7.4
4	48.3 ± 1.4	19.4 ± 0.9	12.1 ± 2.6	207 ± 8.2
6	48.6 ± 1.5	19.9 ± 1.5	13.9 ± 1.6	213 ± 10.4
Fatigue	47.2 ± 2.0	18.5 ± 1.0	18.9 ± 7.3	209 ± 20.7
5	44.4 ± 3.3	17.3 ± 1.4	18.8 ± 7.8	96 ± 15.4
15	39.4[d] ± 2.2	15.5[e] ± 1.8	14.4 ± 6.4	81 ± 11.6
30	35.1 ± 3.4	14.0 ± 1.0	10.5 ± 5.5	67 ± 6.5
45	31.4 ± 3.0	12.6[f] ± 1.1	7.5 ± 4.6	57 ± 9.6
Furosemide				
Dose	32.7 ± 4.5	13.9 ± 1.9	0.5 ± 0.1	37 ± 8.1
Rest	32.5 ± 3.7	13.4 ± 1.5	0.6 ± 0.1	33 ± 4.0
2	47.6 ± 0.6	19.7 ± 0.2	8.8 ± 1.1	195 ± 9.4
4	49.1 ± 1.5	20.6 ± 0.2	11.4 ± 0.3	205 ± 8.2
6	48.8 ± 1.4	20.0 ± 0.4	17.2 ± 0.3	213 ± 9.6
Fatigue	48.0 ± 1.7	19.2 ± 1.1	19.9 ± 6.7	211 ± 14.9
5	45.6 ± 3.8	18.5 ± 1.6	18.9 ± 3.6	89 ± 9.6
15	40.8d ± 2.0	16.9[e] ± 1.3	13.1 ± 4.9	75 ± 8.4
30	36.1 ± 2.4	14.5 ± 0.5	8.8 ± 3.8	63 ± 13.1
45	33.7 ± 3.7	15.1f ± 0.3	6.9 ± 2.9	53 ± 9.2

[1]Data reported as treatment means ±.

[a,b,c,d,e,f] Means with the same superscript differed due to treatment ($p < 0.05$).

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Fatigue Test on a Treadmill