Insulin Tolerance in Laminitic Ponies

J.R. Coffman and C.M. Colles*

ABSTRACT

Sensitivity to insulin was assessed in ponies episodically affected with chronic laminitis by measurement of blood glucose and arterial blood pressure during insulin tolerance tests. In terms of blood glucose values, laminitic ponies were significantly less sensitive to insulin than controls. Conversely, a post-insulin decline in diastolic, systolic and mean blood pressure values was significantly greater in laminitic ponies than in controls.

Key words: Insulin, glucose, blood pressure, laminitis, pony.

RÉSUMÉ

Cette expérience consistait à déterminer la sensibilité à l'insuline, chez des poneys qui souffraient de fourbure chronique récurrente. Les auteurs déterminèrent à cette fin le taux de glucose sanguin et la pression artérielle, durant les tests de tolérance à l'insuline. D'après leur taux de glucose sanguin, ces poneys s'avérèrent significativement moins sensibles à l'insuline que leurs congénères témoins. Après les tests de tolérance à l'insuline, les poneys atteints de fourbure chronique affichèrent toutefois une baisse de la pression sanguine diastolique, systolique et moyenne significativement plus elevée que leurs congénères témoins.

Mots clefs: insuline, glucose, pression sanguine, fourbure, poney.

INTRODUCTION

Insulin and corticosteroids are mutually antagonistic in key areas of energy and electrolyte metabolism. On several occasions this antagonism has been implicated in pathophysiology and therapy of laminitis (1,2,3,4).

In experimentally induced laminitis, hyperglycemia, eosinopenia and lymphopenia have been documented, suggesting increased glucocorticosteroid output (5,6). In another study Hood (7) identified a relative excess of adrenal androgens. Intravenous and oral glucose (8) and simultaneous glucose and insulin (1) have been recommended as therapy.

Both vasoconstriction (9) and vasodilatation (10) have been suggested as affecting the digital circulation during laminitis. However, Hood (7) demonstrated arteriovenous shunting to be the principal cause of the ischemic changes which occur in the digital corium. It has been pointed out, however, that the circulatory changes in the digit are only part of a multisystemic disorder (11). Corticosteroids have been incriminated in iatrogenic induction of laminitis (3,4). Further, Eyre and Elmes (2) demonstrated that hydrocortisone and betamethasone potentiated the vasoconstrictor effect of epinephrine, norepinephrine and serotonin, but not of histamine in an equine digital artery and vein model.

Breed differences in the morbidity of laminitis have been described (12). Ponies are at highest risk (12). Corresponding breed differences in blood glucose and blood lipid values have also been demonstrated (13). Ponies and Morgan horses have higher total lipids in blood than Thoroughbreds and ponies have lower blood glucose values than either Morgans or Thoroughbreds. In addition, it has been suggested that Thoroughbreds are more tolerant for glucose than Morgans (13). Lack of insulin sensitivity has been suggested as a possible cause of the relative glucose intolerance exhibited by Morgans. Risk of laminitis has not been assessed in Morgans.

Because these reports suggest that antagonism of insulin may somehow be involved in the pathophysiology of laminitis, we assessed insulin sensitivity in ponies with a history of recurrent laminitis. Since arterial hypertension has been shown to correlate with the severity of laminitis (11) we measured the effect of insulin on arterial blood pressure as well as blood glucose.

MATERIALS AND METHODS

Twelve ponies (six laminitic and six control) from a closed herd maintained at the Equine Research Station were used in the experiment (Table I). Ponies with no hoof changes and no previous history of laminitis were used as controls and designated group A. Ponies which were known to have

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TABLE I. Description of Animals Used in the Present Study

Group A (controls)				Group B (laminitics)			
Number	Sex	Age	Weight	Number	Sex	Age	Weight
1	Mare	7 year	200 kg	7	Mare	7 year	190 kg
2	Mare	7 year	205 kg	8	Mare	7 year	180 kg
3	Mare	10 year	210 kg	9	Mare	7 year	176 kg
4	Gelding	15 year	215 kg	10	Gelding	29 year	182 kg
5	Gelding	16 year	212 kg	11	Gelding	13 year	204 kg
6	Gelding	7 year	204 kg	12	Gelding	13 year	196 kg
Average age		10.33 year				12.66 year	

developed laminitis during at least one previous spring were used as laminitic ponies and designated group B. Because laminitis morbidity has been shown to be age-related (7) laminitic and control ponies were matched on the basis of age. All 12 ponies were included in an insulin sensitivity test in November 1978 (Trial 1). Insulin sensitivity tests were repeated in June 1979 (Trial 2) at which time blood pressure was evaluated in addition to blood glucose. Pony number 10 was much older than his laminitic mate (4). Due to intervening pathology both ponies were eliminated from Trial 2. Two trials were done because the risk of laminitis in horses at grass is much greater in spring than in fall.

The ponies were kept as a herd on grass. In winter the ration was supplemented with hay ad libitum and one pound of carrots and in severe weather up to five pounds per head of horse and pony cubes. Prior to insulin injection the ponies were stabled and fasted for 12 hours overnight.

Aqueous insulin of porcine origin was administered intravenously at a dose of one unit per 2.27 kg of body weight. Insulin dosage was selected on the basis of prior clinical experience. Blood samples were obtained sequentially via previously placed jugular catheters at 0, 30, 60, 90, 120, 180, 240 and 300 minutes.

Fluoride vacutainers were used for blood collection. Blood glucose determinations were made manually using a glucose oxidase method. The plasma was separated within two hours of sampling.

Arterial blood pressure was measured at the ventral coccygeal artery (Trial 2) by the indirect Doppler shift method described previously (14), at the time each blood sample was obtained. Mean blood pressure was derived by adding one third of the pulse pressure to diastolic pressure.

Analysis of variance (anova) was used for statistical analysis of the data. The paired means were compared by least significant difference.

RESULTS

BLOOD GLUCOSE

In Trial 1, laminitic ponies were significantly less sensitive to insulin at 30, 60, 90, 120, 180 and 240 minutes postinsulin injection than were control ponies (Fig. 1).

When the insulin tolerance test was repeated in Trial 2 laminitic ponies were again less sensitive to insulin, the difference being significant at 120 minutes postinjection (Fig. 2).

ARTERIAL BLOOD PRESSURE

Laminitic ponies were more sensitive to insulin than controls in terms of arterial blood pressure response. Diastolic blood pressure dropped more in laminitic than in control ponies, and was significantly lower at 30 and 300 minutes postinjection (Fig. 3). Mean blood pressure (Fig. 4) was consistently

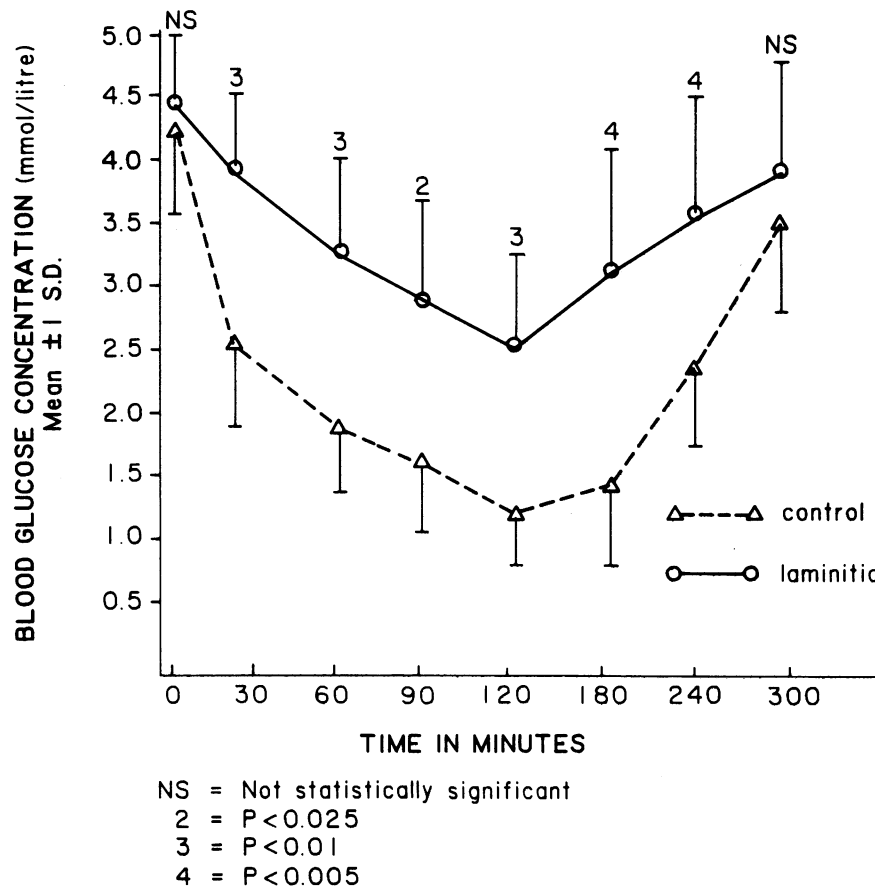

Fig. 1 Effect of insulin on blood glucose levels in six control as compared to six laminitic ponies (Trial 1). Each point represents the mean for six ponies. Each bracket represents ± 1 S.D.

lower in laminitic ponies starting at 30 minutes postinjection and persisting through the 300 minute study period. The difference was significant at 30, 90, 120 and 300 minutes. Systolic blood pressure (Fig. 5) was also lowered to a greater degree in laminitic ponies following insulin injection, the difference being significant at 30, 90 and 120 minutes postinjection.

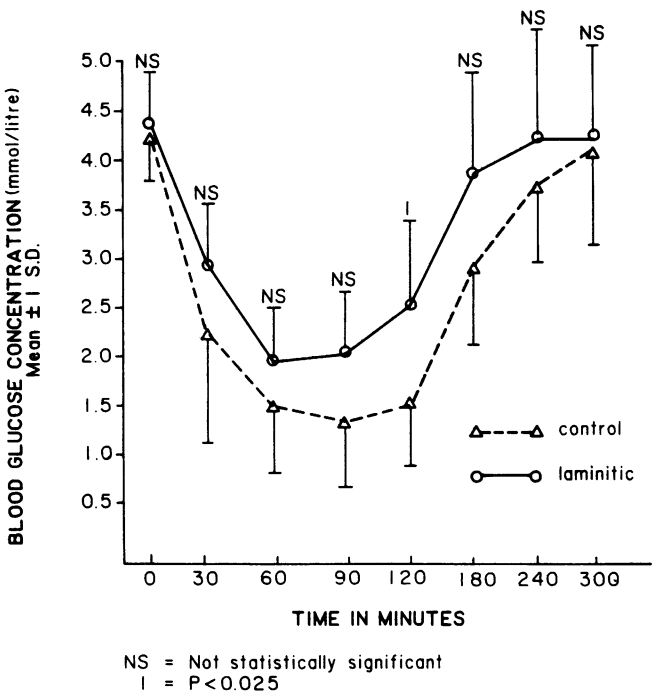

Fig. 2. Effect of insulin on blood glucose levels in six control as compared to six laminitic ponies (Trial 2). Each point represents the mean for six ponies. Each bracket represents ± 1 S.D.

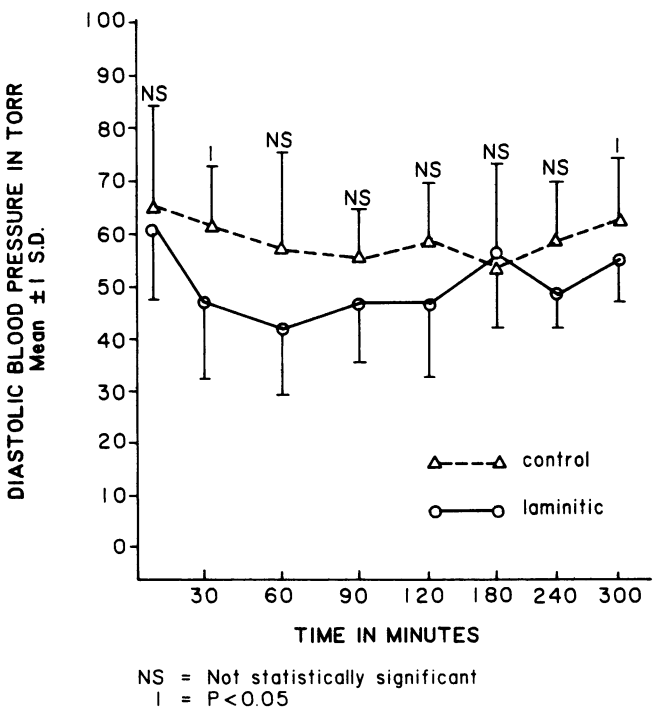

Fig. 3. Effect of insulin on diastolic blood pressure in six control as compared to six laminitic ponies (Trial 2). Each point represents the mean for six ponies. Each bracket represents ± 1 S.D.

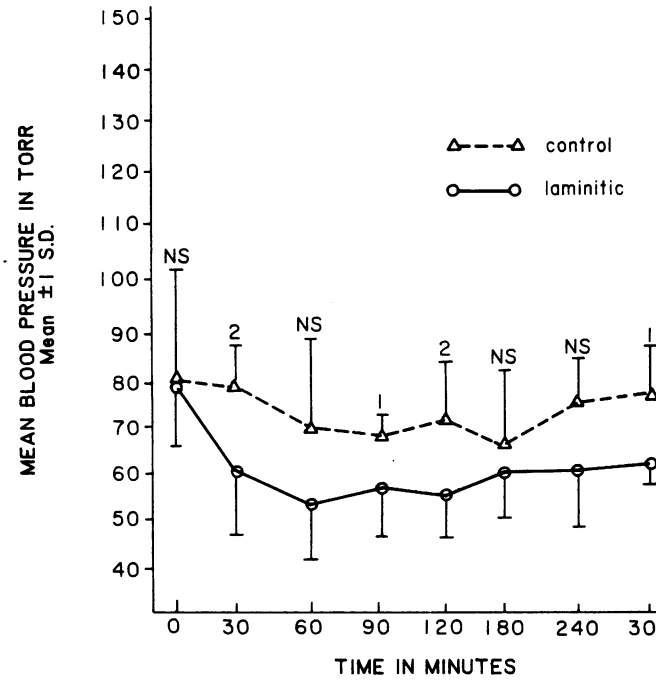

Fig. 4. Effects of insulin on mean blood pressure in six control as compared to six laminitic ponies (Trial 2). Each point represents the mean for six ponies. Each bracket represents ± 1 S.D.

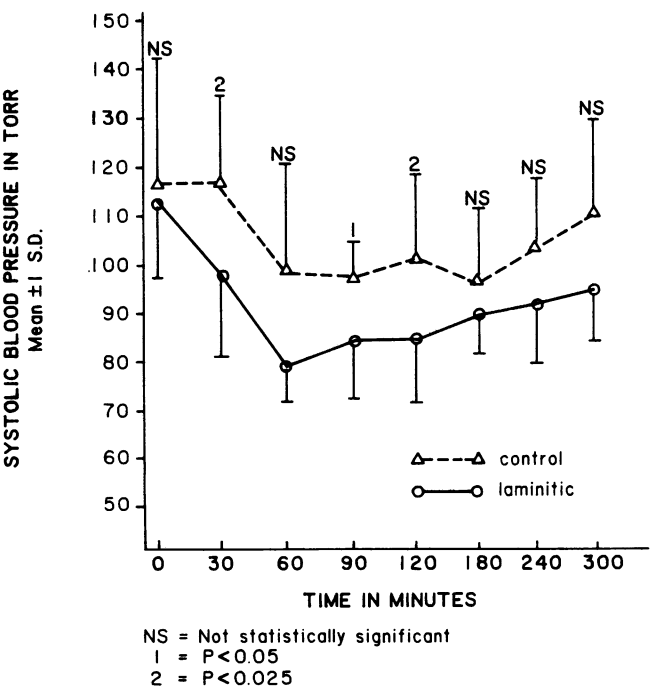

Fig. 5. Effects of insulin on systolic blood pressure in six control as compared to six laminitic ponies (Trial 2). Each point represents the mean for six ponies. Each bracket represents ± 1 S.D.

DISCUSSION

Glucocorticosteroid secretion due to pain logically could be a cause of insulin resistance. However, in Trial 1 the laminitic ponies were not exhibiting pain or signs of lameness. During Trial 2, three ponies were lame and yet the difference in insulin sensitivity response was less. This suggests that pain was not the cause of insulin insensitivity in the laminitic ponies, an intrinsic difference in metabolism being likely.

Arterial hypertension has been shown to be present in laminitis, and to be correlated with the degree of severity (11). Hood (7) demonstrated in an acute laminitis model that pain preceded hypertension and upon relief from pain, blood pressure returned to normal. However, the same study revealed that the longer hypertension persisted, the more difficult it was to reverse or reduce with analgesia. It was suggested by Hood that persistent hypertension may contribute to the irreversible alterations in digital circulation which characterize chronic laminitis (15).

Glucose, given either intravenously or per os, has been suggested as an adjunct to therapy for chronic laminitis in obese horses (8). Insulin and glucose in combination have also been recommended for therapy of refractory laminitis, particularly in instances where the horse had been previously treated with corticosteroids (1). The results of the present study suggest that any beneficial results may have been due, at least in part, to an effect on circulation. Of related interest is the study of perfused equine digital artery and vein strips by Eyre and Elmes (2) demonstrating glucocorticosteroid potentiation of vasoconstrictor substances (epinephrine, norepinephrine and serotonin). They suggested that this may be one reason corticosteroids have been incriminated as an iatrogenic cause of laminitis. The greater drop in arterial blood pressure in laminitic ponies is of particular interest in the light of these observations since insulin and glucocorticosteroids are antagonists.

Insulin has been reported to produce vasodilatation in the hands of humans (16), which was felt to be due to loss of tone rather than active vasodilatation. This effect was originally thought to be due to hypoglycemia but further studies have associated postural hypotension in human diabetic patients with diabetic autonomic neuropathy (16). These investigators found that hypotension could be provoked by insulin administration in diabetic patients with autonomic neuropathy. The hypotension was immediate and appeared to be unrelated to blood glucose values. The same study showed that ionic flux was not the cause of the blood pressure changes and that there was no change in their rate of motor nerve conduction. There was, however, a drop in right atrial pressure which led Page and Watkins (17) to postulate that the hypotension was due to a redistribution of blood flow with pooling in the skin, muscle and splanchnic viscera. This was consistent with the work of Middleton and French (16) and supported by the observation that their patients were clinically vasodilated as evidenced by flushed face and hands.

Mogensen, Christensen and Gundersen (18) showed that insulin-dependent diabetic patients usually experience a slight increase in arterial blood pressure following insulin administration and confirmed that this change was independent of blood glucose values. The combined studies of Page and Watkins (17) and Mogensen *et al* (18) showed that insulin only lowers blood pressure in diabetic patients if the circulatory reflexes are abnormal and that this phenomenon is unrelated to blood glucose changes.

Whether or not there is any analogy between diabetic autonomic neuropathy and the response of laminitic ponies to insulin is not known. However, further study of this phenomenon could lead to an enhanced understanding of the systemic circulatory changes in chronic laminitis as well as the possible development of a therapeutic role for insulin.

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