Effects of chromium yeast supplementation on postprandial glycaemic and insulinaemic responses in insulin-resistant ponies and horses

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Summary

The trace element chromium (Cr) has attracted attention because Cr supplements have been shown to benefit biological functionality and health in both humans and animals. It has been suggested that Cr decreases insulin levels and improves glucose disposal in type 2 diabetic and obese humans. Therefore, the aim of the study was to examine the effect of feeding Cr-enriched yeast on glucose metabolism in insulin-resistant ponies and horses. 27 insulin-resistant ponies and horses, mean age ($\pm$SD) 13.9 ($\pm$4.8) years, mean body mass ($\pm$SD) 422 ($\pm$138) kg, mean body condition score ($\pm$SD) 7.6 ($\pm$0.8) on a scale of 1–9, were used in a placebo-controlled study. The ponies and horses were fed for four weeks either a yeast product without Cr (= placebo, N = 12), or a Cr-enriched yeast (= verum, 2 g organic Cr3+/kg yeast, 25 μg/kg BW, N = 15). During experimental period all animals were on a hay-based diet (1.2 kg hay/100 kg BW). A starch tolerance test (STT, 1.5 g starch/kg BW) was performed at the beginning and at the end of the study. Blood was collected following a standardized protocol. Plasma glucose concentrations were determined by glucose oxidase assay and plasma insulin was determined by radioimmunoassay. The STT revealed exaggerated glucose and insulin responses, reflecting an impaired glucose tolerance in all animals. Postprandial insulin responses were significant higher at the beginning of the study in the group to be fed verum when compared to the placebo group. After supplementation, plasma insulin responses were significantly modified by Cr intake (diet p < 0.05), suggesting an improved glucose regulation. Plasma glucose responses were not affected by the different treatments. Cr supplementation for four weeks improved glucose metabolism in ponies and horses suggesting that Cr facilitated insulin signaling. However, it must be emphasized that the ponies and horses still had impaired glucose regulation as indicated by supraphysiological glucose and insulin responses to the STT when compared to healthy horses.

Keywords: glucose, insulin, insulin resistance, chromium yeast, supplementation, ponies, horses

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Effekte der Chromhefezulage auf die postprandialen Veränderungen von Glucose und Insulin im Blut bei insulin-resistenten Ponys und Pferden

Chrom besitzt eine besondere Bedeutung in der Therapie der Insulinresistenz beim Menschen, da Chrom die Bindung von Insulin am Rezeptor aktivieren kann. Ziel dieser Studie war es, die Supplementierung von Chrom auf die postprandiale Glucosehomöostase bei insulin-resistenten Pferden bzw. Ponys zu überprüfen. Für die Placebo kontrollierte Studie standen 27 insulin-resistente Ponys bzw. Pferde (Alter 13,9 ± 4,8 Jahre, mittlerer Body Condition Score 7,6 ± 0,8 auf einer Skala von 1-9) zur Verfügung. 12 Tiere erhielten entweder ein Placebo (Placebo = Hefe ohne Chrom) oder 15 Ponys bzw. Pferde wurden mit einer chromhaltigen Hefe (= Verum, 2 g organisches Cr3+/kg Hefe, 25 μg Cr/kg KM) über einen Zeitraum von 4 Wochen supplementiert. Während der Versuchsperiode wurden die Ponys bzw. Pferde ausschließlich mit Heu gefüttert (1,2 kg/100 kg KM). Zu Beginn und am Ende der Supplementierungsphase wurde ein Stärketoleranztest (STT 1 und STT 2; 1,5 g Stärke/kg KM) durchgeführt und nach einem standardisierten Protokoll Blutproben zur Glucose- und Insulinbestimmung entnommen. Plasma Glucose wurde enzymatisch mittels Oxidase Assay and Plasma Insulin wurde mittels Radioimmunoassay bestimmt. Alle Ponys bzw. Pferde reagierten mit abnorm hohen Glucose- und Insulinkonzentrationen im Verlaufe der STT 1 und STT 2. Auffällig war, dass die Tiere der Verumgruppe vor Beginn der Supplementierungsperiode signifikant höhere Insulinwerte im Vergleich zur korrespondierenden Placebogruppe aufwiesen. Nach der vierwöchigen Supplementierungsphase konnte bei den Tieren, die Cr erhielten, eine deutliche Reduktion bei der Insulinreaktion im Verlaufe des STT 2 beobachtet werden, wohingegen die Placebopferde nur eine moderate Veränderung in der Insulinreaktion aufwiesen. Ein Effekt der Cr Supplementierung auf die Plasma Glucosekonzentrationen konnte im Verlauf der Studie nicht beobachtet werden. Cr scheint auch bei Ponys bzw. Pferden zu einer Verbesserung der Insulinresistenz zu führen, allerdings muss betont werden, dass die Ponys bzw. Pferde auch weiterhin nach der vierwöchigen Cr-Supplementierungsphase abnorm hohe Insulinreaktionen aufwiesen.

Schlüsselwörter: Glucose, Insulin, Insulinresistenz, Chromhefe, Supplementierung, Ponys, Pferde

Introduction

Insulin resistance (IR) is associated with impaired insulin activity and a compensatory increase in insulin secretion (*Johnson* 2002). The molecular aetiology of IR include defects of insulin signalling, such as reduced insulin receptor tyrosine kinase activity, and reduced post-receptor phosphorylation steps (*Kas-* *hyap* and *DeFronzo* 2007). As a consequence, glucose transport and glucose metabolism such as, glucose phosphorylation, glycogen synthesis or glucose oxidation, is impaired in different tissues. In humans, IR and associated hyperinsulinaemia contribute to the metabolic syndrome that typically includes impaired glucose tolerance or type 2 diabetes, obesity, dyslipidaemia, raised blood pressure and coronary artery dise-

ase (*Reaven* 1998, *Potenza* and *Mechanik* 2009). Currently, the Equine Metabolic Syndrome (EMS) has been defined as a syndrome of insulin resistance; regional or general adiposity; and clinical or subclinical laminitis (ACVIM Consensus Statement 2009). In this context, it is supposed that IR and hyperinsulinaemia alter vascular dynamics and endothelial function (*Asplin* et al. 2007), and obesity creates a proinflammatory state in horses and ponies (*Vick* et al. 2008).

Although epidemiological data are lacking, it seemed that ponies and light horses, like Quarter horses, are more susceptible to EMS than Thoroughbred or Standardbred horses (*Freestone* et al. 1992, ACVIM Consensus Statement 2009). In the horse, dietary interventions aimed at reducing obesity, include energy restriction, mainly by reducing sugar and starch intake (*van Weyenberg* et al. 2008, *Carter* et al. 2009) and should be accompanied by physical activity. In humans, complementary dietary recommendation involve specific supplements such as soluble dietary fibre (e.g. pectins), omega 3 fatty acids (fish, flaxseed oil), sources of polyphenols and isoflavones (e.g. red wine, soy protein), herbs (e.g. cinnamon extract, green tea), and certain major minerals and trace elements (e.g. magnesium, zinc, chromium; *Potenza* and *Mechanick* 2009). In horses, data about complementary dietary strategies in the treatment of EMS are lacking. In humans, chromium (Cr) has been the most studied, and some reports have suggested that Cr supplementation may increase insulin sensitivity and improve glucose tolerance, although the findings were equivocal (*Bartlett* and *Eperjesi* 2008, *Potenza* and *Mechanik* 2009).

Cr is an essential trace element that is involved in the metabolism of carbohydrates, lipids and proteins by amplifying the activity of insulin (*Mertz* 1993). In diabetic humans and rats, Cr supplementation has been shown to increase the cellular uptake of glucose and stimulate insulin metabolism (*Lukaski* 1999, *Cefalu* et al. 2002).

Cr is present in several oxidation states, but is most stable in the trivalent state, the predominant form in biological systems (*McDowell* 2003). However, the Cr content of foods has not been clearly defined and inorganic $Cr3^+$ is poorly absorbed (Table 1). In contrast, Cr^{6+} that is derived mainly from industrial exposure is absorbed more readily (*McDowell* 2003). The daily dietary Cr intake by humans is generally low whereas in animals, it is considered to be adequate to meet physiological need. There is little retention of Cr and that which is absorbed is excreted primarily via the kidneys (*McDowell* 2003). In general, marginal Cr intakes can be compensated by Cr-containing supplements that contain inorganic $CrCl_3$ or the more available organic forms such as Cr-yeast, Cr methionine, Cr nicotinate (CrNic), Cr tripicolinate (CrTri) and Cr picolinate (CrPic).

Equivocal results were obtained with horses following Cr supplementation. *Pagan* et al. (1995) measured lowered blood levels of glucose, insulin and cortisol during exercise in healthy Thoroughbred horses. A trend for a lower insulin response was measured in healthy mares subjected to an intravenous glucose tolerance test (*Gentry* et al. 1999). *Ott* and *Kivipelto* (1999) fed Cr to yearling horses and showed an increased glucose clearance in the supplemented group.

Unlike these results, *Vervuert* et al. (2006) found higher plasma glucose levels during exercise in Cr-supplemented healthy horses. *Cartmill* et al. (2005) found that dietary Cr supplementation had no effect on glucose dynamics or insulin sensitivity in mature horses with high body condition scores and hyperleptinaemia.

As Cr has been proposed as a complementary therapy in the treatment of IR in horses under practical feeding conditions, the aim of the current study was to examine the effect of feeding Cr-enriched yeast on glucose metabolism in insulin-resistant ponies and horses.

Material and methods

In a preliminary trial, a total of 83 ponies and horses were checked for the following criteria: obesity (*Henneke* et al. 1983), history of laminitis and impaired glucose tolerance. Glucose tolerance was assessed by a modified starch tolerance test. The test meal (1.5 g starch/kg BW) was fed at 0730 h following a 12 h overnight fast. Blood samples for plasma glucose and insulin were collected 30 min before feeding the test meal, and thereafter at 60 min intervals for 3 h. Postprandial glycaemic and insulinaemic responses were compared to plasma glucose and insulin profiles of healthy ponies and horses. Those ponies and horses which implement all three criteria were included in the study.

Animals and diets

27 insulin-resistant ponies or horses, mean age (±SD) 13.9 (±4.8) years, mean body mass (±SD) 422 (±138) kg, mean body condition score (BCS) (±SD) 7.6 (±0.8) (*Henneke* et al. 1983) were used in a placebo-controlled study. The animals were individually housed in box stalls and bedded on wood shavings. Ponies and horses had free access to a paddock 8-12 h daily. Additionally, animals were walked daily for 30-60 min. During the experimental period (4 weeks) all animals were on a hay-based diet (1.2 kg hay/100 kg BW).

This project was approved by the ethics committee on animal welfare of Baden-Württemberg in accordance with German legislation on animal rights and welfare.

Supplementation

The ponies and horses were fed for four weeks either a yeast product without Cr (= placebo, N = 12, table 2), or a Cr-enriched yeast (= verum, 2 g organic Cr3+/kg yeast, 25 μg/kg BW, N = 15, table 3). The placebo or the Cr-enriched yeast was blended into a commercial, fiber-enriched compound feed. The supplement was given once a day in the morning. The allocation to the respective group was executed by rotation.

Starch tolerance test

A starch tolerance test (STT, 1.5 g starch/kg BW) was performed at the beginning (STT 1) and at the end (STT 2) of the

Table 1 The biology of Cr (*Mordeni* et al. 1997, *McDowell* 2003, *Anke* et al. 2005)
Beschreibung des Chroms im Stoffwechsel (Mordeni et al. 1997, McDowell 2003, Anke et al. 2005)

Feedstuffs (mg/kg):	Cereals:	0.1 – 20
	Kernels:	oat 0.49, barley 0.35, wheat 0.64, rye 0.6
	Meat:	0.15
	Milk:	0.015
	Egg:	0.005 – 0.02 (egg yolk > 20 times)
	Hay:	0.1 – 10
	Water:	0.001 – 100
	Minerals:	60 – 500
Specification:	Cr^{3+}:	most stable oxidation state, predominant form in biological systems
	Cr^{6+}:	bound to oxygen, strongly oxidizing, toxic properties
	Cr^{0}, Cr^{2+}:	no relevance
Absorption:	Passive absorption (small intestine), presumably active transport mechanism, transport of Cr in blood via transferrin	
	Inorganic Cr^{3+}: <0.5 – 2 % (e.g. $CrCl_3$)	
	Organic Cr^{3+}: 25 – 30 % (e.g. high Cr-yeast, CrNic, CrPic)	
Excretion:	After absorption: mainly via urinary tract with small losses in faeces, sweat and hair	
Storage (mg/kg):	Liver:	0.04 – 1
	Kidney:	0.05 – 6.2
	Spleen:	0.05 – 0.3
	Hair:	0.20 – 3.3
	Muscle:	0.10 – 0.2
Requirements:	Humans:	50.0 – 200 µg/day
	Horses:	no available information
Deficiency:	Decreased sensitivity of peripheral tissues to insulin	
	Impaired protein metabolism	
Toxicity:	Cr^{3+}:	very low toxicity
	Cr^{6+}:	allergic dermatitis, skin ulcers, bronchogenic carcinoma by industrial exposure to Cr

Table 2 Plasma glucose (mmol/L) and plasma insulin (µU/mL) concentrations before and after experimental period for the placebo and Cr group
Plasma Glucose (mmol/l) und Plasma Insulin (µU/ml) im Verlaufe der Beobachtungsperiode für die Placebo- oder Chromgabe

Breed	Age	BCS	N
Shetland Pony	8.5 ± 2.9	7.8 ± 2.8	2
Welsh Pony	14 ± 3.7	7.5 ± 2.7	2
Quarter Horse	13 ± 3.5	9.0 ± 3.0	2
Haflinger Horse	10	8.5	1
Other breeds[1]	16 ± 5.0	8.0 ± 0.6	5

[1]Other breeds: Warmblood horse (N = 1), Knabstrupper horse (N = 1), Arabian horse (N = 1), Andalusian horse (N = 1), Criollo horse (N = 1)

Table 3 Breed, age, BCS and number of animals which were included in the verum group
Rasse, Alter und Anzahl der Tiere, die der Verumgruppe zugeordnet wurden

Breed	Age	BCS	N
Shetland Pony	11.0 ± 3.3	7.3 ± 2.7	2
Welsh Pony	14.8 ± 3.9	7.2 ± 2.7	5
Quarter Horse	13	7.5	1
Haflinger Horse	18.0 ± 4.2	7.5 ± 2.7	2
Other breeds[1]	16.3 ± 4.7	7.5 ± 0.8	5

[1]Other breeds: Warmblood horse (N = 2), Fjord horse (N = 2), Lipizzaner horse (N = 1)

study period. A commercial compounded feed was used as a source of starch. The ingredients of the compounded feed (36 % starch, 6.8 % sugar) were oats and micronised cereals in the following descending order based on inclusion rate: oats, wheat, maize, barley, and wheat feed. The test meal was fed at 0730 h following a 12 h overnight fast. At 0700 h, an indwelling catheter (1.8 × 2.35 mm/12 G, Braun, Melsungen, Germany) was inserted into the jugular vein. The catheter was connected to a 50 cm extension set (Vygon, Aachen, Germany) and sutured in place. The extension set and catheter were flushed with physiological saline after every blood sampling. Blood samples were collected 30 min before feeding the test meal, and thereafter at 30 min intervals for 5 h, and then at 60 min intervals for the following 2 hours. Blood was placed in tubes containing lithium-heparin (15 I.E. Heparin/ml blood, Sarstedt, Nümbrecht, Germany). Blood samples were centrifuged at 2012 g for 10 min within 5 min of collection. Plasma was stored at -20 °C until analysed.

Analysis

Animals were weighed before and after the study using a mobile scale (Firma Tru Test MP Series 600, scaling range 0.5 – 1,500 kg). Plasma glucose concentrations were determined by glucose oxidase assay (Unimate 7 GLUC GDH, Roche Diagnostics GmbH, Mannheim, Germany) and plasma insulin was determined by radioimmunoassay (Insulin RIA, Coat-A-Count [125I], Siemens Healthcare Diagnostics, Eschborn, Germany).

Statistical methods

The results are presented as means ± SD. Incremental area under the plasma glucose and plasma insulin curve (AUC) was calculated using simple non-overlapping polygons, and the area over the baseline without consideration of the area beneath the curve.

Table 4 Mean plasma glucose (mmol/L) and mean plasma insulin (μU/mL) concentrations before and after experimental period for the placebo and verum group
Mittlere Plasma Glucosekonzentrationen (mmol/l) und mittlere Plasma Insulinkonzentrationen (μU/ml) im Verlaufe der Beobachtungsperiode für die Placebo- und Verumgruppe

Parameter	Treatments	N	Experimental period					
			Before			After		
Glucose	Placebo	12	5.53	±	0.91	5.56	±	0.46
	Verum	15	6.25	±	2.08	5.96	±	2.01
Insulin	Placebo	12	42.9	±	47.8	14.4	±	8.3
	Verum	15	63.7	±	81.9	33.2	±	35.7

Table 5 Mean peak plasma glucose (± SD, mmol/L) and mean AUC (± SD, mmol x min/L) before (STT 1) and after experimental period (STT 2) for the placebo and verum group
Mittlere Plasma Glucosepeaks (± SD, mmol/l) und mittlere AUC (± SD, mmol x min/l) vor (SST 1) und nach der Supplementierungsphase (STT 2) für die Placebo- und Verumgabe

Treatments	N	Experimental period	Peak glucose (mmol/L)			AUC$_{glucose}$ (mmol x min/L)		
Placebo	12	STT 1	11.8	±	1.9	1746	±	712
Verum	15		12.4	±	2.6	1788	±	636
Placebo	12	STT 2	10.7	±	2.6	1354	±	945
Verum	15		10.9	±	3.0	1399	±	746

Table 6 Mean peak plasma insulin (± SD, μU/mL) and AUC (± SD, μU x min/mL) before (STT 1) and after experimental period (STT 2) for the placebo and verum group
Mittlere Plasma Insulinpeaks (± SD, μU/ml) und mittlere AUC (± SD, μU x min/ml) vor (SST 1) und nach der Supplementierungsphase (STT 2) für die Placebo- und Verumgabe

Treatments	N	Experimental period	Peak insulin (μU/mL)			AUC$_{insulin}$ (μU x min/mL)		
Placebo	12	STT 1	1158	±	753[a]	281541	±	189698[a]
Verum	15		1901	±	1443[b]	492670	±	358231[b]
Placebo	12	STT 2	883	±	725[a]	220986	±	193617[a]
Verum	15		1277	±	855[a]	318892	±	224850[a]

Means in the same column with different superscripts are significantly different ($P < 0.05$)

Data were subjected to an analysis of variance (ANOVA) for repeated measures (Statistika, StatSoft), factoring the effects of supplementation and time postprandially. When F-values were significant, further analysis was made using the least sig-nificance difference test. A t-test for unpaired samples was used to analyse the AUC for plasma glucose and plasma insulin, peak plasma glucose and peak plasma insulin. Mul-tiple regression was performed to test the relationship bet-
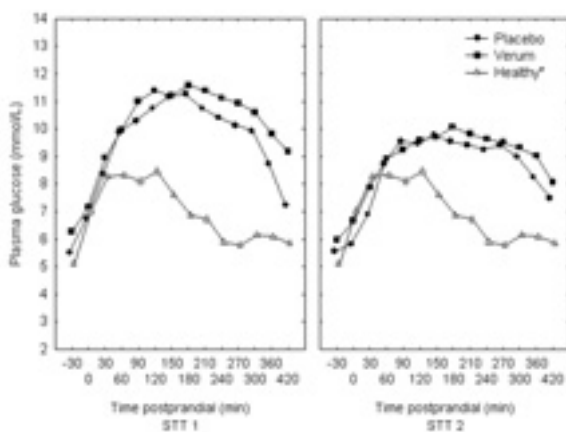

Fig. 1 Mean plasma glucose (mmol/L) before (STT 1) and after experimental period (STT 2) for the placebo and Cr group. *Data for healthy horses are adapted from *Vervuert* et al. (2009)
Mittlere Plasma Glucosekonzentrationen (mmol/l) vor (SST 1) und nach der Supplementierungsphase (STT 2) für die Placebo- oder Chromgabe. Daten der gesunden Pferde sind von Vervuert et al. (2009) entnommen worden
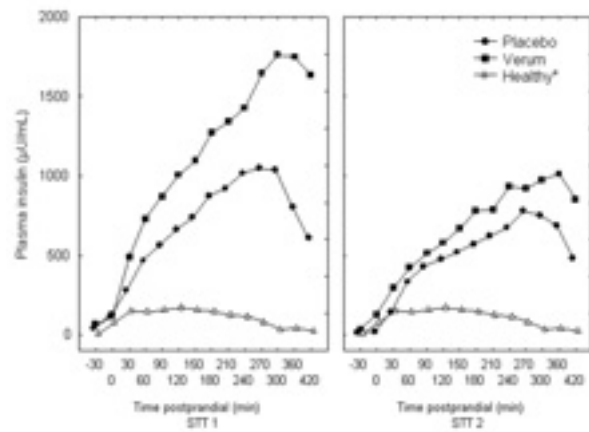

Fig. 2 Mean plasma insulin (μU/mL) before (STT 1) and after experimental period (STT 2) for the placebo and Cr group. *Data for healthy horses are adapted from *Vervuert* et al. (2009)
Mittlere Plasma Insulinkonzentrationen (μU/ml) vor (SST 1) und nach der Supplementierungsphase (STT 2) für die Placebo- oder Chromgabe. Daten der gesunden Pferde sind von Vervuert et al. (2009) entnommen worden

ween body mass, BCS, plasma glucose and plasma insulin. Statistical significance was accepted at P < 0.05.

Results

During the experimental period, horses lost BW in the range of 3.8 ± 4.3 % for the verum group and 2.1 ± 3.2 % for the placebo group (treatment P > 0.05). After 12h feed restriction, baseline plasma glucose and plasma insulin concentrations were similar for the different treatment groups before and after supplementation (Table 4) although numerically lower plasma insulin concentrations were measured for both groups after the supplementation period.

A significant increase in plasma glucose was measured 30-60 min after starch intake for both groups before (STT 1) and after the study period (STT 2, Figure 1). In both groups, the plasma glucose levels did not return to basal levels in STT 1 and STT 2. Mean peak plasma glucose values and mean AUC were similar for both groups without any significant differences before (STT 1) and after the study period (STT 2, Table 4).
A significant rise in plasma insulin was measured 30 min after starch intake in every case; a return to resting levels did not occur during the sampling phase (Figure 2). For STT 1, mean peak plasma insulin levels and AUC were significantly higher for the verum group than for the placebo group (P < 0.05, Table 4, Figure 2), and a significant decrease in peak plasma insulin and AUC was observed after the end of the experimental period (STT 2) following feeding the Cr-enriched yeast (P < 0.05), whereas the decrease in mean peak insulin and AUC was less pronounced for the horses given the placebo (time P > 0.05, Table 5, Figure 2).

Discussion

At the beginning of the study, mean resting insulin levels after feed restriction exceeded 20 μU/mL which provides evidence of IR (ACVIM Consensus Statement 2009). Additionally, the high mean body condition score of the ponies and horses indicated regional or general adiposity, a main risk factor for IR (van Weyenberg et al. 2008, Carter et al. 2009). In contrast, mean resting plasma glucose concentrations were still in the physiological range, suggesting that measurement of resting plasma glucose has limited diagnostic value in identifying cases of IR.

As expected, starch intake increased postprandial plasma glucose and plasma insulin responses of the animals. In healthy horses, postprandial glycaemic and insulinaemic responses to an identical amount of starch were less pronounced (Vervuert et al. 2009) than the responses measured with insulin-resistant animals, suggesting a dysregulation in glucose metabolism. In our study we did not perform dynamic testing for insulin resistance like combined insulin-glucose tolerance test which monitors the glycaemic response to a combination of exogenous glucose and insulin. Although a high glycaemic and insulinaemic response strongly suggests IR, this procedure has not fully validated as tests for insulin resistance in ponies and horses (Durham et al. 2010).

However, a more blunted postprandial insulinaemic response was observed for both groups during STT 2, but with a more pronounced reduction in insulin profile when Cr-enriched yeast was fed. Feeding Cr to diabetic humans has become quite popular as it has been shown to improve insulin sensitivity (Lukaski 1999, Cefalu et al. 2002). It has been suggested that Cr decreases insulin levels and improves glucose disposal in Type 2 diabetic and obese humans. In this context it has been hypothesized that Cr forms a complex between insulin and insulin receptors that facilitates the insulin-tissue interaction (Mertz 1993). The proposed mode of action of Cr is that increases in blood insulin levels stimulate its uptake by insulin-dependent cells, resulting in the binding of Cr to chromodulin. The binding of four Cr ions to chromodulin enables the link to the insulin-stimulated insulin receptor, and hereby amplifies insulin signalling (Davis et al. 1996, Vincent 2000). In the present study, Cr supplementation seemed to improve insulin signalling as postprandial insulin responses were significant lower during STT 2 for the Cr-treated animals. However, it must be emphasized that the animals were still suffering by impaired glucose regulation as indicated by supraphysiological glucose and insulin responses to starch intake when compared to healthy horses (Vervuert et al. 2009).

In the present study, we used a Cr dosage which was adapted from human treatments; a higher dosage might have greater potential. There are no specific Cr requirements stated for equids. It is supposed that Cr absorption from a typical equine diet, including feedstuffs like hay or grains, is < 0.5%, whereas Cr absorption from an organic source like a Cr-enriched yeast exceeded 25% (McDowell 2003). Further studies are required to obtain more information on Cr metabolism and to establish recommendations for Cr intake by the horse.

We are aware that the postprandial insulin responses were significant higher at the beginning of the study in the group to be fed Cr when compared to the placebo group. In consequence, it cannot be excluded that the differences in baseline assessment might have affected the outcome of this study. However, this confounding factor should be addressed in future studies as the great variation in insulin concentrations has also been reported by others (e.g. Freestone et al. 1992) and possibly mirrors different levels/degrees of IR which needs further elucidation.

It was interesting to note that the placebo horses had non-significant changes in resting and postprandial insulin profiles which were presumably linked to body weight loss. Van Weyenberg et al. (2008) observed an improvement in insulin sensitivity in ponies losing up to 18% of their initial body weight by energy restriction. Freestone et al. (1992) improved insulin sensitivity in obese ponies by limit feeding (diet not defined) for a four week period resulting in weight losses of ~3% of BW. A similar scale of body weight loss resulted in our study following hay restriction (most animals previously had access to hay ad libitum) and a low-intensity exercise programme. Diet-induced weight gain in horses resulted in decreased insulin sensitivity that was effectively compensated by an increase in insulin secretory response (Carter et al. 2009).

Adipose tissue is recognized as the largest endocrine organ in the body, secreting so-called adipokines that play a major

role in the regulation of immune, metabolic and vascular physiology (*Hutley* and *Prins* 2005). Adipokines include leptin, adiponectin, tumor necrosis factor alpha, several interleukins (e.g. IL-6) and plasminogen activator-inhibitor-1. The secretion of proinflammatory adipokines are supposed to decrease insulin sensitivity, induce oxidative stress and impair microvascular function. A significant reduction in serum levels of tumor necrosis factor alpha protein was measured following weight loss in horses (*Adams* et al. 2009). In consequence weight loss seemed to modify IR by blunting inflammatory responses via adipose tissue.

In conclusion, data from the literature and from the current study showed that body weight loss moderates IR. A longer experimental period with continuing weight loss would probably further affect insulin sensitivity as previously suggested by *von Weyenberg* et al. (2008). In addition, Cr supplementation (25 µg Cr/kg BW, provided by a Cr-enriched yeast) seemed to have some potential in the treatment of IR in equids. Further studies are necessary to obtain more detailed information on Cr metabolism, suitable dosage and duration/frequency of treatment. Cr supplementation alone is an inadequate therapy and should always be associated with body weight loss due to restriction of energy intake and moderate exercise, key factors in the treatment of EMS.

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