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RESEARCH ARTICLE

Influence of Functional Nutrients on Insulin Resistance in Horses with Equine Metabolic Syndrome

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A B S T R A C T

The obesity is a rising health problem both in veterinary and human medicine. In equine medicine excessive body weight is frequently related to insulin resistance and laminitis as is defined as equine metabolic syndrome (EMS). The dietetic management is considered as the crucial part of treatment strategy in the course of EMS. The main feeding recommendation is to administer the low energy diet in order to restore insulin efficiency and to lower body weight. In this study 14 horses of different breed, both sexes and different ages with diagnosed equine metabolic syndrome were fed, concurrently, with oats (3 g/kg bw), hay (15 g/kg bw) and experimental dietary supplement containing selected herbs, aminoacids, butyric acid derivative, biotin and selected dietetic plant like artichoke. The influence of above dietary protocol on body weight, insulin level, and adipose tissue morphometry was investigated in horses from group A. Horses from group B fed only with oats (3 g/kg bw) and hay (15 g/kg bw) served as a control. Results of the experiment indicated that tested supplement could improve insulin efficiency and reduce body mass in experimental horses group.

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INTRODUCTION

Equine metabolic syndrome (EMS), often connected with Obesity Depended Laminitis (ODL) or Peripheral Cushing's syndrome (Johnson *et al*., 2002; McGowan *et al*., 2012), is becoming a more and more frequent disease in equine veterinary practice. It is considered to be highly related with improper feeding strategies and individual metabolic defects of the suffering animals. EMS is defined by obesity, insulin resistance and predisposition to developing laminitis (Geor and Harris, 2009; Geor, 2010; Johnson, 2012). Some bred predisposition in case of ponies and cold-bloods were indicated, but it should be underlined that every horse could develop EMS particularly under improper diet and management (Frank, 2009). Excessive body weight in EMS horses is not only absolute obesity but it is connected with characteristic fat tissue deposits in particular regions of the body such as tail base, neck or eye area. Pathologically developed adipose tissue is becoming metabolically active and starting to produce crucial hormonal and proinflammatory factors which unable the correct action of insulin to postprandial glucose level (insulin resistance) (Reaven, 2010; Aslam *et al*., 2012).

Diagnostic process of equine metabolic syndrome includes most of all the clinical examination with particular attention to accurate body weight measurement and regional adiposity recognition. Moreover, the history of past laminitis is highly indicative for this disease. Serum examination should reveal high insulin concentration and normal glucose level. To obtain more reliable diagnosis, functional metabolic tests are usually performed, such as glucose tolerance test and combined glucose insulin test (Frank *et al*., 2006).

The treatment process is complicated and not fully worked up yet. It should include increased physical activity, pharmaceutical approach and dietary management. Regular physical exercise in a form of riding and/or longing seems to be effective therapeutic intervention, improving the insulin sensitivity in horses without signs of active laminitis. As far as pharmaceutical approach is concerned, only levothyroxine sodium and metformin have been used in clinical practice (Frank *et al*., 2008). Controlling the horse's diet is very important for two reasons: first as preventative strategy and second, as a treatment itself. The main goal to obtain by the dietary protocol is to reduce the animal weight by feeding the horse with low glicemic, low energy diet (Carter *et al*., 2010). In this study we investigated the influence of diet enriched with chosen herbal elements, dietetic plants and functional nutrients on insulin resistance and body weight.

MATERIALS AND METHODS

Horses (n=14) of different breed (Silesian Breed, Haflingers, Ponies), both sexes, aged between 8-14 years were involved into the study. Horses spent the majority of the day outside with one hour per day of moderate intensity exercise (longing or riding). The experimental horses were chosen on the basis of clinical examination (body weight, regional obesity, clinical features of past laminitis), baseline insulin level, glucose concentration and combined glucose insulin test confirming insulin resistance. The horses selected for the study were allocated into the two groups. Group A, comprising 8 horses, was provided for active test feed supplement. Group B (6 horses) was the control group with only basic feeding as described below. Each group consisted of horses with comparable main features. The horses were kept in four stables in South Poland, each stable comprised of a proportional number of groups A and B horses. All animals had free access to sandy paddocks, but were excluded from pasture. For reasons of practicability under the field conditions we preferred best possible matching of horses to randomization. Agreement of horse owners and local ethical committee was obtained.

Dietary Protocol: Two concentrates were manufactured by Muhle Ebert Dielheim (Germany). Each concentrate consisted of oats, ground and pelleted. Group A pelleted concentrate in addition contained 13.3% of nutrient mixture, outlined in table 1. It is equivalent to commercially available feed experimental dietary supplement. Concentrate of group B instead contained 13.3% of conventional grass hay.

Dietary protocol consisted of two separates phases, namely: 4 weeks of running in period and 3 months active dietary trial. The weight of each individual was measured at the end of each period every day for five days; the results were than averaged. During running in period animals of both groups received 3g of pelleted oats per 1 kg of body weight daily and commercially available timothy grass hay 1.5% per 1 kg of body weight with water *ad libitum*. In the next step, the active dietary trial was conducted. Horses were divided into 2 groups: first group A (n=8) receiving test feed A - pelleted oats (3g/kg bw) + enriched with test supplement+ hay 1.5% and second group B (n=6) receiving test feed B - pelleted oats (3g/kg bw) + hay 1.5% as a control.

Combined Glucose Insulin Test (CGIT): From the examined horses (14 individuals), samples of peripheral blood were collected into EDTA tubes and coagulation tubes by jugular venipuncture. Blood insulin level was determined using the Equine Elisa Test (BioVendor). Baseline blood glucose concentrations were measured by means of glucometer (Glucosens 1040).

Before performing CGIT, all horses were starved overnight with only limited access to Timothy hay (4g/kg bw). The level of stress was minimized by the presence of the owner and conducting the procedure in surroundings familiar to the animals. The blood was collected and the baseline insulin and glucose level were measured. Then, 50% dextrose solution (150 mg/kg body weight) was injected intravenously immediately followed by application of regular insulin bolus (IV 0.10 U/kg bw). Next, blood glucose concentrations were measured at 1, 5, 15, 25, 35, 45, 60, 75, 90, 105, 120, 135 and 150 minutes post infusion by means of glucometer (Glucosens 1040).

All results were analyzed for statistical significant differences between groups, using the student t test (Statistica 9.0) and were considered to be significantly different when $P<0.05$ or $P<0.01$.

RESULTS

Clinical examination revealed that all horses were obese with bcs>7. Initial total body weight ranged from 230 kg to 780 kg with obvious signs of regional adiposity. After 4 weeks running in period, individual body weights were still comparable with the initial body weight, with no statistically significant differences noticed between groups. At the end of the study, reduction of the total body weight was observed in all horses from group A, while horses from group B showed significant increase in body weight (Table 2). Statistical analysis revealed significant differences between these two groups after the feeding period ($P<0.05$).

Combined Glucose Insulin Test (CGIT): All experimental horses exhibited elevated insulin baseline level and were euglicemic. After 4 weeks running in period there was no significant difference of baseline insulin level between group A and B. After the feeding period the insulin level decreased in group A, compared to the insulin concentration in this group before the trial. Horses from group B showed only slight decrease between initial and final insulin baseline levels. Statistical analysis showed significant differences between two groups after feeding period ($P<0.01$) (Table 2).

At the beginning of research all experimental horses demonstrated positive CGIT test result, (serum glucose concentration reached the normal range after 45 minutes post insulin injection). After running up period all horses still exhibited positive CGIT test result. At the end of the study horses from group A (in contrary to group B) showed negative CGIT test results - they reached normal glucose level before 45 minutes after insulin injection (Fig. 1).

Table 1: Quantities of compounds in experimental dietary supplement

Compounds		Dietary additices per kg		Trace elements per kg	
Dry protein	18.0%	Vit. A	50 IE	Iron	150 mg
Cellulose	7.5%	Vit. D3	5.5 IE	Zinc	2.6 mg
Dry fat	7.5%	Vit. E	5.5 mg	Manganese	3.5 mg
Dry ash	13.0%	Vit. B1	100 mg	Copper	850 mg
Calcium	1.0%	Vit. B2	150 mg	Iodine	1 mg
Phosphorus	0.8%	Vit. B6	100 mg	Cobalt	20 mg
Magnesium	1.0%	Vit. B12	150 ug	Selenium	4 mg
Sodium	0.9%	Biotin	10 ug		
		Nicotine acid	150 mg		
		Folic acid	15 mg		
		Pantotenium acid	140 mg		
		Choline chloride	2 mg		

Table 2: Comparison (mean±SD) body weight and blood insulin level measurements at the initial stage and after all feeding periods

Parameters	Group A	Group B	p value
Initial body weight (kg)	565.9±179	554.6±184	P>0.05
Body weight after running in period (kg)	561.4±173	554±179	P>0.05
Body weight after feeding period (kg)	509.1±165	615.2±180	P<0.05
Initial insulin level (μU/ml)	81.13±11.8	85.17±9.4	P>0.05
Insulin level after running in period (μU/ml)	77.38±11.7	81.17±10.2	P>0.05
Insulin level after feeding period (μU/ml)	34.75±6.8	83.33±11.1	P<0.01

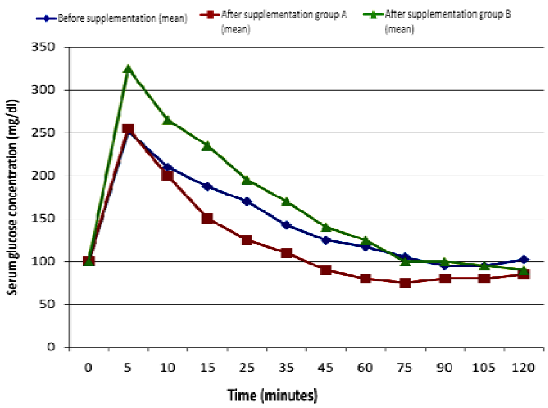

Fig. 1: The results from combined glucose-insulin test.

DISCUSSION

The obesity is the rising health problem both in veterinary and human medicine. Particularly in human beings it is considered to be a civilization disease resulting mostly from improper diet and reduced physical activity of modern societies. Obesity phenomenon is also related to genetic background of the given individual. In equine medicine disorder closely connected with insulin resistance, excessive body weight and laminitis is defined as equine metabolic syndrome (EMS). Laminitis which is frequent consequence of EMS is considered to be second, after colics, equine health problem and in extreme cases can be fatal. Insulin resistance and proinflammatory activity of the fat tissue were documented to play major role in equine metabolic syndrome (Carter *et al*., 2010).

Disability to utilize fat tissue storage is often observed in contemporary horse breeding and management as a result of high carbohydrate and starch feeding protocols. In those circumstances fat tissue plays not longer the role of energy storage, but significantly influences development of insulin resistance. This occurrence is connected with impaired insulin interaction with its peripheral receptors, which is often ascribed to adipose derived glucocorticosteroids, free fatty acids and adipokines (leptin, adiponectin) which are adipose tissue hormones (Slawik and Vidal-Puig, 2007). Although clinical evidence of inflammation is lacking, excessive fat tissue occurs to be an important source of pro-inflammatory cytokines such as IL-6, TNF (tumor necrosis factor) and MCP-1 (monocyte chemoattractant protein), which further complicates the course of the disease.

Complex pathogenesis of EMS could be related to difficulties in treatment of this disease in horses. The administration of pharmaceutics without relevant diet management is usually unsuccessful. Horses affected with EMS should have reduced intake of calories to prevent additional weight gain. Additionally a massive restriction of starch and nonstructural carbohydrates (NSC) diet content, relatively high intake of digestible fiber and medium chain triglycerides (MCT) are recommended. The mentioned diet profile reduces the amount of fermentable sugars, which may cause the increase in blood glucose and insulin levels (Dugdale *et al*., 2010).

In the course of this study, we observed a marked body weight reduction after supplementation period in horses from experimental group, despite receiving 3g/kg bw of oats. It could be deduced that unique composition of feed supplement, namely the content of L-carnitine, biotin, taurin, herbs and chosen plants have the reducing weight properties (Nakaya *et al*., 2000). L-carnitine, is a quaternary amine (β-hydroxy-γ-N-trimethyammonium butyric acid), and is known as a vitamin like and amino acid like substance (Cha, 2008). L-carnitine deficits may interfere with lipids availability as an energy source and their accumulation resulting in obesity (Zeyner and Heimeier, 1999), thus we conclude that the supplementation with this substance improved the body weight decrease in our study. Moreover, contents of an artichoke help to reduce the metabolism of starch, which is particularly important in the maintenance of body weight, and blocks obesity progress (Tormo *et al*., 2004; Nazni *et al*., 2006; Celleno *et al*., 2007). There are some studies describing the positive effect of natural organic substances such as herbal mixtures, biotin, taurin and lipoidic acid, which improve insulin sensitivity and reduce oxidative stress (Dragland *et al*., 2003; Vincent *et al*., 2007). In the course of this research, experimental feed was enriched with Gliucogard® formula comprising *Silybum marianum,* Bilberry (*Vaccinium myrtillus),* Capsella *(Capsella bursa-pastoris),* Anise *(Pimpinella anisum),* fennel *(Foeniculum vulgare)* and cinnamon. Anthocyanin content of bilberry is known as an anti-diabetic factor involved in glucose transport and fat metabolism (Takikawa *et al*., 2010). Moreover cinnamon and anise provide the high concentration of antioxidants (>75 mmol/100 g), which positively affect the glucose/insulin system and enhance the liver glycogen storage (Couturier *et al*., 2010; Couturier *et al*., 2011); these characteristics have found a confirmation in our experiment. Chromium as also important ingredient of tested dietary supplement is an essential nutrient that potentiates insulin action and thus influences carbohydrate, lipid and protein metabolism. It was demonstrated that the insulin resistance could be improved by administration of supplements enriched in chromium (Striffler *et al*., 1998). Additionally, several studies have shown that certain aromatic herbs accumulate high levels of chromium and could contribute to dietary intake of this element. The highest level of chromium among supplemented herbs in this study could be found in garlic, mint, cinnamon and anise (Garcia *et al*., 2000).

In conclusions it should be underlined that, despite feeding horses affected with equine metabolic syndrome with 3g/kg bw of oats per day, the diet enrichment with dietary supplement comprising selected herbs, biotin, L-carnitine and chosen plants (artichoke) could improve insulin serum level, sensitivity and reduce the body mass. Therefore, the proper selection of functional nutrients is able to affect favorably main risk of EMS-induced laminitis. If the underlying nutrient mixture is able to directly prevent or to positively influence the laminitis events remains to be investigated in further research.

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