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EQUINE METABOLIC SYNDROME

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The article defines the disease – the equine metabolic syndrome (EMS) and based on literature data, the leading causes, pathogenesis, diagnosis, prevention, and treatment of complications provoked by equine metabolic syndrome are described. Equine metabolic syndrome is registered in young horses and old animals. For example, Morgan, Paso Fino, Arabian, riding, and thoroughbred horses. Diagnosis of equine metabolic syndrome is based on the analysis of breed and genetic predisposition, determination of insulin resistance, and the degree of obesity. Early diagnosis of equine metabolic syndrome prevents the development of laminitis. Therefore, the primary treatment for equine metabolic syndrome is weight loss, with a combination of diet and exercise in horses without developing laminitis. Treatment and care of an animal with metabolic syndrome require an individual approach. The main strategic direction in solving the problem of insulin resistance should be based on weight loss and increasing insulin sensitivity by changing the diet and increasing physical activity. A change in diet is to reduce energy components and non-structural carbohydrates in its composition. In addition, grazing should be avoided, especially during the season when young, fresh grass appears. It is necessary to pay attention to the pastures, where today the number of grasses of genetically modified species, which are grown for milk production and fattening cattle, is increasing. Such grasses are characterized by a high content of NSC, which is the opposite of the pastures that are necessary for horses. Suppose the equine metabolic syndrome was established after the detection of laminitis. In that case, measures should reduce body weight, but with little physical activity, to not expose further damage to the hooves. Therefore, priority is directed to remove the

animal from the laminitis and reduce obesity with significantly reduced physical activity. A low-carb diet should reduce insulin activity. However, if its activity is very high, you can use drugs to decline its level.

Key words: *horses, insulin resistance, obesity, laminitis, glucose, diet, exercise.*

МЕТАБОЛІЧНИЙ СИНДРОМ У КОНЕЙ

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У статті дано визначення захворювання – метаболічний синдром коней, а також на підставі даних літератури охарактеризовано основні причини, патогенез, діагностику, профілактику та лікування ускладнень, спричинених метаболічним синдромом у коней. Метаболічний синдром коней реєструється в молодих коней, а також у геріатричних тварин. Найбільш поширеним метаболічний синдром коней є в поні, коней породи Морган, Пасо Фіно, арабських, верхових і чистокровних коней. Діагностика метаболічного синдрому коней полягає на аналізі породної та генетичної схильності, визначенні резистентності до інсуліну, а також ступеня розвитку ожиріння. Рання діагностика метаболічного синдрому коней запобігає розвитку ламініту. Основним у лікуванні коней за метаболічного синдрому є зниження маси тіла, з комбінацією дієти і фізичного навантаження в коней без розвитку ламініту. Лікування й догляд за твариною з метаболічним синдромом вимагає індивідуального підходу. Основний стратегічний напрямок у вирішенні проблеми інсулінорезистентності повинен опиратися на втраті маси тіла й підвищенні чутливості до інсуліну за допомогою зміни раціону та збільшенні фізичної активності. Зміна раціону полягає у зниженні енергетичних компонентів і неструктурних вуглеводів у його складі. Крім того, необхідно уникати випасання тварин, особливо в пору року, коли з'являється молода, свіжа трава. Необхідно звертати увагу на пасовище, на яких сьогодні збільшується кількість трав генетично модифікованих видів, які вирощують для виробництва молока та відгодівлі великої рогатої худоби. Така трава характеризуються високим вмістом NSC, що є протилежністю пасовищ, які необхідні для коней. Якщо метаболічний синдром коней був встановлений після виявлення ламініту, то заходи повинні бути спрямовані на зменшення маси тіла, але з обмеженим фізичним навантаженням, щоби не наражати на подальше пошкодження копит. Першочергова увага має бути спрямована на лікування ламініту у тварини, а також зменшення ожиріння зі значно зниженою фізичною активністю. Низьковуглеводна дієта повинна знижувати активність інсуліну. Якщо його активність є дуже високою, можна використовувати препарати для зниження його рівня.

Ключові слова: *коні, метаболічний синдром, інсулінорезистентність, ожиріння, ламініт, інсулін, глюкоза, дієта, фізичне навантаження.*

Metabolic syndrome was first described in humans in developed countries due to limited physical activity, combined with easy access to high-calorie drinks and food. With the change in methods of use and feeding, similar observations were later investigated in horses [14].

Equine Metabolic Syndrome (EMS) – a clinical syndrome that is a collection of interrelated pathological changes related to obesity, insulin resistance, and laminitis [23].

EMS is registered in young horses and old animals. For example, Morgan, Paso Fino, Arabian, riding, and thoroughbred horses [33]. As already mentioned, the main elements of EMS are insulin resistance, obesity, and laminitis. However, it is assumed that the syndrome covers a much more comprehensive range of problems that adversely affect energy metabolism, which can promote thrombosis, cause chronic inflammation and excessive free radical formation, and develop oxidative stress [1]. In addition, such animals develop endocrinological changes, leading to cardiovascular disease [38].

Therefore, the use of the term EMS is beneficial for distinguishing horses with Cushing's syndrome or cases of hypothyroidism, with which it is often confused [22].

Pathophysiology of EMS. Adiposity. Genetically, horses, like many other animals, can accumulate fat. Bodyweight and subcutaneous fat deposition are influenced by environmental factors, including diet, season, physical activity, and genetic factors [2].

The mechanisms underlying general obesity in horses have not been thoroughly studied, but overfeeding combined with limited physical activity, which slows metabolism, are considered significant factors in developing obesity, as in humans and other species [3, 31].

"Local" obesity is associated with the development of fatty tissue only in certain parts of the body. For example, in horses, adipose tissue accumulates around the neck, foreskin, breast, and sides of the body. An informative EMS test is the distribution of fat along the entire neck length. This condition is known as "cresty neck" and, regardless of its degree, causes an increase in neck volume [18].

Insulin resistance is an insufficient biological response of cells to the action of insulin at its sufficient concentration in the blood [29].

There are two theories linking obesity to insulin resistance. The first is related to regulating insulin signaling pathways induced by cytokines and adipokines synthesized in adipose tissue. The second refers to the intracellular accumulation of lipids in insulin-sensitive tissues such as skeletal muscle, adipose tissue, liver [27].

A natural diet for horses is low in fat and carbohydrates quickly converted into fat. Such fat is used for energy production or is deposited and stored intracellularly. When fat exceeds the capacity of cells, it accumulates in other places, such as skeletal muscle, liver, and pancreas. Despite the increase in beta-oxidation, lipids disrupt the normal functioning of cells in these organs, including the signaling pathway through which insulin causes a biological effect in target cells [4].

Insulin resistance is associated with defects in insulin signaling, including a decrease in tyrosine kinase activity and insulin receptors [8].

The development of insulin resistance is pathogenetically associated with laminitis, when regular insulin activity does not elicit the expected response in target cells [6, 7, 42]. The primary function of insulin is to stimulate glucose uptake by tissues. The two main sites of indirect glucose uptake are skeletal muscle and adipose tissue, but we must also consider the liver, which also absorbs glucose from the blood [9].

Insulin resistance results from a decrease in the density of insulin receptors, their malfunction, damage to internal signaling pathways, and dysfunction of insulin-dependent hepatic glucose transporter protein in the liver GLUT4 (glucose transporter type 4) [24].

Laminitis is one of the most severe and common disorders of the extremities in horses. The disease is defined as an aseptic, diffuse inflammation of the connective skin tissue of the hoof. Although changes in the hoof manifest the disease, it is currently considered a systemic disorder accompanied by changes in other organs [25].

The occurrence of chronic laminitis should always refer the veterinarian to further differential diagnosis and the possibility of developing EMS. Still, it should be remembered that laminitis is a separate illness [20].

Predisposition to laminitis may be determined by the body's ability to supply glucose to hoof tissues. It has been suggested that insulin resistance affects the supply of nutrients to the hoof tissues by changing the pressure in the blood vessels. In addition, insulin has a vasodilating effect, increasing blood flow to tissues [26].

Diagnosing EMS. The diagnosis of EMS should be based on the patient's medical history, the results of a clinical study, the evaluation of radiographs of the hooves, and the results of laboratory tests. For example, the best laboratory test for the diagnosis of insulin resistance is an intravenous test for glucose tolerance. Still, from the point of view of practice, an alternative approach to diagnosis is recommended [13].

The most straightforward diagnostic test for EMS is to determine the insulin level in the blood. However, the interpretation of the obtained results should be careful – taking into account the factors that may affect the reliability of the results. The concentration of insulin in the blood is influenced by many factors – feeding horses, especially in recent times (diet, its amount). It is also necessary to determine the cortisol concentration in the blood (daily fluctuations, emotions, pain, stress), physiological condition (reproductive status), obesity, comorbidities. Insulin activity and fasting glucose concentration are relatively stable and can diagnose [10]. The animal must be prepared before the study for 24 hours. Restrict feeding, including non-structural carbohydrates (NSCs) (starch, pectin, fructans), and a starvation diet 8 to 10 hours before the study. Horses that are on pasture are placed in places without access to feed. Blood samples should be sent to the same laboratory because different laboratories may use different methods to determine insulin in the blood, leading to incredible results [44].

Horses and ponies with EMS are characterized by slightly elevated or high serum glucose (reference ranges of 80–115 mg/dL) and hyperinsulinemia (upper reference limit <20 μOd/ml) [16].

In horses with active inflammation of the hoof base, it is not advised to perform the above tests until eliminating the acute phase of the disease, when each sympathetic nervous system activation leads to decreased insulin sensitivity and hyperglycemia [19].

Insulin content determination in the blood indicates a false-negative result in horses and ponies that receive a diet low in NSC. It is recommended to perform dynamic tests on such animals. Executing dynamic tests is necessary when the animal has clinical symptoms of EMS, but the results of previous tests were not in doubt. Such studies are advised to assess the degree of insulin resistance and monitor illness progression [39]. Intravenous insulin-glucose tests (CGIT) should be combined to diagnose insulin resistance effectively. This test can be successfully used in the field. Administration of these two drugs (glucose 150 mg/kg, insulin 0.1 IU/kg) requires several determinations of blood glucose with a glucometer (before the introduction of 1, 5, 15, 25, 35, 45, 60, 75, 90, 105, 120, 135 and 150 minutes from the moment of introduction). The obtained result is characterized by forming a two-phase curve with positive (hyperglycemic) and negative (hypoglycemic) particles. Also, it is evaluated concerning the time for which the concentration of glucose in the blood returns to baseline. Insulin sensitivity is confirmed by returning the glucose content to baseline within 45 minutes [12]. Patients rarely develop symptoms of hypoglycemia due to insulin administration (weakness, tremor, increased sweating). If such symptoms occur, 40 % glucose solution quantity 120 ml is administered intravenously [34].

False-negative results confirming the absence of insulin resistance may be due to the action of stressors before the study. Therefore, the study should be performed in a quiet and peaceful environment, and the intravenous catheter is best placed the day before the study [35]. The combined test gives more useful clinical results because they are more informative than each test alone [28]. However, the main reason for erroneous results of glucose and insulin in the blood during the collection of individual blood samples is the animal's stress. Therefore, the constant determination of glucose is a kind of innovation and helps to eliminate stressors. This method consists of the subcutaneous placement of a sensor to determine the glucose blood content, which registers its level every 5 minutes for up to 7 days. It is a beneficial solution for both the patient and the veterinarian [32].

Assessment of obesity. The best way to assess obesity is the Body Condition Score (BCS) method, which allows you to assess the degree of obesity objectively. The method determines the level from 1 (exhaustion) to 9 (severe overweight). Horses are evaluated visually and empirically by manually examining six body areas where fatty tissue accumulates. To assess the degree of obesity also considers the physical characteristics of horses, described in the original works [43].

Obesity in horses occurs according to the proposed scheme. Fat deposition begins behind the shoulder blades. Then it covers the ribs, above the back of the body, and finally along the shoulder girdle in the direction of the neck and head. Condition assessment (BCS system) determines the amount of fat accumulated in these areas. It may be useful to measure the neck circumference in “local” obesity, which, as already mentioned, is a symptom of EMS [1].

Recommendations. Treatment and care of an animal with metabolic syndrome require an individual approach. The main strategic direction in solving the problem of insulin resistance should be based on weight loss and increasing insulin sensitivity by changing the diet and increasing physical activity. A change in diet is to reduce energy components and non-structural carbohydrates (NSC) in the diet. In addition, grazing should be avoided, especially during the season when young, fresh grass appears [18].

Suppose the EMS was established after the detection of laminitis. In that case, measures should reduce body weight, but with little physical activity, to not expose further damage to the hooves. Therefore, priority is directed to remove the animal from the laminitis and reduce obesity with significantly reduced physical activity [5].

Obesity prevention. Reducing obesity has the most significant positive effect on restoring insulin sensitivity. It is necessary to remember to limit grazing when returning to pasture when the grass has the highest concentration of NSC – in spring, early summer, the transition period between autumn and winter, as well as in the hours when the concentration is highest (lowest 3 : 00 – 9 : 00). Weight loss should be gradual, as sudden weight loss can lead to hyperlipidemia and fatty liver disease. Reducing obesity should increase physical activity and limit food intake [45].

Focused that laminitis eliminates physical activity. Therefore, the diet should include hay with a low NSC content. It is best to perform a laboratory test of hay to determine the content of NSC. If the animal reacts negatively to reducing the daily diet, the portion is divided into several smaller ones to reduce periods of hunger. You can also use food bags, which take longer to feed. Hay should be introduced into the diet first at a dose of 1.5 % of body weight, and within a month, the dose is reduced to 1 % of body weight if the animal does not lose weight [11].

It is necessary to pay attention to the pastures, where today the number of grasses of genetically modified species, which are grown for milk production and fattening cattle, is increasing. Such grasses are

characterized by a high NSC content, which is the opposite of the necessary pastures for horses [21]. Summing up, the hay should be low in NSC and should not contain alfalfa and grain. The NSC reduction can be achieved by soaking hay for 30 minutes in warm water or 60 minutes in the cold. In addition, you can use commercial feed with low NSC content. However, the feeding of low NSC foods is accompanied by a decrease in protein, vitamins, and minerals, so it is counseled to include them in the diet in addition [30].

Treatment. A low-carb diet should reduce insulin activity. However, if its activity is very high, you can use drugs to decline its level [37].

Levothyroxine sodium. Weight loss can be increased by using a special diet and increasing exercise. Administration of the drug in high doses causes weight loss in horses. The drug causes weight loss due to increased thyroxine concentration by stimulating basal metabolism. Horses should not graze because levothyroxine causes hyperphagia. It can be used for 3–6 months at a 0.1 mg/kg [15, 17].

Metformin hydrochloride. Metformin is a drug used in human medicine to control hyperglycemia and increase insulin sensitivity in patients with diabetes. It inhibits glucose synthesis in the liver. Studies in horses have shown improvement in insulin sensitivity in patients with insulin resistance at a dose of 15–30 mg/kg after oral administration for two weeks. It was also found that the bioavailability of the drug after oral administration is low in horses, but its use in combination with moderate exercise has a positive effect [36, 40, 41].

Conclusions

Equine metabolic syndrome is a clinical syndrome registered in horses and is characterized by obesity, insulin resistance, and the development of laminitis. Understanding the mechanisms underlying this disease is still limited but is an area of active research. Diagnosis of equine metabolic syndrome is based on the analysis of breed and genetic predisposition, determination of insulin resistance, and the degree of obesity. Early diagnosis of equine metabolic syndrome prevents the development of laminitis. Therefore, the primary treatment for equine metabolic syndrome is weight loss, with a combination of diet and exercise in horses without developing laminitis.

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