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Establishment of Temporary Criteria for Metabolic Syndrome (MS) Diagnosis and Assessment of the Occurrence Rate of MS in Cats

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Abstract: In this study, researchers attempted to establish temporary criteria for Metabolic Syndrome (MS) diagnosis in cats. To verify the usefulness of the selected criteria, we investigated changes in plasma glucose, Triglyceride (TG), Total Cholesterol (TC), Alanine Aminotransferase (ALT) insulin and adiponectin levels as diagnostic factors in 50 clinically healthy cats. Cats with obesity as an essential factor in addition to any two of the three conditions, namely increased plasma glucose levels, elevated TG and/or TC levels and higher ALT activity were diagnosed with MS. Presence of additional factors such as reduced plasma adiponectin and/or raised insulin levels, confirmed the MS diagnosis. Based on these criteria, 9 (18.0%) cats were diagnosed with MS. In these cats, the plasma glucose, TC and ALT levels were significantly higher than those in the control cats (n = 41) without MS. MS was not detected in cats with body condition score <3 and the occurrence rate of MS was the highest in 5-10 years old cats. In the MS cats, reduced plasma adiponectin levels appeared to be an essential factor that defined the early stage of the disease.

Key words: Adiponectin, cat insulin, metabolic syndrome, disease, Japan

INTRODUCTION

Changes reflective of a Western lifestyle are thought to be responsible for the rapid rise in obesity and type 2 diabetes mellitus. Epidemiological evidence strongly suggests that changes in diet and physical activity levels are the main contributory lifestyle factors in humans (Tuomilehto *et al*., 2001; Emberson *et al*., 2005; Johnston *et al*., 2010). In dogs and cats, the occurrence of glucose/lipid abnormalities with obesity has markedly increased in recent years (Johnson, 2005; Mori *et al*., 2010; Muranaka *et al*., 2011). Cat obesity is commonly associated with insulin resistance that leads to cat diabetes, closely resembling human type 2 diabetes mellitus (Hoenig, 2006; Hoenig *et al*., 2007) and also with Metabolic Syndrome (MS). In humans, MS is considered to be a cluster of the most dangerous heart attack risk factors i.e., diabetes with raised fasting plasma glucose, abdominal obesity, high cholesterol and high blood pressure (IDF, 2005). Presently, criteria for MS diagnosis in dogs and cats are similar to those in humans. In this study, researchers tried to establish new temporary criteria for MS diagnosis in cats and verified by comparing with values in healthy cats.

MATERIALS AND METHODS

A total of 50 client-owned (volunteered) cats (26 female, 24 male, 2-18 years old) from 11 veterinary clinics in the Setagaya district of the Tokyo metropolitan area were used to evaluate the criteria for MS diagnosis. The degree of obesity was assessed by Body Condition Score (BCS) on the following five-point scale: very thin, underweight, ideal, overweight and obese. Blood samples were collected from jugular veins of overnight-fasted cats (without any nutrients for >10 h since, the last meal) into heparinized tubes. Plasma was separated by centrifugation at 4°C and stored at -25°C until use. Glucose, Triglyceride (TG) and Total Cholesterol (TC) levels and Alanine aminotransferase (ALT) activity were measured with an auto analyzer (AU680, Olympus Corporation, Tokyo, Japan) using the manufacturer's reagents.

Commercial ELISA kits such as the Lbis Cat Insulin kit (Shibayagi Co., Gunma, Japan) and mouse/rat adiponectin ELISA kit (Otsuka Pharmaceutical Co., Tokyo, Japan) were used to measure plasma insulin and adiponectin levels, respectively. Results are presented as mean±95% C.I. Statistical significance was determined by

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student's t-test using Sigmaplot (Version 11.2, Build 11.2.0.5, Systat Software Inc., San Diego, CA, USA). The significance level was set at $p<0.05$.

RESULTS AND DISCUSSION

The temporary criteria for MS diagnosis in cats are discussed in the study. Temporary criteria for Metabolic Syndrome (MS) diagnosis in cats to be defined as having MS, cats must have the following:

- Central obesity (defined as over 10% increase in normal BW or BCS >3.0 and any two of the following 3 factors
- Plasma glucose level ≥120 mg dL^{-1}
- TG level ≥165 mg dL^{-1} and/or TC level ≥180 mg dL^{-1}
- ALT level ≥100 IU L^{-1} (Additionally, diagnosis of MS is confirmed by the following two factors)
- An adiponectin level <3.0 μg mL^{-1} and/or an insulin level >3.0 ng mL^{-1}

All values are measured in plasma of overnight fasted cats. BW = Body Weight; BCS = Body Condition Score; TG = Triglyceride; TC = Total Cholesterol and ALT = Alanine Transaminase.

These criteria were developed based on the previous study with >142 normal healthy cats (Hatano *et al*., 2010). Cat MS was diagnosed according to human MS criteria (IDF, 2005). Cats with obesity as an essential factor in addition to any two of the three factors, namely raised glucose levels, elevated TG and/or TC levels and increased ALT activity were diagnosed with MS. The diagnosis was confirmed by presence of additional factors such as reduced adiponectin and/or raised insulin levels. Plasma metabolite and hormone levels and ALT activity in cats with and without MS are shown in Table 1. Nine (18.0%) of 50 cats were diagnosed with MS according to the new selected criteria. In MS cats, plasma glucose, TC and ALT levels were significantly higher than those in control cats without MS. Plasma TG and insulin levels in the MS cats were higher than those in the controls whereas plasma adiponectin levels in the MS cats were lower than those in the controls however, the differences were not significant. The occurrence rate of MS was investigated in cats with different BCS and ages (Table 2). MS was not observed in cats with BCS <3.0. The occurrence rate of MS was highest in 5-10 years old cats.

Visceral fat accumulation with insulin resistance is an important risk factor for MS in humans. In cats, glucose and lipid metabolism disorders with obesity have remarkably increased in recent years and are defined as MS in cats in this study. In cat MS, hyperglycemia, hyperlipidemia and fatty liver disease with insulin resistance appear to occur similar to the human condition. These abnormalities were examined as factors in establishing criteria for MS diagnosis in cats. Researchers found that obesity (BCS>4.0) with visceral fat accumulation is an essential factor. Hyperglycemia, hyperlipidemia (hypertriglyceridemia and/or hypercholesterolemia) and fatty liver disease are also necessary factors. ALT is considered to be an indicator of liver disease (Satter *et al*., 2004) and MS cats were found to have raised plasma ALT activity. According to cat MS criteria, hypertension is not considered as a necessary factor which differs from human MS criteria (IDF, 2005). Plasma insulin levels in cats without MS were higher compared with those in MS cats therefore, raised plasma insulin levels may not to be an essential factor for MS in cats.

It has recently become widely accepted that obesity is characterized by chronic low-grade inflammation of adipose tissue that predisposes affected individuals to insulin resistance (Yang *et al*., 2010; Gauthier and Ruderman, 2010). Adipose tissue of obese individuals secretes a multitude of proinflammatory cytokines and chemokines whereas secretion of adiponectin, an adipocytokine that activates AMP-activated Protein Kinase (AMPK) and has well known anti-inflammatory and insulin-sensitizing properties is significantly decreased (Weiss *et al*., 2005). Adiponectin levels show a strong negative correlation with insulin resistance and obesity (Wijesekara *et al*., 2010). Reduced plasma adiponectin levels are one of the essential factors for MS diagnosis and adiponectin may represent a novel target for the prevention and treatment of visceral obesity associated with MS (Okamaoto *et al*., 2006).

Table 1: Comparison of metabolite, enzyme and hormone levels in cats with and without Metabolic Syndrome (MS)

Factors	With MS (n = 9)	Without MS (n = 41)
Glucose (mg dL^{-1})	218.0±106*	111.0±9.00
TG (mg dL^{-1})	142.0±112	89.0±31.0
TC (mg dL^{-1})	213.0±67*	162.0±15.0
ALT (IU L^{-1})	104.0±46*	52.0±7.00
Adiponectin (μg mL^{-1})	2.2±1.1	3.8±1.10
Insulin (ng mL^{-1})	4.1±1.4	3.6±1.10

TG = Triglyceride; TC = Total Cholesterol; ALT = Alanine Transaminase; Values are presented as mean±95% CI; *Significantly different ($p<0.05$) from values without MS

Table 2: Occurrence rate of Metabolic Syndrome (MS) in cats with different Body Condition Scores (BCS) and ages

Parameters	Rate of MS (%)
BCS (1-5)	
<3	0/5 (0.0)
3-4	1/9 (6.7)
>4	8/36 (22.2)
Age (years)	
1-4	1/13 (7.7)
5-10	4/17 (23.5)
>10	4/20 (20.0)

CONCLUSION

In this study, MS cats had lower blood adiponectin levels compared to the controls. Development of MS causes severe metabolic disorders such as diabetes mellitus therefore, proper treatment appears to be a key factor to prevent the progression to severe metabolic disorders. The criteria presented here for cats are not absolute and should be adjusted based on further examination of additional data to be confirmed as reliable.

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