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New Criteria of Hyperlipidemia with Insulin Resistance in Dogs

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Abstract: Researchers attempted to establish temporary criteria to detect hyperlipidemia at early stage in dogs. To verify the usefulness of the criteria, researchers investigated plasma Glucose (GLU) Triglyceride (TG), Total Cholesterol (TC) and Non-Esterified Fatty Acid (NEFA), Alanine Aminotransferase (ALT) and insulin levels as diagnostic markers in 38 clinically healthy dogs. Hyperlipidemia dogs were detected based on the any two of the following three factors, namely elevated the TG, TC and NEFA levels. In addition, measurement of raised insulin levels, the dogs were diagnosed as hyperlipidemia with insulin resistance. Based on these criteria, nine (23.7%) of 38 dogs were diagnosed as hyperlipidemia. In these dogs, plasma TG, NEFA and insulin levels were significantly higher than those in the control dogs without hyperlipidemia (n = 29).

Key words: Dog, hyperlipidemia, insulin resistance, plasma, glucose

INTRODUCTION

In dogs and cats, occurrence of glucose and lipid metabolism disorders such as obesity and diabetes has increased markedly in recent years (Hatano *et al*., 2010; Mori *et al*., 2010). Obesity with insulin resistance is an important risk factor for Metabolic Syndrome (MS). Hyperlipidemia is a common sign of obese animals (Mori *et al*., 2011). Hyperlipidemia is diagnosed clinically as >300 mg dL^{-1} of plasma Total Cholesterol (TC) concentration in dogs (Whitney, 1992) and hyperlipidemia with the above plasma TC level is considered to be severe stage. Plasma Triglyceride (TG) concentrations of 150-400 mg dL^{-1} are considered mildly elevated for clinical assessment in dogs (Whitney, 1992). In the present study, researchers attempted to establish the new criteria to detect hyperlipidemia at early stage in dogs and to prevent the hyperlipidemia progresses to MS and severe metabolic disorders in dogs. The aim of this study is to make the new criteria for hyperlipidemia to prevent the severe metabolic disorders and to discuss the availability of the criteria in veterinary medicine.

MATERIALS AND METHODS

Thirty eight client-owned (volunteered) dogs (16 female, 22 male and 0-14 years old) of 5 veterinary clinics in Kanto district in Japan were used to evaluate the criteria for hyperlipidemia. Four dogs were excluded due to having disorders such as diabetes mellitus. The degree of obesity was assessed by Body Condition Score (BCS) on the following five-point scale: very thin, underweight, ideal, over weight and obese. Blood samples were taken from jugular veins of dogs fasted overnight (without any nutrient for >8 h after the last meal) in heparinized tubes. Plasma was recovered by centrifugation at 4°C and stored at -25°C until use. Glucose (GLU), Triglyceride (TG), Total Cholesterol (TC), Alanine aminotransferase (ALT) levels were measured using an autoanalyzer (AU680, Beckman Coulter, CA, USA) with manufacture's reagents. Plasma Insulin (ISN) concentrations were measured with commercial ELISA kits, Lbis dog insulin kit (Shibayagi Co., Gunma, Japan) and Non-Esterified Fatty Acid (NEFA) was measured using commercial kit (NEFA-C test, Wako Pure Chemical Industries, Inc., Tokyo, Japan). Results are presented as mean±95% C.I. Statistical significance was determined by student's t-test. The significance level was set at $p<0.05$.

RESULTS AND DISCUSSION

The temporary criteria for hyperlipidemia in dogs are discussed in this study. Temporary criteria to detect hyperlipidemia with insulin resistance in dogs must have the following factors:

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- Any two of the following 3 factors
  - Raised TG level ≥165 mg dL^{-1}
  - Raised TC level ≥200 mg dL^{-1}
  - Raised NEFA level ≥1.5 mEq L^{-1}
- Additional diagnosis of insulin resistance is fixed with the following factors
  - Raised insulin level ≥2.5 ng mL^{-1}

Based on the new criteria, 9 (23.7%) of 38 dogs were diagnosed as hyperlipidemia. In hyperlipidemia dogs, plasma TG, NEFA and insulin levels were significantly higher than those in the control dogs without hyperlipidemia. Plasma TC and ALT levels in the hyperlipidemia dogs were higher than those in the controls whereas there was no difference in plasma glucose levels between control and hyperlipidemia dogs (Table 1). The occurrence ratio of hyperlipidemia was investigated in dogs with different BCS and ages (Table 2). About 6 (33%, highest ratio) hyperlipidemia dogs were detected in dogs with BCS 4. The occurrence ratio of hyperlipidemia dogs increased with aging.

Criteria for hyperlipidemia proposed here showed lower plasma TG and TC concentrations compared to those for clinicians (500 mg dL^{-1} of TG, 500 mg dL^{-1} of TC) (Xenoulis and Steiner, 2010) which researchers think the criteria for clinical treatment. Actually hyperlipidemia dogs diagnosed by the new criteria did not show the typical symptom as hyperlipidemia diagnosed with criteria as in the past. Researchers think this hyperlipidemia is at early stage without the tangible signs and researchers think they can prevent the hyperlipidemia to develop severe metabolic disorders by detecting hyperlipidemia at the early stage with the new criteria.

Table 1: Comparison of metabolite, enzyme and hormone levels in hyperlipidemia and control dogs

Plasma contents	Hyperlipidemia (n = 9)	Control (n = 29)
Glucose (mg dL^{-1})	106.70±10.3	103.10±7.00
TG (mg dL^{-1})	129.60±70.7*	55.20±13.2
NEFA (mEq L^{-1})	1.36±0.63*	0.78±0.18
TC (mg dL^{-1})	246.90±27.2	212.40±28.6
ALT (IU L^{-1})	78.70±34.0	59.00±16.0
Insulin (ng mL^{-1})	2.39±2.41*	0.99±0.27

Values are presented mean±95% CI. *Significantly different ($p<0.05$) from control dogs values

Table 2: Occurrence ratio of hyperlipidemia in dogs with various body condition score or age

Factors	Ratio of hyperlipidemia (%)
BCS	
2	0/1 (0.0)
3	2/18 (11.1)
4	6/18 (33.3)
5	1/1 (100.0)
Age	
1-4	1/10 (10.0)
5-10	3/19 (15.8)
>10	5/9 (55.5)

Researchers suggest that plasma insulin concentrations could be elevated significantly compared to the controls in the early stage of hyperlipidemia when plasma glucose concentrations were not elevated. The condition with high plasma insulin and high plasma lipid levels observed in hyperlipidemia dogs is considered to be insulin resistance which becomes a key factor to induce Metabolic Syndrome (MS) (Wang *et al*., 2012).

The effect of canine obesity has been studied since at least 1960's (Finlayson *et al*., 1960; Krook *et al*., 1960). Today, abdominal obesity due to visceral fat accumulation with insulin resistance has been an important risk factor for metabolic syndrome in dogs as well as in cats. Compared to cats, insulin resistance is not frequently observed in dogs (Hoenig, 2006; Hoenig *et al*., 2007). However, since development of hyperlipidemia could cause severe metabolic syndrome such as diabetes mellitus, proper treatment such as food restriction and exercise, appears to be a key factor to prevent the progression to sever metabolic disorders.

CONCLUSION

The criteria for dogs are not absolute and should be adjusted based on further examination of additional data to be confirm as reliable. Hyperlipidemia was detected highest in dogs with Body Condition Score (BCS) 4 and the occurrence rate of hyperlipidemia increased associated with age.

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