Preemptive Veterinary Medicine of Feline Obesity Disease

Summary of Doctoral Thesis

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Summary

Obesity is defined as "a condition in which adipose tissue has accumulated excessively". Furthermore, it is classified into subcutaneous fat type obesity in which fat accumulates subcutaneously and visceral fat type obesity in which fat accumulates around the viscera such as the small intestine, depending on a site where fat tissue accumulates. In particular, obesity with visceral fat accumulation is a risk factor for type 2 diabetes, hypertension, arteriosclerosis, cardiovascular disorders, and cancer. One of the characteristics of obesity is that chronic mild inflammation persists, which causes metabolic disorders such as insulin resistance and dyslipidemia, infiltrating immune cells into tissues and increasing production of inflammatory cytokines in adipose tissues is observed. In response to these inflammatory signals, adipose tissue releases inflammatory mediators and acute phase proteins. These are the main causes of obesity-related complications. Obesity is also known to increase with age, and its onset will increase in the future, but not decrease. For these reasons, obesity is said to be "an epidemic of the 21st century", and overcoming it is an urgent issue for human race. On the other hand, obesity continues to increase in dogs and cats, which is a major health problem in the veterinary field. There are many common pathologies of obesity in humans, dogs and cats, and researching and unraveling the mechanisms and connecting them to prevention and treatment is consistent with the concept of One Health that protects human and animal health together. It can be greatly expected as a field of future research.

Although we often encounter obese dogs and cats in daily small animal practice, we have not investigated the incidence of overweight to obesity in animals actually visited. This time, we examined dogs and cats who visited our hospital for the purpose of medical examination. According to the 2018 Pet Population Forecast by the American Pet Supplies Association (APPA), an estimated 56 million cats and 50 million dogs are overweight

to obese nationwide. In a similar study in 2017, 60% of cats (26.5% overweight / 33.5% obesity) and 56% dogs (36.4% / 19.6%) were overweight to obese. At present, the ratio of overweight to obesity in dogs and cats is 30 to 40%, the ratio tends to increase year by year, and the tendency is similar to the incidence of human beings. In our survey, overweight to obesity in dogs in 2019 was 38.3%, and cats were 49.1%. In dogs, the ratio of overweight to obesity has been fixed at around 30% since 2017, and in cats, the ratio has been fixed at nearly 50% since the beginning of 2016. It become clear that cats had a higher incidence of obesity than dogs. This survey was aimed at health check-up animals that are relatively interested in health compared to general owners, so it is expected that the ratio of actual visiting animals will be higher. In the current situation where life with pets has greatly helped alleviate stress in society, research on obesity in dogs and cats and promoting their prevention and treatment agree with One Health's concept, "health of people, animals, and the environment (ecosystem)are interrelated and one" ,and have a great significance for "symbiosis between humans and animals" .

The incidence of obesity in cats is 30-40% and tends to increase worldwide. Cats are more likely to be obese than dogs because of their unique glycolipid metabolism characteristics. Based on these metabolic characteristics of cats, we developed a flowchart and criteria for determining obesity. BCS grade 7 or higher is determined to be obesity. Primary obesity is a condition in which excess triglyceride accumulates in adipose tissue due to excessive energy intake and lack of exercise。 This is distinguished from secondary obesity caused by abnormal hormonal secretion from the thyroid, pituitary gland, gonadal and the like. Primary obesity is further classified by the presence or absence of health problems. Those without health problems are simply obese, and those with health problems are divided into subcutaneous fat types and visceral fat types according to the presence or absence of visceral fat accumulation (somewhat). Visceral fat type often accompanies an inflammatory response and is the basis for metabolic syndrome. Obesity disease was determined when the patient was overweight with a BCS of 7 or

more and showed two or more of the three symptoms of hyperlipidemia (TG>
165mg / 100mL or T-chol> 180mg / 100mL), low adiponectin (<3μg / mL), high
SAA (> 200 ng / mL).Various factors such as heredity, nutrition, and
lifestyle are involved in the development of obesity to obesity disease,
and the factors that occur vary from individual to individual. Early
diagnosis and appropriate early response are effective in suppressing
obesity. Obesity is one of the non-infectious diseases (NCD), and
preemptive medicine with thorough prevention of individuals is effective
in suppressing NCD. It is important to apply the analysis data of genomics,
proteomics and metabolomics accumulated in the process of developing and
quantifying markers for early diagnosis as big data. In addition, it is
considered that early diagnosis and prevention of obesity disease can be
promoted if regular cat health checkups and the like can be made customary,
as in the diagnosis of metabolic syndrome in humans. If such a series of
systems can be established, it will be possible for cats to be healthy and
live long, leading to the construction of a society where both humans and
animals can live healthy and live longer.

 One of the causes of the development of obesity disease is tissue damage
to inflammation caused by reactive oxygen species (ROS) produced
excessively with the increase in fatty acid β-oxidation. Therefore,
administration of antioxidants and anti-inflammatory agents that can
suppress this series of reactions is thought to lead to reduction of obesity
symptoms. Many plant-derived active ingredients, phytochemicals, are known
to have antioxidant and anti-inflammatory effects. We investigated the
effects of quercetin derivative Rv-PEM01, one of these phytochemicals, on
healthy and obesity disease cats for 4 weeks. The dose was 2.5 to 2.8 mg
/ kg / day in terms of quercetin. In healthy cats, plasma NEFA and SAA
concentrations significantly decreased after 4 weeks of administration of
quercetin derivatives. Body weight, BCS, and blood glucose levels did not
change. When quercetin derivative Rv-PEM01 was administered to 3 cats
(mongrel, female, 5, 6 and 9 years old) determined to be obesity disease
provided by clinical facilities in Tokyo, all 3 animals received Rv-PEM01

for 4 weeks later, no significant changes in body weight or BCS were observed. Blood lipid (TG, T-chol, NEFA) and SAA concentrations decreased in all three animals, but the low adiponectin state was not resolved. LDH, AST, and ALT activities were slight, but all three animals decreased after Rv-PEM01 administration. The most prominent effect of administration of the quercetin derivative Rv-PEM01 was increased liver function-improved lipid metabolism. Active use of plant-derived active ingredients such as quercetin in the veterinary field is required. Quercetin derivatives can be expected to have anti-oxidant and anti-inflammatory effects even when administered to healthy animals. Therefore, quercetin derivatives can be applied to prevent metabolic disorders such as obesity, hyperlipidemia and type 2 diabetes.

Obesity is now a major global health problem. The incidence is rising not only in developed countries but also in developing countries in recent years. Obesity is a non-infectious disease that is a risk factor for serious metabolic diseases such as type 2 diabetes, hypertension, cardiovascular disorders, and cancer, so overcoming it is an urgent issue for mankind. In the future, in the super-aging society facing Japan, the importance of extending healthy life expectancy rather than average life expectancy will be noticed, and obesity is a living condition that cannot be overlooked as a life prognostic factor. In addition, obesity is not simply regarded as a nutritional disorder, but in order to understand its pathology, it is very important to consider various aspects such as nutrition, genetics, behavior, immunology, endocrinology infectious diseases and microbiology.

On the other hand, dogs and cats who visit animal hospitals have the same tendency as people. With the dramatic progress of veterinary medical technology in recent years, pets have entered the age of aging as well as human society, and in obesity and overweight dogs and cats that are obvious in daily clinics of animal hospitals as well Many encounters. And many owners know that their pet is obese is not good for their health, but they

haven't taken a step to improve it, or if they do, it is extremely difficult to achieve good results. There are many common pathologies for obesity in humans, dogs and cats, and this is a trend of modern medicine, and it is necessary to respond within the framework of the One Health research to protect the health of humans and animals together. The study of obesity in dogs and cats can be a reference for human medicine and vice versa.

Early diagnosis and appropriate early response are effective in suppressing obesity. If preventive and preemptive medicine is used to detect obesity early and lifestyle-related diseases are eradicated, medical expenses will be reduced for a super-aged society, and healthy life expectancy will be extended. I believe that it will definitely contribute to the realization of a happy society.