Evaluation of exercise in diabetic dogs and temporal relationship between exercise and meal

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Exercise therapy as well as dietary therapy is one of the basic therapies for diabetic patients. In human study, primary effects of exercise therapy include improving blood glucose control, lipid metabolism and insulin sensitivity. Exercise therapy had been a therapy directed to obese patients and type 2 diabetic patients. But recently, it also directed to type 1 diabetic patient. It was reported that any exercise could be done for type 1 diabetic patients, if they did not have any progressed complication or inadequate blood glucose control. Today, in patients with type 1 diabetes for whom exercise therapy is incorporated, correction of postprandial hyperglycemia and decrease in HbA1c, as well as effects of preventing complication and extending life expectancy have been reported, thus increasing significance of exercise therapy. On the other hand, depending on dosage of insulin or timing of mealtime, various side effects such as hypoglycemia or delayed digestion and absorption might be occurred in exercise therapy. However, effect of exercise therapy on glucose metabolism is not clear in dogs.

Therefore, objective of this study was to determine usefulness of exercise therapy in diabetic dogs and to elucidate relationship between exercise and meals.

Chapter 2 Changes in heart rates, blood lactate concentration and number of steps with different exercise intensity in healthy dogs

In order to set exercise intensity, changes in heart rates, blood lactate concentrations and number of steps with different exercise speeds (running at 6, 8, 13, 16 km/h for 30 minutes) were determined in this chapter. Five healthy beagle dogs maintained in our laboratory were used in this study. In the results, heart rates with different exercise intensity (rest, 6 km/h, 8 km/h, 13 km/h, 16 km/h) were 94±11/min, 118±10/min, 121±7/min, 121±7/min and 144±12/min, respectively. Higher exercise intensity induces higher heart rate, suggesting increase of exercise stress. Blood lactate concentrations did not changed between at rest,6 and 8 km/h after exercise therapy. However, significant increase was observed at 13 and 16 km/h compared to at rest. Furthermore, lactate concentrations at 16 km/h were significantly higher than at 13 km/h. Heart rate itself is insufficient for index of exercise intensity. In human, it has been demonstrated that lactate concentrations (lactate curve) during exercise show two-phase variations: the first phase is aerobic variations fluctuating under 2 mmol/L of lactate concentration (under LT) and the second phase is anaerobic variations rapidly increasing to 4 mmol/L or above (over LT). Exercise therapy at 6 and 8 km/h used in this experiment did not induce any changes of blood lactate concentrations, these speeds might be low intensity. Therefore we determined exercise therapy at 6 km/h and 8 km/h as aerobic exercise. In regards of exercise therapy at 13 and 16 km/h, highest lactate concentration after exercise were 1.53±0.49 mmol/L (20 minutes) and 1.97±0.57 mmol/L(30 minutes), respectively, but they (average concentration) remained under 2 mmol/L. Therefore, these two exercise intensity were also determined as aerobic exercise.

In conclusion, heart rates and blood lactate concentrations might be appropriate

indexes for exercise therapy in dogs. Furthermore, exercises therapy at 6, 8, 13 and 16 km/h used in this experiment were determined as aerobic exercise.

Chapter 3 Changes in blood biochemical parameter and gene expression of skeletal muscle after therapeutic exercise in diabetic dogs.

In this study, we investigated whether therapeutic exercise affect for blood biochemical parameters (Glycated albumin(GA), Non-esterified fatty acid(NEFA), creatine kinase(CK), lactase dehydrogenase(LDH), 3-hydroxybutyric acid(3HB), adiponectin), and muscular mRNA expression (insulin receptor substrate1, 2(IRS-1, IRS-2), phosphatidylinositol 3-kinase(PI3-K), Akt kinase 2(AKT2), AMP-activated protein kinase(AMPK), glucose transporter 4(GLUT4), uncoupling protein 3(UCP3), acetyl-coA carboxylase (ACC)) in diabetic dogs. The results showed that continuous one-month exercise in diabetic dogs significantly decreased GA level. Temporal analysis of postprandial glucose concentration after therapeutic exercises were tended to decreased.

CK and LDH concentration were significantly decreased after exercise therapy, suggesting continuous exercise induced training effects. In regards to lipid metabolism, NEFA concentration was significantly decreased and adiponectin was elevated after exercise therapy, suggesting decrease of body fat percentage owing to continuous exercise. AMPK and GLUT4 gene expression were elevated to 1.54 and 1.4 times after one month exercise therapy, respectively, suggesting glucose uptake by skeletal muscle in diabetic dogs. Furthermore, IRS-1, PI3-K,

and AKT2 gene expression were elevated to 1.52, 1.73 and 1.5 times after exercise therapy, respectively, suggesting exercise therapy might induce up-regulation of insulin signaling pathway in diabetic dogs.

In conclusion, therapeutic exercise decreased the GA level and thus improved glycemic control in diabetic dogs. Furthermore, changes in some gene expression suggested that therapeutic exercise affected glucose uptake in skeletal muscle and insulin signaling gene expression in diabetic dogs.

Chapter 4 Relationship between exercise therapy and mealtime in healthy and diabetic dogs

Changes in blood glucose concentration due to exercise therapy was reported to induce various side effects such as hypoglycemia and delayed digestion and absorption depending on dosage of insulin or timing of mealtime. Postprandial hypoglycemia has been reported in a dog during hunting. Therefore the purpose of this study was to investigate relationship between exercise therapy and mealtime. In Paragraph 1, we evaluated blood biochemical parameter before and after oral glucose tolerance test (OGTT) test in healthy 4 dogs. Exercise therapy was performed after 30 minutes of OGTT. The results suggested that exercise therapy induce decreasing blood glucose and insulin concentrations after OGTT. As such, conditions with both hyperglycemia and hyperinsulinemia might have higher risk of lowering blood glucose concentrations. In the Paragraph 2, we studied influence of exercise therapy performed with different time periods after a meal on glucose and lipid metabolism in healthy 4 dogs. The results showed that exercise therapy induced rapid decrease of blood glucose concentration in 1, 2, 3 and 4h after meals groups. However, 5h after meals group from exercise therapy was

not observed any changes of blood glucose concentration after exercise therapy, suggesting postprandial exercise with 5h after meals did not affect for blood glucose concentrations in healthy dogs. In Paragraph 3, we studied influence of exercise therapy performed with different time periods after a meal (6h and 8h after meals group) on glucose and lipid metabolism in 2 diabetic dogs. As a result, decrease of blood glucose concentrations was observed in two diabetic dogs with 6h after meals. However, 8h after meals group was not observed any changes of blood glucose concentration after exercise therapy, suggesting postprandial exercise with 8h after meals did not affect for blood glucose concentrations in two diabetic dogs. Therefore, time period of exercise therapy might be better to do at 8h after meals.

The current study showed that the establishment a standard for exercise therapy in healthy dogs and its application for diabetic dogs. These evidences provide useful information for exercise therapy of diabetes mellitus in dogs.