Journal of Advanced Biomedical Sciences | Winter 2022 | Vol 12 | 1 | https://doi.org/10.18502/jabs.v12i1.8874

Original Article

The Effect of Vertical Sleeve Gastrectomy on Weight Loss, Insulin and Glucose Levels in Dogs

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Received: 23 Sep 2021 Accepted: 13 Nov 2021

Abstract

Background & Objective: This study was designed to evaluate the effect of sleeve-gastrectomy procedure on weight loss, glucose and insulin blood levels in overweight dogs.
Materials & Methods: In the current study, 5 overweight dogs (31.6±3.03kg) were selected for sleeve-gastrectomy procedure. Insulin and glucose levels were measured from the blood samples that were taken before the surgery and weekly 1.5 month post-operatively. The weight of the dogs was also measured at the same time. The surgery was performed according to the technique described by Gagner 2009, and the dogs received special diet during the recovery period to end of the study.
Results: One dog died due to dehiscence and leakage 48 hours post-operatively. Decrease in mean weight was 6.25±0.44 in the first week after surgery and the weight loss process continued to end of the study. Changes in insulin and glucose blood levels demonstrated to have pulsatile patterns. Insulin levels decreased for the first week, but its level increased in the second week period. Again, insulin levels demonstrated to have decreasing pattern in the following 4 weeks. On the other hand, the glucose levels changed each week and did not show any certain pattern.
Conclusion: Post-operative weight loss was observed in all cases but it was not statistically significant. It could be due to limited number of the samples. The glucose and insulin changes were attributed to hormonal changes particularly gut hormones that were affected by sleeve-gastrectomy procedure but further detailed studies on hormonal effect are required.

Keywords: obesity, Sleeve Gastrectomy, insulin, blood glucose, dogs

Introduction

Obesity is the result of an imbalance between the calorie intake and its expenditure. These extra calories are accumulated as fat tissue in different organs in the body and leads to serious comorbid conditions (1-3).

Overweight dogs are defined as the dogs that are 10 to 20% over the ideal weight, and obese dogs have 20% more weight, above the ideal weight (4). Also, some other studies mention that a dog with body composition of 25 to 35% body fat is considered as overweight and more than 35% as obese (5). The obesity prevalence of the canine population in developed countries ranges from 11.2% to 59.4% (6-10).

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[DOI: 10.18502/jabs.v12i1.8874]

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Obesity is a multifactorial condition, and several factors are involved to create a positive energy balance, and consequently to develop weight gain. These factors include genetics and breeds (6, 11, 12), age (10, 12-14), sex and neutering (6, 10, 12, 15), and owner-related factors.

Obesity is considered as a significant risk factor for several comorbidities in dogs and has a negative impact on the life span (16, 17). It is beneficial for many obese and overweight dogs that suffer from cardiovascular, endocrine, urinary, renal, respiratory and orthopedic disease to lose weight and alleviate the related clinical signs (18). In addition to these problems, the obese patients need meticulous consideration during anesthesia, since they are at higher risk than normal patients (19, 20).

There are several ways to manage obesity and to reduce the Body Condition Score (BCS) accordingly. Nutritional management, behavioral management, increase in physical activity and exercise are some methods considered for this purpose (18). The main goal of these procedures is to reduce the energy intake or to increase the energy expenditure.

With the nutritional management, depending on the individual's weight, a weight loss program demands several months and sometimes more than a year to be done successfully (18). It has been demonstrated that in the dogs experiencing the dietary reforming program to lose weight, the weight loss rate did not continue in the same gradient as the first weeks and declined over 12 weeks (21). Free access to food following a successful weight loss program results in gaining weight at a faster rate and thereafter less amount of calories is needed to get to the same level of weight than the initial time prior to the weight loss program (22, 23).

Behavioral management includes understanding and improvement in human-animal interactions should be accompanied by dietary management and exercise plan in order to be a successful program (18). The owners' intense emotions and attachment can affect the treatment in either a positive or negative way (18).

Several studies demonstrate that inactivity in dogs could predispose them to obesity development (7, 13). There are some comorbidities accompanied by obesity, including osteoarthritis, exercise intolerance and muscle wasting. These factors limit the amount of exercise which a dog can perform, this obstacle in turn makes restriction on increasing the energy expenditure and limits their maximum exercise tolerance (18).

In humans, bariatric surgery is one of the most appropriate ways to treat obesity (24). Vertical sleeve gastrectomy (VSG) is one the most potent bariatric surgeries that has many advantages over the other methods in this category, and it has a comparative outcome in comparison with gastric bypass, while it is less invasive (24). This surgery method causes better results in comparison with other bariatric surgeries in weight loss and glucose metabolism (25).

It is also shown in human medicine that gastrectomy leads to hyperglycemia and insulin secretion accordingly. This is due to the limited capacity of stomach to store ingested nutrients temporarily after the procedure, and then, this will lead to accelerated absorption of nutrients (26, 27), although by actions of Incretins (28-30) and Adipokines (adiponectin), the glycemia is maintained at a normal range.

This article aimed to study the alteration occurred after VSG in body weight, fasting glucose and insulin levels in dogs, and possible postoperative hypoglycemia or hyperglycemia consequently. To our knowledge, this is the first time that sleeve gastrectomy is performed in dogs to evaluate weight loss, glucose and insulin blood levels.

Materials & Methods

Study population

A total of 5 mixed-breed dogs (4 males and 1 female) were included in this study. The mean preoperative BCS was 5 and the mean body weight was 31.6±3.03 kg.

Operative technique

The animals were anesthetized by standard anesthetic regimen. This protocol included premedication with intramuscular Acepromazine (0.02-0.04 mg/kg), followed by an induction with IV Ketamine (5 mg/kg) and IV midazolam (0.5 mg/kg). Then, all dogs were intubated and maintained with Isoflurane 2% during surgery.

The dogs were positioned dorsal recumbency and the surgical area was prepared routinely. The bucket handle incision was made in the skin from the Xiphoid process to either side bilaterally and subcostally to access the stomach properly (Figure 1) (31). Through the latter method, the whole stomach is more accessible. The subcutaneous and muscles were incised on the same lines.

The branches of left gastroepiploic vessels were ligated along the greater curvature. (Figure 2) Sleeve Gastrectomy (SG) procedure was performed according to the human surgery technique described by Gagner (32).

The greater curvature was resected from 6 cm proximal to the pylorus to the angle of His, along the 48fr tube, which was inserted previously and trans-orally along the lesser curvature, from hiatus to duodenum. Fundus and most part of the body of the stomach were transected and removed. The remaining parts were over-sewn by Parkerker suture technique with absorbable suture material (2/0 vicryl) (Figure 3). The muscles, subcutaneous and skin were closed in three layers with the same suture material and by simple continuous, subcutaneous and subcuticular technique respectively.

Post-operative care

Ringer lactate and Duphalyte serum were administered for all cases 24hrs after surgery. On the 2nd postoperative day, if no vomiting was observed, the ROYAL CANIN recovery powder, according to the weight of each case, was given via nasogastric (NG) tube and free access to the water was provided from this day on. After the 4th day post-operative, a low-calorie diet was provided for 2 weeks. On the third week post-operative, a low-fat and low-calorie diet started and continued until the end of the study. All dogs received IV Cefazolin 25 mg/kg bid for 5 days, IV Ondansetron 0.2 mg/kg bid for 5 days, SC Meloxicam 0.2 mg/kg sid for the first day, and SC 0.1 mg/kg sid for the next 2 following days. Also, IV 2 mg/kg Tramadol bid was administered for 2 days postoperatively.

Sampling

Before the procedure, blood samples were taken after an overnight pre-operative fasting, and weekly after surgery for 1.5 month. The clotted samples were centrifuged to separate out blood plasma, then fasting insulin and glucose levels were measured.

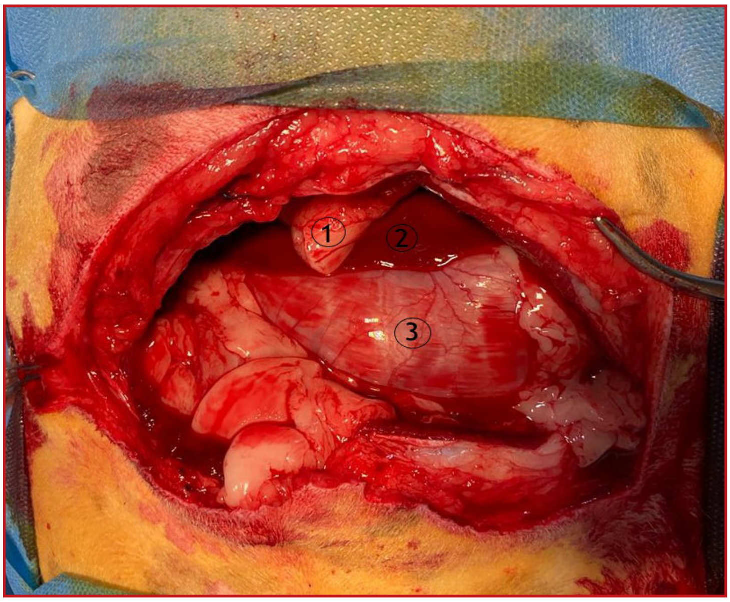

Figure 1. Bucket handle incision. 1. Falciform ligament 2. Liver 3. Stomach

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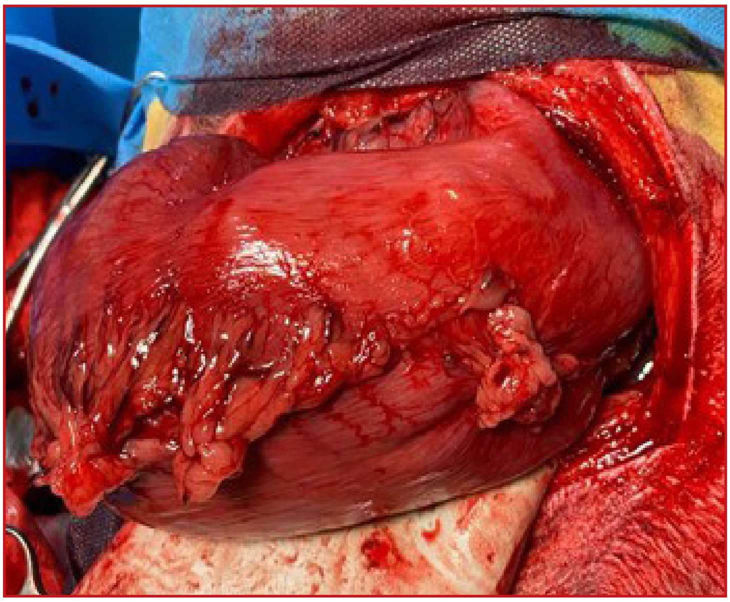

Figure 2. Left gastroepiploic vessels after ligation

Statistical Analysis

Data analysis was performed using SPSS software for windows. Wilcoxon Signed Ranks Test was used to assess differences between data before and after surgery. Test results were presented as Means and standard deviation (Mean ± SD). A value of $p \leq 0.05$ was considered statistically significant.

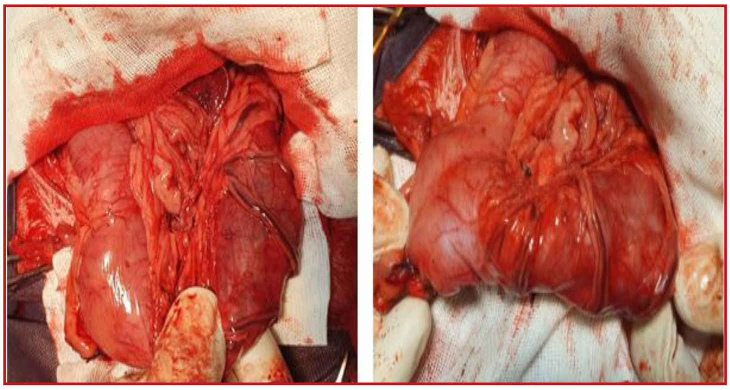

Figure 3. The stomach after Sleeve Gastrectomy

Result

Table 1 shows the weight values for all 4 cases during 1.5 months of study.

Table 2 presents the insulin values during 1.5 months of the study for all 4 cases.

Table 3 has the same format like the two aforementioned tables.

In total of 5 dogs, one dog died within 48 hours post-operatively, due to the gastric suture dehiscence and leakage. During 6 weeks follow-up, as expected, in comparison with the time prior to the operation, weight loss was observed in all of the cases starting from a week after surgery (Weight 2) (31.62±3.03 kg vs. 25.37±2.59 kg), but this weight loss was not statistically significant (p=0.066) (Table 1). The weight loss rate continued constantly for weeks and accordingly (Table 2). The weight reached 21.50±3.87 kg at the end of the study (p=0.068) (Table 4). The weight loss process according to time is presented in Figure 1. None of the weight values were statistically significant (Table 4).

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Table 1. weight changes during study

	N	Minimum	Maximum	Mean	Std. Deviation
Weight1*	4	28.00	35.00	31.6250	3.03795
Weight2**	4	23.00	28.50	25.3750	2.59406
Weight3	4	22.50	28.00	24.8750	2.59406
Weight4	4	22.20	28.00	24.8000	2.68825
Weight5	4	21.00	27.50	24.2500	2.84312
Weight6	4	18.00	27.00	23.1250	3.88104
Weight7	4	17.00	26.00	21.5000	3.87298
Valid N (listwise)	4				

* All the values are presented in kg. Weight 1 indicates the minimum, maximum, mean and standard deviation of the weights among the all 4 dogs at the time of surgery. Weight 2 shows the aforementioned values for the 1st week after surgery and so on.
**Weight 2 is the weight measured at the one week after surgery

Remarkable reduction in mean fasting glucose and insulin levels were observed during the first week after surgery (Table 2 and 3). For the week after surgery (insulin 2) the insulin level was 11.40±2.08 µu/mL when compared to insulin level before surgery 17.33±2.94 µu/mL ($p=0.068$).

This value increased for the second week after surgery and reached 15.32±2.26 µu/mL ($p=0.068$), but again the value decreased for the third week (14.32±3.69 µu/mL) ($p=0.465$). During three following weeks, this level had a constant reduction and at the end of the study it reached 11.75±2.37 µu/mL ($p=0.068$) (Figure 2).

During the study, the glucose levels after surgery had a pulsatile pattern. Glucose level at the start of the study (Glucose 1) was 129.75±5.05 mg/dL. For the first week, glucose level (Glucose 2) decreased and reached 95±6.87 mg/dL ($p=0.068$). The second week (Glucose 3) revealed an increase to 101.87±13.59 mg/dl ($p=0.068$) and the third week (Glucose 4), it decreased again and reached 98.62±10.43 mg/dL ($p=0.068$). This level was 107.87±9.27 mg/dL ($p=0.068$), 95.62±9.62 mg/dL ($p=0.068$) and 114.00±10.70 mg/dL ($p=0.066$) for the fourth, fifth and sixth week respectively. During 1.5 month follow up no statistically significant reduction in mean fasting insulin and glucose levels was observed between post-operative and pre-operative values (Table 4).

Table 1. weight changes during study

	N	Minimum	Maximum	Mean	Std. Deviation
Insulin1*	4	13.18	19.52	17.3325	2.94047
Insulin2**	4	8.74	13.52	11.4000	2.08391
Insulin3	4	12.53	17.65	15.3200	2.26566
Insulin4	4	9.28	18.16	14.3250	3.69555
Insulin5	4	8.25	18.76	13.8325	5.35174

Insulin6	4	9.89	15.36	12.4000	2.56602
Insulin7	4	9.66	15.17	11.7500	2.37690
Valid N (listwise)	4				

*All the values are presented in µu/ml. Insulin 1 indicates the minimum, maximum, mean and standard deviation of the weights among the all 4 dogs at the time of surgery. Insulin 2 shows the aforementioned values for the 1st week after surgery and so on.
**Insulin 2 is the insulin value measured at the one week after surgery

Table 3. Glucose changes during study

	N	Minimum	Maximum	Mean	Std. Deviation
Glucose1*	4	124.00	134.00	129.7500	5.05800
Glucose2**	4	90.00	105.00	95.0000	6.87992
Glucose3	4	83.50	116.00	101.8750	13.59151
Glucose4	4	86.50	110.00	98.6250	10.43532
Glucose5	4	97.50	120.00	107.8750	9.27699
Glucose6	4	84.50	108.00	95.6250	9.69858
Glucose7	4	100.00	126.00	114.0000	10.70825
Valid N (listwise)	4				

*All the values are presented in mg/dl. Glucose 1 indicates the minimum, maximum, mean and standard deviation of the weights among the all 4 dogs at the time of surgery. Glucose 2 shows the aforementioned values for the 1st week after surgery and so on.
**Glucose 2 is the glucose value measured at the one week after surgery

Table 4. Changes in weight, insulin and glucose levels on the 1st, 2nd, 3rd, 4th, 5th and 6th week post-operative

	Prior To Surgery	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6
Parameters	Mean	Mean p	Mean P	Mean P	Mean P	Mean p	Mean P
weight	31.62±3.03	25.37±2.59 0.066	24.87±2.59 0.066	24.80±2.68 0.066	24.25±2.84 0.066	23.12±3.88 0.066	21.50±3.87 0.068
Insulin	17.33±2.94	11.40±2.08 0.465	15.32±2.26 0.068	14.32±3.69 0.465	13.83±5.35 0.144	12.40±2.56 0.144	11.75±2.37 0.068
Glucose	129.75±5.05	95.00±6.87 0.068	101.87±13.59 0.068	98.62±10.43 0.068	107.87±9.27 0.068	95.62±9.69 0.068	114.00±10.70 0.066

*P<0.05 considered as significant

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Discussion

Obesity has been considered as a disease in human population for many years. Recently, at a World Small Animal Veterinary Association One Health meeting, canine obesity was also officially classified as a disease (33, 34).

The prevalence of canine obesity was reported in several manuscripts. According to the studies, this value was 44.4% for China (9), 59% for UK (7) and 34.1% in the United States (35).

In human medicine, when the long-term medical treatment and weight loss management of obesity are unsuccessful, bariatric surgeries are considered as a salvation procedure and has a beneficial effect on comorbidities related to the obesity (36, 37). Also, bariatric surgery is considered as an only effective modality in controlling and treatment of super morbid obesity and maintains weight loss for the Long-term (38). Therefore, we aimed to design a study and to perform such a surgery in dogs and evaluate some specific parameters to see whether it is applicable to dogs or not.

In the current study, weight loss happened immediately after surgery and for the first week afterwards, a 6.25 kg reduction in mean weight of cases was observed. This reduction continued at a slower rate till the end of study. Hady et al. (38) demonstrated that weight loss after SG procedure occurs through two mechanisms: caloric restriction and hormonal modulation. Because of resection of the fundus, the plasma level of ghrelin decreased after 7 days post-operatively. (39, 40). The increase in insulin level observed for the 2nd week post-operation could be related to slower gradient in the weight loss that is mentioned before.

Also, in this study, the glucose level reduced to a basal level in the first week after surgery due to weight loss and hormonal changes. It seems that because of glucose homeostasis through different physiological processes, the body maintains glucose level at a certain range and therefore no hypoglycemia or hyperglycemia was observed after surgery. Hady et al. (38) demonstrated that weight loss improved glucose metabolism and insulin sensitivity after SG.

During the following week (from the 2nd week after surgery to the end of study) the glucose levels did not decrease to the basal level and demonstrated a pulsatile pattern that could be due to the adaptation of β-cell to the new conditions. It is shown that β-cell function adapts after bariatric surgeries to optimize or maintain glucose homeostasis (41). It is also mentioned that β-cell sensitivity to the factors such as glucose and GLP-1 will be reduced after surgery to prevent hyper secretion of insulin and hypoglycemia subsequently (42, 43).

The insulin reduction observed in the current study from 3rd week after operation is possibly related to β-cell adaptation, but further detailed studies are required.

Also, it is observed that insulin changes did not follow the glucose changes in the following weeks after surgery and despite the pulsatile pattern changes in glucose level, the insulin level decreased in an already stable pattern from the third week to the end of study. This pattern could also possibly happen due to both hormonal changes that affect the insulin sensitivity and β-cell adaptation.

As it is demonstrated by the study, the reduction in insulin level at the first week could be related to the sudden decrease in glucose level in the blood and hormonal effects.

It has been proved that extra pancreatic and extra intestinal factors can affect insulin secretion, and these can be triggered by SG procedure (36).

Insulin levels would be regulated mainly by serum glucose levels, and can be reduced through improvement in insulin sensitivity (36). By improving insulin sensitivity, the insulin secretion would be decreased (41).

Kubosaki et al. (44) and Henquin et al. (45) demonstrated that, there is a factor that inhibits the insulin response to the intra peritoneal infusion of glucose in mice, and this factor is extrinsic to the Langerhans islets. Basso et al. showed that this factor could be ghrelin (36), that decreases insulin sensitivity, so the removal of gastric fundus, as happens in SG procedure, could help improve insulin sensitivity (46).

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SG has been proved to have a remarkable reductive effect on ghrelin level in humans (36, 39) and rodents (47). It seems that SG surgery can also reduce the ghrelin level in dogs, but further detailed studies are needed.

SG causes increased hepatic insulin sensitivity in mice 5 days after surgery (48) that continues for 30 days postoperatively. Also, SG has a significant reductive effect on insulin level a week after surgery (38, 49).

GLP-1 is responsible for stimulation of pancreatic β-cells for insulin biosynthesis, the restoration of insulin sensitivity, and inhibition of glucagon secretion, which may result in decreasing hepatic glucose production (50). It is speculated that the decrease in glucose plasma level that is observed in the present study in the first week after surgery, could be attributed to the increased GLP-1 secretion.

Adipose tissue is the source of secretion of adiponectin (49). Although the adiponectin is an adipokine secreted by adipose tissue, in obese patients the adiponectin level is demonstrated to be low and it has a reverse relationship with insulin level (49). While the adiponectin is an adipokine, the plasma level of adiponectin is demonstrated to be increased during caloric restriction in both human and animal populations. A recent study showed that this could be due to an increase in the adipose tissue within the bone marrow during caloric restriction (51).

It is also shown that adiponectin and leptin completely reverse insulin resistance in mice, (52) and adiponectin improves the insulin sensitivity through regulation of fatty acid oxidation and suppression of hepatic glucose production (53).

It is also demonstrated that ghrelin, suppresses the insulin sensitizing hormone adiponectin (49).

So, the insulin level reduction that observed in our study, can be explained by ghrelin level reduction, increase in Adiponectin level, GLP-1 and PYY level.

Glucose levels also dropped a week after SG surgery in mice as a weight independent process (48). SG also caused a decrease in glucose levels a week after surgery in obese patients (49, 54).

The pulsatile pattern of glucose levels that was observed during the follow up after surgery in the current study, was also observed in other experiments (49).

In the current study for the surgical technique, because of the approach related difficulties to access the fundus through routine ventral midline incision, it is decided to use Handle Bucket Incision technique. This technique used widely in human operations for specific purposes.

One of the main limitations of the present study was the sample size. Therefore, a bigger population for better evaluation is suggested.

Additionally, as animals were not obese or diabetic, the insulin and glucose level was in normal range, so it is suggested that a study be conducted on such a group of patients as well.

Finally, it is suggested to follow-up these cases for a longer period of time to confirm these data.

Conclusion

In summary, sleeve gastrectomy surgery was well tolerated by dogs. The insulin and glucose plasma levels were maintained in normal range. Remarkable reduction in weight, insulin and glucose was observed one week after surgery in the current study, but it was not significant in comparison with the pre-operative values. This could be due to the small sample size and non-diabetic and non-obese animals. 1.5 month after surgery, the clinical parameters measured in the study were still in the normal range.

These observations may help evaluate the role and indication of SG surgery in proposed surgical therapy for obese and diabetic dogs. However, several hypotheses still need to be confirmed in order to accurately evaluate the role of SG in these types of patients.

Conflict of Interests

The authors declared that there is no conflict of interests.

Acknowledgments

The authors are grateful to Mr. Mohsen Norouzi, Daryoush Sarikhani and Esmaeil Dehdashti for their technical assistance during all procedures in the department of veterinary surgery. The authors also respect Shiraz University for their support.

The ethical approval number of Shiraz University statement on veterinary research is: 9330103.

Conflict of Interests

The authors declared that there is no conflict of interests.

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[DOR: 20.1001.1.22285105.2022.12.1.1.5]
[DOI: 10.18502/jabs.v12i1.8874]

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