Sonorous plunge of serum magnesium levels among pre-diabetic and diabetic cats

Research Article

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Article info
Submission: 11-05-2023
Accepted: 19-09-2023
Online First: 20-09-2023
Publication: 15-12-2023

e-ISSN: 2548-1150
doi prefix: 10.31797/vetbio
http://dergipark.org.tr/vetbio

ABSTRACT

Diabetes mellitus is a frequently occurring endocrine disorder in felines, and the impact of magnesium deficiency on the incidence of diabetes and related complications has garnered significant interest in the realm of human research. Our objective was to investigate the levels of magnesium present in the serum of cats with pre-diabetes and diabetes. Although magnesium levels in pre-diabetic and healthy cats did not exhibit a significant statistical difference, a notable contrast was evident in diabetic cats in this study. Specifically, diabetic cats exhibited considerably lower magnesium levels in comparison to non-diabetic felines. In conclusion it should not be unwise to draw preliminary conclusion that magnesium levels should have helped better understanding molecular insight and consequences in both pre-diabetic and diabetic cats. If necessary, as evidenced by hypomagnesemia also at this study, dietary supplementation should be considered.

Keywords: Diabetes mellitus, feline, hypomagnesemia, insulin

INTRODUCTION

Diabetes is in general practice, frequently been detected among cats even if clinical signs are existed (O'Neill et al., 2016). Diagnostic criteria for prediabetic status among cats have not been explored. On the other hand, as aforementioned previously (Gottlieb and Rand, 2018) hence, there are no longitudinal research searching for nondiabetic cats with elevated glucose concentrations, cats experiencing diabetic remission through lightly elevated glucose levels (7.5 to <9 mmol/L or >135 to <162 mg/dL) are under high risk of switching to diabetes within 270 days (Gottlieb et al., 2015). Thus, so far detection of probable prediabetic and subclinical diabetic conditions among cats should be of beneficial for suitable measurements for delaying/preventing clinical diabetes (Gottlieb and Rand, 2018). For better understanding of readers Table 1 showed useful glossary for feline diabetes, adopted from well-reviewed literature data by Gottlieb and Rand (2018).

To the best of the current authors' knowledge, there has been no documented scientific investigation conducted thus far that has examined and compared the occurrence and prevalence of hypomagnesemia among healthy cats, as well as those with diabetes and pre-diabetes. For this purpose, we aimed to determine the serum magnesium (Mg) levels among pre-diabetic and diabetic cats.

How to cite this article
Ural, K., Erdoğan, S., Erdoğan, H. (2023). Sonorous plunge of serum magnesium levels among pre-diabetic and diabetic cats. *Journal of Advances in VetBio Science and Techniques*, *8*(3), 191-195. https://doi.org/10.31797/vetbio.1295598

Table 1. Useful glossary for feline diabetes. Adopted from well-reviewed literature data by Gottlieb and Rand (2018).

Factors	Glucose levels	Caution
Fasted blood glucose concentration*	~3.0–6.5 mmol/L (117 mg/dL)	By use of portable glucose meter (calibrated for feline blood)
Monitorization of blood glucose	Upper limit for cut point of 166 mg/dL (9.2 mmol/L),	Denoting probable influence of stress on diagnosing diabetes among cats (Reeve-Johnson et al., 2012)
Acute stress	-	-
Struggling	Might be responsible for elevated glucose levels on average by 74 mg/dL (4.1 mmol/L) and up to 195 mg/dL (10.8 mmol/L) even in 10 minutes	Due to elevated lactate and norepinephrine concentrations (Rand et al., 2002)
Cats ≥8 years of age	Presenting an initial blood glucose >117 mg/dL (6.5 mmol/L) should be subjected to retesting 4 hours later	If not <117 mg/dL (6.5 mmol/L) could thus be subjected to retesting after 24 hours (Gootlieb and Rand, 2018; Rand et al., 2002)

*Withdrawal of food for 18–24 hours (Gootlieb et al., 2015; Reeve-Johnson et al., 2013).

MATERIALS AND METHODS

Animals

A total of 20 cats from different breeds, ages, and both genders were enrolled. The diseased cats, comprising the subjects of this research, were chosen from among those presenting at the small animal clinics of the faculty that had received a routine diagnosis of diabetes. In contrast, the healthy cats were selected from individuals brought to the clinic for general health check-up or vaccination, having been deemed healthy based on clinical and laboratory assessments. Written consent was obtained from the owners of both the afflicted and healthy group animals for their participation in the study.

Classification to groups were healthy cats (n=10) and diseased cats with pre-diabetes (n=8) and diabetes mellitus (n=10). Inclusion criteria was partially shown in Table 1. Whether if blood glucose was >9.8 mmol/L, the cat was diagnosed as diabetic. Whether if blood glucose was between 6.5 to 9.8 mmol/L the case was considered pre-diabetic (Reeve-Johnson et al., 2016). Exclusion criteria includes diabetic ketoacidosis, thyroidal illness, renal failure or liver failure that may have interfere with blood glucose levels.

Laboratory analysis

Following an 18/24-h fast, sera samples were withdrawn gently from either ear/paw for blood glucose measurement via a portable glucose meter.

Magnesium levels were measured using the xylidyl blue colorimetric method in an autoanalyzer (Randox Daytona Plus®, Randox Laboratories Ltd, UK), utilizing serum samples obtained after blood collection.

Statistical analysis

Descriptive statistics were conducted on the levels of magnesium in healthy, pre-diabetic, and diabetic cats, and the data were presented in the form of mean and standard error. For comparisons between groups, the non-parametric test technique Kruskal-Wallis-H was used. Dunn's test were used for post hoc comparisons. Cases where the obtained p-values were less than 0.05 were considered statistically significant. All analyses were performed using the GraphPad Prism® 9.5.1 software (GraphPad Software Inc., San Diego, CA, USA).

RESULTS

All cats enrolled herein (at pre-diabetes group) existed a pre-diabetic state with a fairly elevated blood glucose levels, reaching up to 200 mg/dL

(11 mmol/L), but show no symptoms of the disease. All of them were not requiring an insulin supportive therapy, whether we suggested modification of nutrition [i.e. low carbohydrate diet (17%), low glycemic home prepared functional foods with lifestyle changes.

Magnesium levels in prediabetic and healthy cats did not change statistically, but they were shown to be substantially different in diabetic cats. Also, it was shown that diabetic cats had much lower Mg levels than non-diabetic cats, as shown in Table 2 and Figure 1 below.

Tablo 2. Mean Mg (mg/dL) concentrations among cats enrolled at this study

Parameter	Healthy cats (n=10)	Pre-diabetic cats (n=8)	Diabetic cats (n=10)
Mg (mg/dL)	2.11±0.15[a]	1.73±0.13[a]	0.90±0.16[b]
P value	0.002		

[a-b]: Values indicated by different letters on the same line are statistically significantly different.

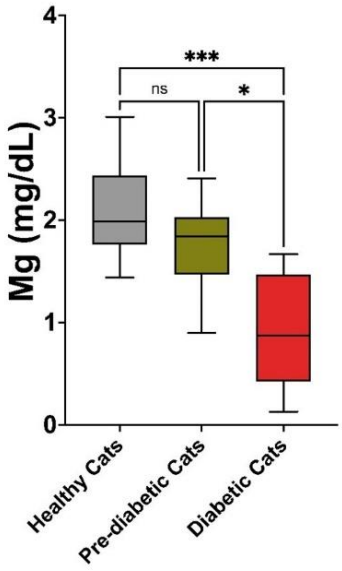

Figure 1. Boxplot analytes of magnesium median (min-max.) Mg (mg/dL) levels among healthy, pre-diabetic and diabetic cats. ns: Non-significant, *: p<0.05, ***: p<0.01.

DISCUSSION

In this study, we aimed to determine the serum Mg levels of pre-diabetic and diabetic cats. In this context we observed that the levels of magnesium in diabetic cats were less than those observed in both healthy and prediabetic cats. Beginning with 1940s, it has been well recognized that type 2 diabetes mellitus has been related to hypomagnesemia (Martin and Wertman, 1947; Pham et al., 2007). Diminished serum magnesium (Mg^{2+}) levels in relationship with type 2 diabetes mellitus in cohort studies have been explored (Chaudhary et al., 2010). In human being type 2 diabetes mellitus, the prevalence of hypomagnesemia varied between 14 and 48% in comparison to 2.5-15% detected among healthy controls (Pham et al., 2007). To the present authors knowledge herein, there has been no reported research detecting the incidence/prevalence of hypomagnesemia in diabetic, pre-diabetic and healthy cats in comparison up to date. The results that we obtained at this study, therefore, would highlight this era of endocrinology. On the other hand, a previous study reported magnesium status in cats with diabetes mellitus (n=21) and diabetic ketoacidosis (n=7), in comparison to 12 healthy cats (controls), 21 cats with DM, and 7 cats with DKA. Cats with diabetes mellitus (n=2 vs 13) and diabetic ketoacidosis (n=1 vs. 4) presented serum total Mg and ionized Mg lower than the reference ranges, in which in which hypomagnesemia was reported as a common finding (Norris et al., 1999). In the present study considering available results mean Mg (mg/dL) values among healthy cats vs. pre-diabetic and diabetic cats were 2.11, 1.73 and 0.90, respectively. Furthermore, diabetic cats presented statistically lower Mg values in contrast to both pre-diabetic and healthy control cats, (p=0.0002) (Figure 1 and Table 2).

Hypomagnesemia in relationship with a severely quick, diminishing renal function in type 2 diabetes mellitus patients (Pham et al., 2005), through a contrary correlation among oral Mg^{2+} intake and diabetes mellitus risk (Dong et al., 2011). Mg^{2+} supplementation on glucose metabolism and insulin sensitivity (Guerrero-

Romero and Rodríguez-Morán, 2014; Guerrero-Romero et al., 2015; Rodríguez-Morán and Guerrero-Romero, 2003) has been well reported.

Given endocrine/metabolic disease conditions in relationship with Mg deficiency, diabetes mellitus is quite common. Several research dedicated that mean plasma concentrations are diminished both in type 1 and type 2 diabetes in comparison to nondiabetic controls along with marked negative correlations between Mg and fasting plasma glucose (Kim et al., 2010; Sales and Pedrosa, 2006). Several different causes of hypomagnesemia among diabetics comprised i) dietary intake of low magnesium (Schulze et al., 2007), ii) osmotic diuresis related to elevated renal excretion of magnesium, iii) imperceptive relation with insulin influencing intracellular magnesium transportation and thereof resulting with elevated extracellular Mg loss (Paolisso et al., 1986), iv) uncontrollable usage of loop/thiazide diuretics resulting with Mg wasting, v) diabetic autonomic neuropathies (Pham et al., 2007) and diminished tubular reabsorption because of insulin resistance (Barbagallo and Dominguez, 2007). Herein at the present study we did not investigate underlying etiology, other than diabetes control, however there were no usage of diuretics, nor osmotic diuresis. Although we did not evaluate low dietary intake of Mg, as all cats were fed with different commercially available foods, enabling us to investigate such kind of variety, this might be a causing factor especially among pre-diabetic cats herein involved. On the other hand, probable insulin resistance might participate as a co-factor among both diabetic and pre-diabetic cats herein comprised.

CONCLUSION

In conclusion, taking into account data obtained at this research, it should not be unwise to draw preliminary conclusion that magnesium levels should have helped better understanding molecular insight and consequences in both pre-diabetic and diabetic cats. This is because Mg has a pivotal role for utilization and transportation of carbohydrates whereas if necessary, as evidenced by hypomagnesemia also at this study, dietary supplementation should be considered.

ACKNOWLEDGMENT

Financial support: No financial assistance or grant was received for this study.

Conflict of interest: The authors declare that they have no potential conflict of interest with respect to the authorship and/or publication of this article.

Ethical statement: In the Regulation on the Working Procedure and Principles of the Animal Experiments Ethics Committee published in the newspaper numbered 28914 dated 15.02.2014, in the second clause's sub-clause b, it is clearly stated that there is no need for ethics committee approval for non-experimental clinical veterinary practices. In this study, since a commercial product presented as a feed additive and not considered as a drug was used both for health and for the control of the disease picture, and additionally, an informed owner consent form was obtained, there was no need for ethics committee approval.

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