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Effect of Experimental Diabetes Mellitus on Plasma Lactate Dehydrogenase and Glutamic Oxaloacetic Transaminase Levels in Rabbits*

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Abstract: Hyperglycemia was induced in 20 male, white, New Zealand rabbits (2-3 kg) (Oryctolagus cuniculus huxley) by alloxan (100 mg/kg body weight, I.V.) and maintained for 16 weeks without insulin treatment. Blood samples were taken from both diabetic and non-diabetic rabbits at the same time for measurement of plasma enzymes. Levels of glutamic oxalacetic transaminase (GOT) and lactate dehydrogenase (LDH) were determined after treatment. The levels of LDH and GOT were 155.6 ± 41.9 U/L and 47.0 ± 20.4 U/L in the control group respectively. These parameters were 286.9 ± 142.9 U/L and 93.9 ± 62.5 U/L in the diabetic group respectively. It was observed that LDH ($p < 0.05$) was significantly increased, whereas GOT was not significantly increased ($p > 0.05$) in the diabetic group. In conclusion, we agree that routine use of LDH measurement to monitor diabetic status may be useful, but the characteristic parameters of diabetes mellitus are better indicators.

Key Words: Diabetes mellitus, LDH, GOT, Rabbit

Tavşanlarda Deneysel Diyabetin Plazma Laktat Dehidrogenaz ve Glutamik Oksalasetik Transaminaz Enzim Düzeylerine Etkisi

Özet: Bu çalışmada, diabet 20 erkek, beyaz, Yeni Zelanda ırkı tavşan (Oryctolagus cuniculus huxley) alloxan verilerek (100 mg/kg vucut i.v.) oluşturuldu ve insulin tedavisi yapılmaksızın 16 hafta bekletildi. Plazma enzimlerini ölçümü için kan örnekleri hem diabetik hemde kontrol grublarından alındı. Muameleden sonra laktat dehidrogenaz (LDH) ve glutamik oksalasetik transaminaz (GOT) seviyeleri belirlendi. LDH ve GOT seviyeleri sırasıyla, kontrol grubunda 155,6 ± 41,9 U/L ve 47,0 ± 20,4 U/L iken, diabetli grubunda 286,9 ± 142,9 U/L ve 93,9 ± 62,5 U/L idi. Yapılan istatistiki analiz sonucu, diabetli, plazma LDH değerinin önemli oranda ($p < 0,05$) yükseldiği ancak GOT yüksekliğinin önemsiz olduğu ($p > 0,05$) görüldü. Sonuç olarak, LDH diabetes mellitus için bir indikatör olabilirler ancak, diabetes mellitus'un mevcut karakteristik paremetreleri daha iyi birer indikatördürler.

Anahtar Sözcükler: Diabetes mellitus, LDH, GOT, Tavşan

Introduction

Diabetes mellitus is known in dogs, cats, rats and mice and probably occurs in most mammals, although it is only likely to be diagnosed in laboratory animals (1). The disease is accepted to be the commonest endocrine disease, which are multi-systemic disorders resulting from deficiency in the secretion or action of the pancreatic hormone insulin, which in turn produces profound abnormalities of metabolism (2). On the basis of a case history, the clinical and paraclinical manifestation of diabetes mellitus are reviewed.

Since muscle and liver dysfunction is frequently associated with diabetes mellitus, many clinical reports have indicated that serum enzyme activities derived from the muscle and liver such as creatine phosphokinase (CPK), LDH and GOT are elevated.

The levels of enzyme increased in diabetes mellitus is a metabolic result already treatable with pancreas hormones. Before the availability of sensitive pancreas hormone analysis, increased serum or plasma enzyme levels were considered important evidence supporting the diagnosis of diabetes mellitus (1).

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In widespread enzyme screening programs, although a number of studies have been carried out in patients with hyperglycemia comparing serum enzyme levels (3-21), the results are mostly conflicting.

In spite of the reason explained above, there is still great contradiction between results. Therefore, the purpose of this study was to assess the predictive value of LDH and GOT in discriminating between rabbits with experimental diabetes mellitus and control rabbits.

Materials and Methods

Subjects: Twenty male New Zealand rabbits (2-3 kg in weight) from the serum animal farm were used. The animals were fed a diet of rabbit pellets and water ad libitum.

Induction of experimental diabetes in rabbits: Hyperglycemia was produced by iv administration of alloxan (100 mg/kg body weight) in 16 h fasting rabbits. After 72 h of alloxan administration, fasting blood glucose was measured. The rabbits were not treated with insulin and the animals with fasting blood glucose ≥ 250 mg/dl were considered diabetic. Four months after administration of alloxan monohydrate, blood samples were obtained from a cardiac puncture for the determination of plasma glucose, LDH and GOT. Five milliliters of blood were drawn immediately into ice-chilled siliconized disposable glass tubes contained EDTA (1 mg/ml). The plasma samples were obtained by centrifuging blood samples at 3000 rpm for 30 minutes at 4 °C. The measurement of enzymes and glucose levels was carried out in these plasma samples.

Measurement of Enzyme: Plasma enzyme levels were measured by autoanalyzer (Hitachi 705, Japan) using commercial kits.

Analysis of Data: All data were expressed as mean ± standard deviation (SD). For statistical analysis the SPSS/PC+ package (SPSS/PC+, Chicago, IL, USA) was used. For all parameters, means and SE were calculated according to the standard methods. The Mann-Whitney U test was used to test for differences between means of the treatments and the control rabbits. The significance level was $p = 0.05$ for all tests.

Result

The body weights and plasma glucose concentrations of each group are shown in Table 1. and Figure 1. Hyperglycemia in experimental group confirmed by blood glucose concentration (BGC) was significantly higher than that in the control group ($p < 0.001$). The body weights of each group did not change significantly during the study.

LDH and GOT data are given in Table 2. and Figure 2. An increase in LDH was observed in the diabetic group, but GOT was slightly higher in the diabetic group than in the control group.

Discussion

This study showed that glucose and LDH were significantly higher. As for GOT, no significant differences existed between the levels in rabbits with diabetes mellitus compared with control rabbits. Correlation analysis showed that LDH is correlated with BGC. According to these results, it may be speculated that LDH provides additional information about diabetes mellitus. We also found that high BGC, a multi-systemic disorder resulting from deficiency in the secretion or action of the pancreatic hormone insulin, is a better indicator of diabetes mellitus than plasma enzyme. These findings are

Table 1. Physical and physiological characteristics of the rabbits (Mean ± SD).

	Control $\bar{X} \pm \bar{x}$	Diabetic $\bar{X} \pm \bar{x}$	P
N	10	10	--
Body weight (g)	2425 ± 125	2385 ± 113	ns
Plasma glucose (mg/dl)	89.6 ± 7.4	404 ± 79.3	< 0.001

ns: not significant

Table 2. LDH and GOT levels (Mean ± SD).

	Control $\bar{X} \pm \bar{x}$	Diabetic $\bar{X} \pm \bar{x}$	P
LDH U/L	155.6 ± 41.9	286.9 ± 142.0	<0.05
GOT U/L	47.0 ± 20.4	93.9 ± 62.5	ns

ns: not significant

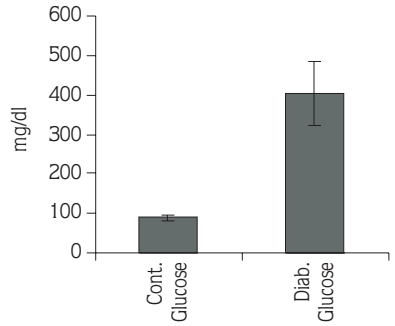

Figure 1. Glucose in Control and Diabetic Rabbits.

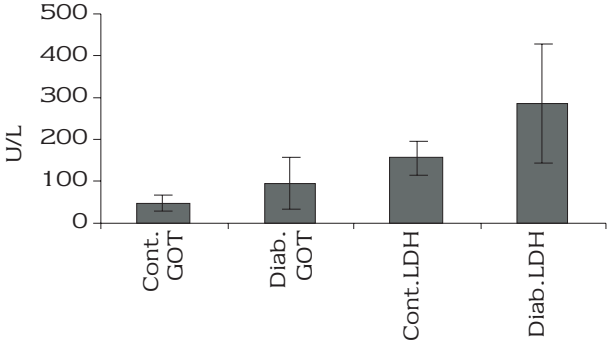

Figure 2. Enzymes in Control and Diabetic Rabbits.

in accordance with and in contradiction with other studies in which the subjects were generally human.

The results of the present study indicated that plasma LDH levels in rabbits with diabetes mellitus were significantly higher when compared with the controls. To date, no study examining plasma enzyme in diabetes mellitus has been reported in rabbits. Therefore, we were not able to compare our results with others. Although a number of studies about LDH and GOT levels in diabetes mellitus have been carried out, the results are mostly in conflict. Oliver et al. (3), Tanaka et al. (9) and Margiavichene et al. (12) did not observe any increases in LDH between diabetes and controls; consequently their results are not in accordance with ours. Melinkeri et al. (5), Awaji et al. (6), Nikolaeva et al. (8), Jones et al. (10), Cheshchevik (13), Zappacosta et al. (14) and Goldberg et al. (20) indicated that LDH levels were higher in patients with diabetes mellitus than those in normal subjects. Consequently, these reports are in accordance with our findings. On the other hand, Cai (7) and Ryder et al. (11) observed decreases in LDH in diabetic subjects. These results are in contradiction with our findings and those of other studies. In addition, Fernandez et al. (15) indicated that the level of GOT did not change in diabetes mellitus compared with normal subjects. Consequently, their report is in accordance with ours. Tanaka et al. (9), Jones et al. (10), Piyachaturawat et al. (16), Nanbara et al. (17), Rao et al. (18), Henderson et al. (19), Goldberg et al. (20) and Awadallah and El-Dessoukey (21) indicated that GOT levels were higher in diabetes mellitus than those of normal subjects, but Awaji et al. (6) observed decreases in GOT between diabetes and controls. Consequently, their report is in contradiction with ours. These controversial data may be due to using different animals as study subjects or different experimental treatment.

Even though several theories have been proposed to explain these differences, the mechanism of enzymes are not well understood. Some investigators have suggested that the increase in enzymes levels in patients with diabetes mellitus resulted from the influence of insulin on liver and muscle tissue (2). The other possibilities include malnutrition, hepatic anoxia and infection in diabetes mellitus. However, the enzyme released from other organs may contribute to the change in levels in enzyme. Our results indicating the fact that plasma LDH levels were significantly higher in diabetic rabbits than those in the control group support these possibilities.

In conclusion, the present study demonstrated that the serum enzymes levels were elevated in alloxan-induced diabetic rabbits compared with the control values. Our results also showed that GOT did not increase significantly in hyperglycemic animals ($p > 0.05$). However, this study indicated that further experiments should be performed to investigate what is responsible for the elevation of enzymes in muscle and liver. This test may be used in forensic study if more studies confirm our findings, because of the unstability of serum enzyme. Such a test could also be of value in population studies, and it would be of interest to understand the molecular basis of refractoriness of hyperglycemia.

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