Letter to the Editor

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High-fat diet and low-dose streptozotocin induced type 2 diabetes: a methodological critique

DEAR EDITOR,

The high-fat diet (HFD)- fed, streptozotocin (STZ)- treated rat model is one of the experimentally-induced animal models of diabetes. This model is often used to evaluate the antidiabetic activity of several agents. According to Srinivasan et al., prolonged exposure of high-fat diet leads to insulin resistance, and the development of diabetes occurs only in insulin-resistant HFD-fed rats following low dose STZ, because the HFD-fed rats are already mildly hyperglycemic due to insulin resistance [1].

In HFD/STZ model, the rats are fed with high-fat diet for 2-4 weeks or for a relatively long time (≥ 3 months) in order to simulate the insulin resistance and/or glucose intolerance. After induction of diabetes with multiple or single low-dose of STZ (30- 35 mg/kg), some of the diabetic rats receive treatment [2]. In this way, the impact of treatment can be determined by comparing the differences between groups. In this experimental model, all rats should be allowed to continue to feed on their respective diets until the end of the study. Diabetic rats should be fed the HFD throughout the study. However, there is a lack of methodological information concerning the feeding time in some recently published studies [3,4].

In our experience, we observed changes in some parameters after switching the HFD to normal pellet diet (NPD) in the diabetic rats. The feeding of NPD for 4 weeks significantly decreased FBG in diabetic rats compared to HFD-fed diabetic rats (234.40 ± 42.71 mg/dl vs. 464.00 ± 23.88 mg/dl, $p < 0.05$). Although diet regulation could not restore normal blood glucose, such a decrease was unexpected. In addition, the body weights of the NPD-fed diabetic rats were significantly lower than the body weights of the HFD- fed diabetic rats (249 ± 6.00 g vs. 288.00 ± 4.41 g, $p < 0.05$). There was no significant difference in body weight between nondiabetic control rats and diabetic rats fed NPD for 4 weeks. Further details can be found in Table 1.

Diet regulation and weight loss may prevent, control and reverse diabetes. However, at later stages of the disease, it is difficult to improve blood glucose control without medication, because the disease progresses from insulin resistance to insulin deficiency [5]. According to some diabetes researchers, the amount of residual functional beta-cells mass is an important issue, and another important question is whether HFD/STZ rat mimics an early or late stage of type 2 diabetes [6]. These preliminary findings suggest the possibility that HFD/STZ rat model may simulate the characteristics of early stage more than the final stage of type 2 diabetes, and hyperglicemia in the experimental model can partially reverse with diet regulation.

Table 1. Effects of diet changes on HFD/STZ induced diabetes in rats

	Initial values	After induction of diabetes (3rd week)	After NPD/ HFD (7th week)
Fasting Blood Glucose (mg/dl)			
C	67.00±1.51	72.40±2.60	74.20±3.10
D+NPD	74.00±2.50	344.60±26.19*	234.40±42.71*
D+HFD	78.00±4.72	377.40±18.50*	464.00±23.88*#
Body weight (g)			
C	220.00±4.47	228.00±4.63	231.00±4.84
D+NPD	220.00±5.14	255.00±2.73*	249.00±6.00
D+HFD	230.00±4.30	260.00±4.47*	288.00±4.41*#

C: control rats, D+NPD: diabetic rats fed NPD after induction of diabetes, D+HFD: diabetic rats fed HFD after induction of diabetes.
*different from C ($p<0.05$);
different from D+NPD ($p<0.05$).
Diabetes was induced by a HFD (2 weeks) combined with low dose streptozotocin (35 mg/kg) injection. Values are means ± S.E.M., n=5 in each group. Statistical significance was determined using one- way ANOVA followed by Tukey's test.

Zeynep Ozturk
Izmir Ataturk Training and Research Hospital, Clinical Pharmacology and Toxicology, Izmir, Turkey.

Address for correspondence:
Zeynep Ozturk,
Izmir Ataturk Training and Research Hospital, Clinical Pharmacology and Toxicology, Izmir, Turkey.
dr.zeyneb@hotmail.com

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REFERENCES

1. Srinivasan K, Viswanad B, Asrat L, Kaul CL, Ramarao P. Combination of high-fat diet-fed and low-dose streptozotocin-treated rat: a model for type 2 diabetes and pharmacological screening. Pharmacol Res 2005; 52:313-320.
2. Ozturk Z, Gurpinar T, Vural K, Boyacioglu S, Korkmaz M, Var A. Effects of selenium on endothelial dysfunction and metabolic profile in low dose streptozotocin induced diabetic rats fed a high fat diet. Biotech Histochem 2015; 90:506-515.
3. Soliman A. Potential impact of Paracentrotus lividus extract on diabetic rat models induced by high fat diet/streptozotocin. The Journal of Basic & Applied Zoology 2016;77:8-20.
4. Stalin A, Irudayaraj SS, Gandhi GR, Balakrishna K, Ignacimuthu S, Al-Dhabi NA. Hypoglycemic activity of 6-bromoembelin and vilangin in high-fat diet fed-streptozotocin-induced type 2 diabetic rats and molecular docking studies. Life Sci. 2016; 153: 100-117.
5. Franz MJ. The dilemma of weight loss in diabetes. Diabetes Spectr 2007; 20:133-136.
6. Skovsø S. Modeling type 2 diabetes in rats using high fat diet and streptozotocin. J Diabetes Invest 2014; 5:349-358.

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