OPEN ACCESS

GAVIN PUBLISHERS

Journal of Diabetes and Treatment

Cheng KC, et al. J Diabetes Treat: JDBT-146.

Editorial

DOI: 10.29011/ 2574-7568. 000046

Limitations of Oral Glucose Tolerance Test in Animal Studies

Kai-Chun Cheng[1], Yingxiao Li[1,2], Juei-Tang Cheng[2,3*]

[1]Department of Psychosomatic Internal Medicine, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan

[2]Department of Medical Research, Chi-Mei Medical Center, Yong Kang, Tainan Taiwan

[3]Institute of Medical Science, College of Health Science, Chang Jung Christian University, Guei-Ren, Tainan, Taiwan

[*]**Corresponding author:** Juei-Tang Cheng, Institute of Medical Sciences, Chang Jung Christian University, Gueiren, Tainan City, Taiwan. Tel: +88662517864; Fax: +88662832639; Email: jtcheng@mail.cjcu.edu.tw

Citation: Cheng KC, Li Y, Cheng JT (2018) Limitations of Oral Glucose Tolerance Test in Animal Studies. J Diabetes Treat: JDBT-146. DOI: 10.29011/ 2574-7568. 000046

Received Date: 26 February, 2018; **Accepted Date:** 22 March, 2018; **Published Date:** 30 March, 2018

Abstract

Oral Glucose Tolerance Test (OGTT) is widely used in basic research. But, limitation(s) of OGTT in animal studies were not conducted. In the current report, six limitations involved in OGTT were discussed. It could be the reference for one who is interested in animal research using OGTT.

Introduction

Oral Glucose Tolerance Test (OGTT) is widely used in clinics to diagnose for the Impaired Glucose Tolerance (IGT) and/or type-2 DM (T2DM) [1]. Recently, the risk of transient postprandial hypoglycemia in patients with Non-Alcoholic Fatty Liver Disease (NAFLD) has also been identified using OGTT [2]. Moreover, non-alcoholic steatohepatitis (NASH) linked with T2DM has been focused, because a high prevalence of NASH (56.49%) observed in patients with T2DM with duration of more than 5 years [3]. Therefore, application of OGTT for diagnosis of NAFLD or NASH without overt T2DM is also performed in clinical practice.

In basic research, OGTT is also used in animal studies focusing on glucose homeostasis in main. Insulin Resistance (IR) or insulin sensitivity has ever been characterized in animals using the data named glucose-insulin index obtaining from OGTT [4]. Additionally, OGTT has also been used as a model to mimic the postprandial state of hyperglycemia, which may provide information on the glucose-lowering effect as a consequence of changes in glucose utilization [5]. Generally, OGTT or meal tolerance test mimics the glucose and insulin dynamics under physiological conditions more closely than glucose clamp or insulin sensitivity test in animal studies. The postprandial rise in plasma insulin enables appropriate disposal of blood glucose in the absorptive state, while the fall in plasma insulin contributes to keeping the glucose homeostasis in the post-absorptive state and during the starvation. Therefore, it is not suitable to ignore the blood insulin level, which indicated the ability of pancreatic β-cells in response to plasma glucose. Moreover, some limitations for application of OGTT in animal studies shall be concerned.

First, results are easily affected by many physiological and environmental factors in addition to the pathological conditions. Therefore, an adequate experience of the test is important to avoid the bias in animal studies of OGTT. Next, anesthesia is another factor that may influence the data of OGTT, such as isoflurane has been documented to inhibit OGTT [6].

In addition to the dynamic response of β cells, many factors are known to involve in the response of OGTT including the total Glucagon-Like Peptide 1 (GLP-1), Glucose-Dependent Insulinotropic Polypeptide (GIP), and pancreatic polypeptide. Thus, application of OGTT in the understanding of impaired glucose tolerance in animals is useful, but it seems still limited in the study of glucose utilization in T2DM without another indicator(s).

The 4th limitation is that diabetic disorders are known to be progressive [7] in addition to the variations between rodents and human subjects [8]. Impaired glucose tolerance is mostly reflected in a larger incremental Area Under the Curve (AUC) of the plasma glucose disappearance curve during OGTT. Results in OGTT showed a marked increase in AUC0-120 min from the diabetic group indicating the success of the diabetic model. Then,

diabetic animals were used to treat with the test substance, either herbal extract or nutrient. Once the slope of the glucose disposal phase is markedly increased and AUC is more decreased than the vehicle-treated control, it means that the test substance has an ability to alleviate the impaired glucose tolerance. However, researcher(s) did not concern the differences between patients and diabetic animals. Then, the obtained results are not easy to link with clinical applications.

Interestingly, a test substance usually induced the attenuation of AUC from OGTT in animal studies when it has the ability to enhance glucose utilization [9]. However, results from a marked reduction in AUC only using OGTT are not enough to support the conclusion indicating increased glucose utilization as the action mechanism for test substance because the α-glucosidase inhibitor-like action may result in the same changes [10]. Therefore, more studies are basically required, such as insulin-tolerance test, glucose uptake, glycolysis and others [11].

Finally, the basal glucose level in each group that received treatment with test substance was not the same during OGTT. Similarly, the basal glucose level is also significantly varied in mutant mice from the wild-type littermates [12]. It can be criticized that glucose tolerance is changed due to the difference in basal glucose level. Correction of the data in basal glucose level has been suggested [12]. But no paper ignored the values of basal glucose level in OGTT during the calculation of AUC. Therefore, scientific evidence for the important role of basal glucose level showing at the 0 min during OGTT is required.

Conclusion

Taken together, OGTT applied in the clinic is also useful in animal studies while the diagnosis of diseases is not included in the basic research. The impaired glucose tolerance in animals is the main target used in basic studies. However, many limitations observed in the application of OGTT in animal studies. We indicate six factors as potential limitations as a reference in the current report.

References

1. Adam JM, Josten D (2008) Isolated post-challenge hyperglycemia: concept and clinical significance. Acta Med Indones 40: 171-175.
2. Morio R, Hyogo H, Hatooka M, Morio K, Kan H, et al. (2017) The risk of transient postprandial oxyhypoglycemia in nonalcoholic fatty liver disease. J Gastroenterol 52: 253-262.
3. Seetlani NK, Memon AR, Tanveer S, Ali A, Ali P, et al. (2016) Frequency of Non-Alcoholic Steatohepatitis on Histopathology in Patients of Type 2 Diabetes Mellitus with Duration of More than 5 Years. J Coll Physicians Surg Pak 26: 643-646.
4. Peth JA, Kinnick TR, Youngblood EB, Tritschler HJ, Henriksen EJ (2000) Effects of a unique conjugate of alpha-lipoic acid and gamma-linolenic acid on insulin action in obese Zucker rats. Am J Physiol Regul Integr Comp Physiol 278: R453-459.
5. Lefebvre PJ, Scheen AJ (1998) The postprandial state and risk of cardiovascular disease. Diabet Med 15: S63-S68.
6. Tanaka K, Kawano T, Tomino T, Kawano H, Okada T, et al. (2009) Mechanisms of impaired glucose tolerance and insulin secretion during Isoflurane anesthesia. Anesthesiology 111: 1044-1051.
7. Vandamme TF (2015) Rodent models for human diseases. Europ J Pharmacol 759: 84-89.
8. Chandrasekera PC, Pippin JJ (2013) Of Rodents and Men: Species-Specific Glucose Regulation and Type 2 Diabetes Research. ALTEX 31: 157-176.
9. Song P, Kim JH, Ghim J, Yoon JH, Lee A, et al. (2013) Emodin Regulates Glucose Utilization by Activating AMP-activated Protein Kinase. J Biol Chem 288: 5732-5742.
10. Priya CL, Bhaskara Rao KV (2016) Postprandial Antihyperglycemic And Antioxidant Activities of Acalypha indica Linn Stem Extract: An In-vivo Study. Pharmacogn Mag 12: S475-S481.
11. Chen A, Brar B, Choi CS, Rousso D, Vaughan J, et al. (2006) Urocortin 2 modulates glucose utilization and insulin sensitivity in skeletal muscle. Proc Natl Acad Sci U S A 103: 16580-16585.
12. Siegelaar SE, Holleman F, Hoekstra JBL, J. Hans DeVries JH (2010) Glucose Variability; Does It Matter? End Rev 31: 171-182.