

Editorial

## Nutritional Therapy and Glycemic Variability among People with Diabetes

Refaat A Hegazi<sup>\*1</sup>, Rachel A Johnson<sup>1</sup>, Amy A Devitt<sup>1</sup>

<sup>1</sup>Abbott Nutrition Research & Development.

*\*Corresponding author: Dr. Refaat A. Hegazi, Medical Director, Adult Nutrition, Research and Development, Abbott Nutrition, Affiliate Research Associate Professor, Department of Internal Medicine, The Brody School of Medicine - East Carolina University, NC, 3300 Stelzer Rd, Columbus, OH 43219, Tel: 614-624-7811; Fax: 614-727-7811; Mob: 614-208-9389; Email: Refaat.Hegazi@abbott.com*

Received: 08-01-2014

Accepted: 08-04-2014

Published: 08-08-2014

Copyright: © 2014 Hegazi

Glycemic variability (GV) represents the acute fluctuation of blood glucose levels from peak to nadir. Over the last decade, GV has increasingly become part of the dialogue surrounding glycemic control, as evidenced by the growing number of articles published on this topic over the past few years. Zaccardi and colleagues[9] have proposed that the risk of complications among people with diabetes (PWD) may actually be based on a foundation of four factors: GV, fasting plasma glucose, postprandial glucose, and hemoglobin A1c levels.

Despite the majority is overweight or obese, hospitalized PWD are commonly malnourished. A recent multicenter study of 35 Spanish hospitals, malnutrition was assessed using the mini-nutritional assessment (MNA) tool. The study included 1,090 hospitalized subjects DM with an average age of 78 ( $\pm$  7.1 years). The study showed that 39.1% had risk of malnutrition, and 21.2% of the study subjects had malnutrition[7]. Similarly, a prospective study of 146 consecutive diabetic patients admitted to geriatric service showed that malnutrition is highly prevalent[8].

Enteral or parenteral nutrition therapy is an effective intervention to fulfill the nutritional needs of malnourished hospitalized patients who cannot meet these needs orally. Whether these nutritional interventions could exert an effect on GV in hospitalized PWD is an interesting topic. In this article, we review the available literature of the association of nutritional interventions and GV among PWD and highlight the effects of the type of feeding route as well as the type of feeding formula on GV.

GV has been associated with poor outcome among critically ill patients. However, this association has not been observed among parenteral nutrition (PN) fed patients. In 2008, Krinsley et al. showed that GV is an

independent risk factor for mortality in critically ill patients. In this retrospective study, the authors correlated GV with mortality in 3,252 ICU patients[3]. The study showed that mortality was 12.1% in patients with the lowest GV vs 37.8% in patients with the highest GV. The authors concluded that GV conferred an independent risk for mortality in critically ill patients. Measures to lower GV may have a positive impact on mortality as well as length of intensive care unit (ICU) stay. Interestingly, a recent study showed that GV in PN-fed PWD was not associated with increased mortality[2]. This study included 276 hospitalized medical and surgical patients on PN, nineteen percent of whom had a history of diabetes and 74% were in the ICU. Patients with a known history of diabetes had higher GV compared to those without diabetes. The association of mortality and GV was only significant for patients without a history of diabetes ( $p = 0.02$ ) and no significant association was seen in those with diabetes ( $p = 0.32$ ). This was suggested to result from the fact that PWD were accustomed to fluctuations in GV, unlike those without the disease. This study does not; however address questions of how differing routes or types of nutrition support affect the clinical impact of GV among PWD.

In enterally fed patients, studies have shown that the type of feeding formula could lessen the extent of GV. For instance, the continuous glucose responses of tube-fed PWD who consumed either diabetes specific formula (DSF) or standard nutrition formula (SNF) as sole-source nutrition were compared [1] This was an open label, 2-group, and crossover study of 12 long term care subjects with type 2 diabetes. Subjects were administered feeding formula for 16 hours a day for 5 days via a tube and blood glucose was measured using continuous glucose monitoring. Results demonstrated that as compared to the SNF, the DSF formula resulted in lower GV, There were significantly

more glucose measurements in the target range of 70-180mg/dL and less measure over 200 mg/dl during continuous administration with DSF compared with SNF. A significant reduction in the amount of short-acting insulin administered to subjects when fed DSF compared to SNF was also reported.

Mori and colleagues [4] found similar results in which patients tube fed a DSF experienced significantly less GV than patients fed SNF. Mori and colleagues [6] conducted 3 month follow up to assess the impact of a DSF formula on long term glucose control on subjects requiring insulin therapy. Subjects were continued on a DSF and after 3 months, glucose levels were monitored for 2 consecutive days using continuous glucose monitoring. After 3 months, compared to the feeding period with a standard formula, various measures for GV were significantly improved. Similarly, portion of time spent in hyperglycemia (>180 mg/dl), A1c values and insulin requirement were also significantly decreased when compared to the feeding period with the SNF product. The same group [5] conducted a three-period crossover study of 14 elderly patients with type 2 diabetes assessed GV feeding a DSF containing low-carbohydrate/high-monounsaturated fatty acid liquid diet and an isoleucine containing liquid diet (ICD) against SNF. Overall, GV was improved with the DSF formula compared to both the ICD and SNF formulas. This work strongly supports the finding that during tube feeding the amount and type of carbohydrate provided has significant impact on a patient's GV.

Collectively, the effect of nutritional therapy on glycemic variability is a novel question that warrants further research. While initial reports show that parenterally fed diabetic patients could tolerate GV better than non-diabetics, the effect of enteral nutrition on GV and its consequent effects on outcomes in PWD is under-studied. Furthermore, the limited published research suggests that the type of enteral feeding formulas (standard or diabetes specific) impacts GV in PWD. Due to the potential for significant positive clinical impact, additional research is warranted to fully characterize the benefits associated with the type of nutrition therapy in PWD.

## References

1. Alish C J, Garvey W T, Maki K C, Sacks G S, Hustead D S et al. A Diabetes-Specific Enteral Formula Improves Glycemic Variability in Patients with Type 2 Diabetes. *Diabetes Technology and Therapeutics*. 2010, 12(6): 419-425.
2. Farrokhi F, Chandra P, Smiley D, Pasquel F J, Peng L et al. Glucose variability is an independent predictor of mortality in hospitalized patients treated with total parenteral nutrition. *Endocrine Practice*. 2014, 20: 41-45.
3. Krinsley J. Glycemic Variability: A Strong Independent Predictor of Mortality in Critically Ill Patients. *Critical Care Medicine*. 2008, 36(11): 3008-3013.
4. Mori Y, Ohta T, Tanaka T et al. Effects of a low-carbohydrate diabetes-specific formula in type 2 diabetic patients during tube feeding evaluated by continuous glucose monitoring. *European Journal of Clinical Nutrition*. 2011, 6.
5. Mori Y, Ohta T, Shiozaki M, Yokoyama J, Utsonomiya K. The effect of a low-carbohydrate/ high-monounsaturated fatty acid liquid diet and an isoleucine-containing liquid diet on 24-h glycemic variability in diabetes patients on tube feeding: a comparison by continuous glucose monitoring. *Diabetes Technology and Therapeutics*. 2012, 14(7): 619-623.
6. Mori Y, Ohta T, Yokoyama J, Utsonomiya K. Effects of Low-Carbohydrate/High-Monounsaturated Fatty Acid Liquid Diets on Diurnal Glucose Variability and Insulin Dose in Type 2 Diabetes Patients on Tube Feeding Who Require Insulin Therapy. *Diabetes Technology and Therapeutics*. 2013, 15(9): 762-767.
7. Sanz París A, García J M, Gómez-Candela C, Burgos R, Martín Á et al. Malnutrition prevalence in hospitalized elderly diabetic patients. *NutrHop*. 2013, 28(3): 592-599.
8. Vischer U M, Perrenoud L, Genet C, Ardigo S, Registe-Rameau Y et al. The high prevalence of malnutrition in elderly diabetic patients: implications for anti-diabetic drug treatments. *Diabetic Medicine*. 2010, 27: 918-924.
9. Zaccardi F, Pitocco D, Ghirlanda D. Glycemic risk factors of diabetic vascular complications: the role of glycemic variability. *Diabetes Metab Res Rev*. 2009, 25: 199-207.