

Finally Some Light in Diabetes Management

Haris Riaz¹

¹Department of Medicine, Cleveland Clinic Foundation, Ohio, USA

Diabetes is an evolving pandemic and with the rising prevalence of obesity across the globe, the number of diabetics is estimated to increase. At present, approximately 300 million people are affected with diabetes.

Since hyperglycemia is the hallmark of the condition, it is logical to hypothesize that reducing blood sugars will be associated with improved outcomes in diabetes. Unfortunately, improving outcomes in diabetics have been elusive. Despite clinical trials of a number of medications that act on different metabolic pathways, no medication has been shown to alter cardiovascular morbidity associated with diabetes.

More worrisome is the fact that instead of reducing the risks, some of these medications may be associated with increased risk of cardiovascular morbidity and mortality. The most well-known example is that of thiazolidinediones [1, 2]. Rosiglitazone was shown to be associated with increased risk of cardiovascular events after it was approved by the Food and Drug Administration (FDA) while muraglitazar was near FDA approval when pooled analysis of phase II and III trials showed increased risk of cardiovascular events and the drug was not licensed [3]. More recently, saxagliptin has been shown to increase the risk of heart failure related hospitalizations [4].

Some of the issues about the effect of anti-diabetic medications on the hard clinical end points were highlighted by Dr. Lehman in a thought provoking article in one of the previous issues of this journal [5]. Recently, the EMPA-REG OUTCOME trial found that patients treated with empagliflozin had lower risk of cardiovascular events and mortality as compared to placebo. Empagliflozin decreases blood sugars by blocking the sodium glucose channel and thereby increasing the efflux of glucose in the urine. The primary end point of time to first cardiovascular death, nonfatal myocardial infarction or stroke was significantly reduced in the empagliflozin group (hazard ratio = 0.86, 95% CI=0.74- 0.99). In addition, there was significant reduction in all-cause mortality, cardiovascular mortality, and hospitalization for heart failure in the empagliflozin group. The risk of urinary tract infection and renal function

deterioration was similar in both the groups albeit urosepsis was more common in empagliflozin group. This most likely represents the first randomized controlled trial that has clearly shown to impact the hard clinical end points of macrovascular significance in diabetes. Traditionally, the UKPDS study (metformin) has been suggested to reduce the incidence of these end points.

While this certainly represents a significant advancement in reducing the long term complications of the disease, the long term effects of the drug remain unknown. It is also unclear if the effects of the trial will translate into the "real world".

The pivoting of diabetes management towards the amelioration of clinical end points and away from surrogate markers frequently used to monitor the drug responses is a recent development. Thus clinicians should focus on endpoints of clinical significance while treating patients. With the discovery of new drugs, clinicians should continue to emphasize the importance of diet and exercise (lifestyle changes) when counseling their diabetic patients.

REFERENCES

1. Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. *N Engl J Med.* 2007;356:2457-2471.
2. Nissen SE, Wolski K. Rosiglitazone revisited: an updated meta-analysis of risk for myocardial infarction and cardiovascular mortality. *Arch Intern Med.* 2010 26;170(14):1191-1201.
3. Nissen SE, Wolski K, Topol EJ. Effect of muraglitazar on death and major adverse cardiovascular events in patients with type 2 diabetes mellitus. *JAMA.* 2005;294(20):2581-6.
4. Scirica BM, Bhatt DL, Braunwald E, Steg PG, Davidson J, et al. SAVOR-TIMI 53 Steering Committee and Investigators. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. *N Engl J Med.* 2013; 369: 1317-1326
5. Lehman R. New Drugs for Type 2 Diabetes – No Sweetness, No Light. *J Pak Med Stud.* 2012; 2(3):82-83.
6. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. *N Engl J Med.* 2015 Sep 17. [Epub before print]

Conflict of Interest: None declared

This article has been peer reviewed.

Article Submitted on: 23rd September 2015

Article Accepted on: 1st October 2015

Funding Sources: None declared

Correspondence to: Dr Haris Riaz

Address: Department of Medicine, Cleveland Clinic Foundation, Ohio, USA

Email Address: harisriaz73@yahoo.com

Cite this article: Riaz H. Finally some light in diabetes management. *J Pioneer Med Sci* 2015; 5(4):136