



Hypoglycemia: A Preventable and Avoidable Barrier to Glycemic Control

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Editorial

In the treatment of Type 2 Diabetes, the goal of the primary care physician is to utilize medications that will physiologically mimic the normal pattern of insulin production by the pancreas. This may be better done with the use of Insulin pump or the use of multiple daily insulin regimen using the basal-bolus approach. The main goal in the treatment of diabetes is plainly to reduce the patient's glucose toxicity and improve the acute sense of wellbeing and likewise help achieve a reduction of the long-term complications like cardiovascular disease, kidney failure and blindness.

Studies including DCCT and UKPDS have shown that tight control do matter provided early intervention is key [1,2]. Aggressive intervention after long duration of uncontrolled diabetes is harmful long term as seen in the ACCORD and VADT trials due to the so called "Bad Glycemic Legacy" [3]. So the key in managing diabetes is early screening and early aggressive intervention using safe drugs that have low risk to cause hypoglycemia.

The challenge to clinicians however lies in the choice of medications and to balance cost, efficacy and safety of these medicines. Several options are available for oral medications including Sulfonylureas, Metformin, DPP4 Inhibitors, SGLT 2 Inhibitors as well as injectables like Insulin and GLP1 Agonists.

Among the drugs that give us the highest risk of hypoglycemia and a major cause of hospitalization in our setting is the use of Sulfonylureas [4]. In my part of the world, it is the number one commonly used agent to treat Diabetes due to its cheap cost and availability of generic equivalents [5]. Majority of cases admitted in our hospital occurs among the elderly who have erratic schedule for food intake and unpredictable appetite. The major co-morbidities associated with the elderly patients like renal insufficiency and liver disease also further increase the risk of hypoglycemia. At the same time, the lack of empathy of some physicians dealing with diabetes exacerbates this risk as patients don't understand the risk and benefit of the agents used, the risk of both hyperglycemia and hypoglycemia to their well-being and how these complications can be easily avoided [6].

Agents that are safer for the elderly like DPP4 inhibitors or metformin should therefore be considered as initial therapy for their management. One caveat that reduces the use of DPP4 inhibitors in our workplace is cost as generic brands and equivalents are still not available. Metformin on the other is cheap but its glucose lowering effect is not as robust as a sulfonylurea or DPP4 Inhibitors. Metformin use also has a major gastrointestinal side effect which makes it not acceptable to the elderly [7]. SGLT 2 Inhibitors have been shown to be safe as they don't cause hypoglycemia but caution should be taken among those elderly due to risk of hypotension and dizziness especially if taken together with a diuretic [8]. The symptoms of hypotension and dizziness occasionally maybe mistaken for a hypoglycemic episode.

GLP1 agonists are great drugs to use as they have good efficacy and safety record. They work great in suppressing appetite and therefore suited best among obese uncontrolled diabetics [9]. Caution however should be used if these drugs are taken together with drugs known to cause hypoglycemia like sulfonylureas. By suppressing appetite and delaying gastric emptying, a patient on GLP1 agonist may have cut down on his calories but continues to take the same dose of his sulfonylureas.

One of the main barriers of Insulin utilization and intensification among physicians and patients alike is hypoglycemia [10]. Due to lack of training and experience, primary care physicians fear most is the risk of hypoglycemia. As a result, initiation of insulin is often delayed. Likewise, Insulin is always reserved as the last resort once oral medications fail. The clinical inertia therefore results in delayed initiation of insulin among patients who really need it and less aggressiveness to intensification in achieving A1C goal due to fear of hypoglycemia [11].

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Received Date: 05 Apr 2017

Accepted Date: 20 Apr 2017

Published Date: 22 Apr 2017

Citation:

Gerry H Tan. Hypoglycemia: A
Preventable and Avoidable Barrier to
Glycemic Control. *Ann Diabetes Res.*
2017; 1(1): 1001.

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The availability of new insulin's in the market however has changed that perspective. New basal long acting analogues like Insulin Degludec of Novo Nordisk and Glargine U300 by Sanofi have made it easier for us to convince patients to start insulin.

The long duration of action of Insulin Degludec for example has resulted in a major reduction in the risk of hypoglycemia compared to the usual basal insulin Glargine U100. Due to its unique protraction mechanism of action, Degludec has a flat peak-less profile that has a long half-life of 25 hours and is a true once a day insulin that lasts for 42 hours [12]. Several studies have shown that the use of this long acting insulin's resulted in a 50% reduction in the risk of nocturnal hypoglycemia [13]. This property allows patients to sleep well at night and they literally feel comfortable since there is no feeling of hypoglycemia that usually wakes them up at night.

Caution however should be exercised if Insulin is taken together with daytime sulfonylureas as the combination may lead to increased risk of hypoglycemia. The best combination medication with insulin to avoid hypoglycemia is with DPP4 inhibitors, Metformin and SGLT2 Inhibitors.

Cases of hypoglycemia in our daily practice are characteristically preventable and avoidable. The most common scenario is good compliance with meds but erratic food intake due to busy work schedule. Patients need to realize that if sulfonylureas or insulin are used, the medications should be balanced by proper nutrition in terms of quantity and timing as well as proper lifestyle. And to always caution patients to monitor frequently if in doubt.

In summary, the author continues to emphasize that empathy is key to diabetes management [6]. Physicians should take time to talk with patients and include them in decision making. Complete understanding of the disease process of diabetes, the pros and cons of the different drug regimens and combinations, the risks of hyperglycemia and hypoglycemia and the ways to avoid them should be emphasized at each visit.

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