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CLINICAL PRACTICE UPDATE IN
ENDOCRINOLOGY & DIABETES

Staying In Range: Timely Basal Insulin Optimization

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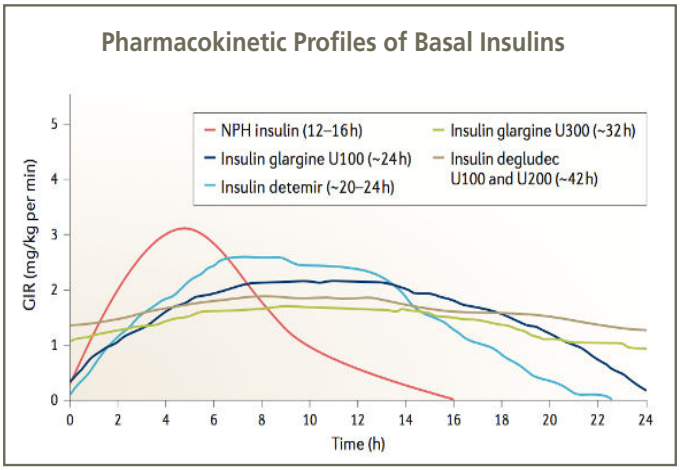
Basal insulins are a very valuable therapy in managing hyperglycemia in people with type 2 diabetes. Initiating basal insulin therapy is a recommended option for people living with type 2 diabetes whose A1c goals are not reached after 3 months on existing therapy or who have significantly elevated A1c levels (>11.0%), symptoms of hyperglycemia, or evidence of catabolism such as weight loss [1]. The use of other antihyperglycemic agents (metformin, DPP4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors) with insulin often results in lower doses of basal insulin being necessary to achieve glycemic control [2]. The role of basal insulin in managing type 2 diabetes is fundamental based on the pathogenesis of type 2 diabetes; insulin is often under-produced by the pancreas over time and requires replacement. Compared with mixed insulin or basal bolus regimens, basal insulin often numerous advantages including resulting in less hypoglycemia, less weight gain, and less complexity [3].

The Landscape of Basal Insulins

In Canada, basal insulin therapies include intermediate-acting NPH and long-acting analogues such as degludec U-100, degludec U-200, detemir, glargine U-100 and glargine U-300. These therapies differ in how they are absorbed into circulation from the subcutaneous tissue and their duration of action [4,5]. In particular, the newer generation basal analogues, degludec and glargine U-300, can be given once per day with lower rates of hypoglycemia than other basal insulins [6]. As well, the newer generation basal insulin analogues offer more flexibility and can be given in the morning or evening with equal effectiveness and safety [6]. The Flex Study illustrates the amazing flexibility of degludec by varying injection timing without compromising glycemic control or



safety vs. same-time-daily degludec or glargine administration [6]. The Diabetes Canada guidelines comment on the various types of basal insulin and provide recommendations on the different options. They emphasize that if minimizing the risk of hypoglycemia is a priority, to use long-acting insulin analogues (insulin glargine U-100, glargine U-300, detemir, degludec) over NPH insulin to reduce the risk of nocturnal and symptomatic hypoglycemia [8]. This recommendation is very practical since reducing hypoglycemia is almost always a priority for all people living with diabetes. To help differentiate amongst the basal insulin options, Diabetes Canada suggests using insulin degludec or insulin glargine U-300 over insulin glargine U-100 to reduce overall and nocturnal hypoglycemia; and severe hypoglycemia in patients at high CV risk [8].

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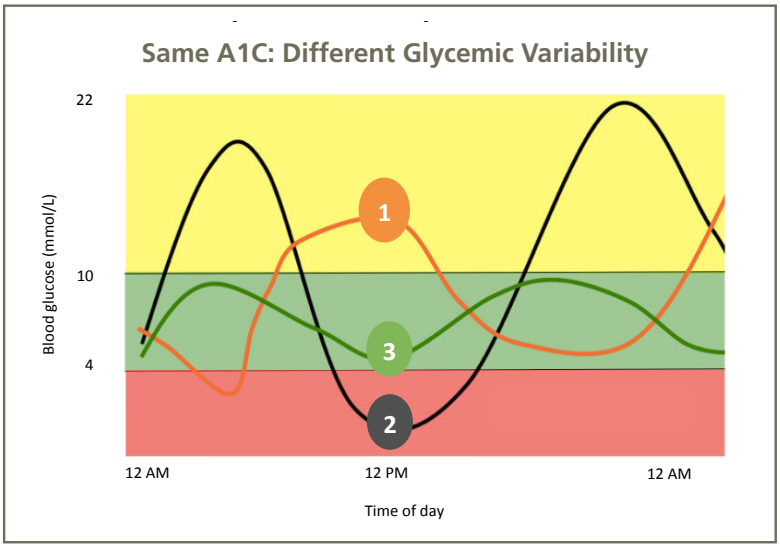
Time in Range: A Best Practice Consequence

Since the advent of glucose sensing technology with continuous glucose monitors and flash glucose monitors, the ability for people living with diabetes to monitor their glucose in real time accurately has greatly improved. This can lead people to make better decisions around lifestyle and pharmacotherapy. This is especially valuable for people using insulin to reduce the risk of hypoglycemia and prevent or correct hyperglycemia effectively. Those with hypoglycemia unawareness or populations at higher risk of hypoglycemia (children, elderly) also derive benefits. As well, these new glucose sensing technologies can generate reports, such as the ambulatory glucose profile, that gives valuable information to the person living with diabetes and health care professionals. These technologies improve care offered by health care teams and promote patient self-management. The ADA has noted that these technologies can reduce the incidence of diabetes related complications and mortality [12].

Traditionally, "glycemic control" was evaluated based on a person's A1c. This is because the A1c represents the average glucose over about a 3-month



period and is directly related to the risk of microvascular complications (and possibly macrovascular disease) related to diabetes. However, the A1c has numerous disadvantages including the fact that is does not take in to account glycemic variability, does not lead to real-time actions since it is only measured every few months, and may be inaccurate in individuals who have certain medical conditions that affect hemoglobin [9].

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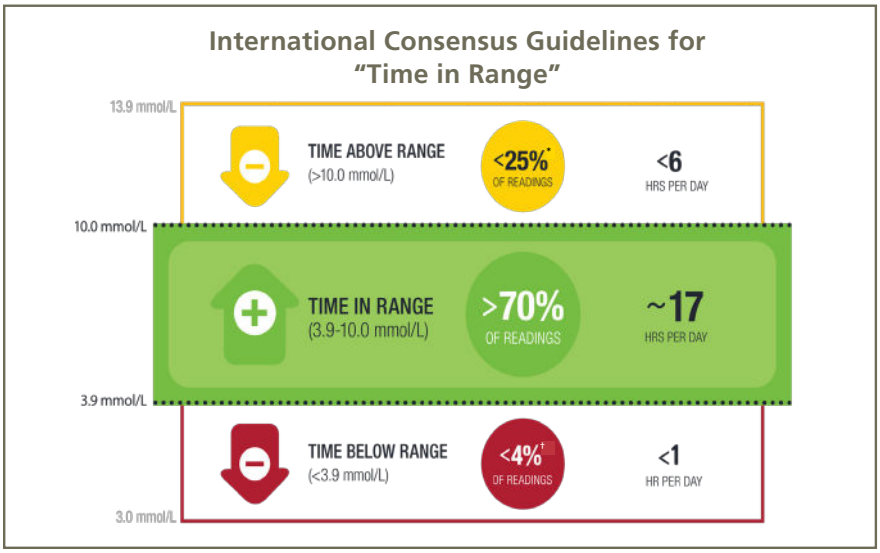
As result, another parameter for "glycemic control" that has been adopted globally is the 'Time in Range', defined in most cases as the percentage of time in which a person's glucose is between 3.9-10 mmol/L. For most people with diabetes, it is recommended that >70% of time be in range, < 25% of the time above range (> 10.0 mmol/L), and < 4% of the time below range (< 3.9 mmol/L) [10]. For people with diabetes in pregnancy, children, or frail elderly, these international consensus recommendations are different allowing for the individualization of diabetes care. Another very useful parameter is the coefficient of variation, which reflects the degree of glycemic variability that exists for the person with diabetes (target < 36%). Suboptimal glycemic variability leads to more diabetes distress and an increases risk of complications [13, 14]. Time in range and

other parameters can be viewed by the person living with diabetes and their health care professionals in real-time, permitting beneficial adjustments to diabetes management.



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New basal insulins, such as degludec and glargine U-300, have been shown to improve time in range and result in less time below range compared with other basal insulin therapies. As well, they improve the coefficient of variation emphasizing their value in reducing glycemic variability [6].

Key Takeaways

Diabetes is a chronic condition that is largely managed by primary care physicians [11]. Given that about 9.3% of people in Canada have diabetes, it is not realistic for all people living with diabetes to be managed by endocrinologists [9]. The adoption of new glucose sensing technologies by primary care physicians is a necessity. Fortunately, these technologies are user-friendly and often preferred by people living with diabetes. It is important to be aware of challenges that exist with continuous glucose monitoring sensors, such as irritation from the adhesives attached to the skin or the sensor falling off. There are strategies to help minimize these unwanted adverse events such as adding medical tape on top of the sensor and placing it on a flat surface. It is important to remember that continuous glucose monitoring devices measure interstitial glucose while self-monitoring blood glucose monitors measure capillary blood glucose so the values may not be the same. Therefore, reassuring the person living with diabetes that the glucose values are different and "not wrong" can enhance the person's trust in the glucose sensor in proving accurate information. If glucose values are changing rapidly or don't make sense, advise the person to double check with a different glucose sensing device.

Similar to the value of newer glucose sensing technologies, the newer basal insulin analogues (degludec, glargine U-300) provide people living with type 2 diabetes an effective and safer treatment option. Both glucose sensing technology and newer basal insulin analogues (compared with older basal insulins) reduce the risk of hypoglycemia and glycemic variability. Further, the ability to inject degludec and glargine U-300 daily with greater flexibility is undoubtedly patient-centred. Primary care physicians should be aware of these basal insulins and consider using them when starting or switching therapy to achieve novel targets for the person living with diabetes.

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