Insulin Glargine: A treatment option in Pakistan

Professor Dr. Rauf Niazi (Professor of Medicine / Endocrinology, MB; BS (Pb), MRCP (UK), FRCP (Edin), FRCP (Glasg), FRCP (Lond), FACP (USA), FCPS (Pak Hon). Pakistan Institute of Medical Sciences, Islamabad, Pakistan.)

Insulin analogues have made a dramatic entrance into the diabetes management armamentarium. Most attention has focused on short-acting insulin analogues. Recently, a new long-acting insulin analogue, glargine, has been introduced for patient use. A single injection of basal insulin with insulin boluses for meal coverage mimics physiological insulin secretion. Early clinical experience with glargine has shown improved blood glucose control, particularly of the fasting glucose levels, in many cases. Additionally, there is less likelihood of hypoglycaemia, especially nocturnal hypoglycaemia, with glargine than with more traditional basal insulin, in both type 1 and type 2 diabetes.[1,2]

It consists of microcrystals that slowly release insulin, giving a long duration of action of 18 to 24 hours, with a "peak less" profile. Pharmacokinetically, it resembles basal insulin secretion of non-diabetic pancreatic beta cells. Sometimes, in type 2 diabetes and in combination with, metformin with meals or a short acting sulfonylurea or meglitinides (Rapaglinide, Nateglinide), it can offer moderate control of serum glucose levels. In the absence of endogenous insulin — type 1 diabetes, depleted type 2 (in some cases) or latent autoimmune diabetes of adults in late stage — insulin glargine needs the support of fast acting insulin taken with food to reduce the effect of prandially derived glucose.

Type 2 diabetes is a progressive disease characterized by insulin resistance and progressive b-cell dysfunction. With the prevalence of type 2 diabetes increasing and with people being diagnosed at an early age, the use of insulin in type 2 diabetes will become increasingly important as patients develop severe insulin deficiency due to pancreatic b-cell loss over time. Although the decision to implement insulin therapy in patients who are on multiple oral agents and present with severe hyperglycaemia, polyuria, and weight loss may be obviously warranted, the choice to initiate insulin therapy in many other patients with type 2 diabetes is less clear.

Factors to be considered when deciding whether to start insulin therapy for a given patient can be diverse and are often complex. Important considerations both in favour of and against the initiation of insulin therapy can include contraindications or intolerance to alternative therapies, cost, and physician and patient preferences, among others. Varying viewpoints also exist regarding whether insulin treatment should be considered early in type 2 diabetes or only as a last resort once oral and other alternative therapies have proven ineffective. The burden falls on the health care team to carefully weigh all of these and other pertinent factors against treatment guidelines and patient-specific treatment goals when determining the optimal therapeutic strategy.

Undoubtedly, one of the largest hurdles concerning the initiation of insulin is overcoming patients' fears and misconceptions regarding insulin use. Preconceived patient perceptions regarding injection pain, weight gain, regimen complexity and its impact on quality of life, and risks and consequences of hypoglycaemia, often hinder successful initiation of therapy. Some patients even believe that their need for insulin reflects a personal failure and that they have somehow failed their family or health care providers.[3]

Given these common concerns, patient education is paramount when starting insulin. In fact, it may often prove beneficial for patients to receive education early regarding the progressive nature of type 2 diabetes so that they understand that, despite their best efforts, their disease will inevitably progress over time. Once patients develop an understanding that a need to add or transition to insulin therapy does not mean they have failed, they may be more likely to readily accept insulin therapy in the future. Although few would argue against the importance of patient education, the overwhelming need and time commitment for intense education in people starting insulin is often itself a barrier for both patients and health care providers. So why initiate insulin early in type 2 diabetes when efficacious

antidiabetic agents such as sulfonylureas, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, GLP-1 receptor agonists, nonsulfonylurea secretagogues, and a-glucosidase inhibitors are available in our pharmacological armamentarium? Such therapies are often sought in lieu of insulin because of their increased acceptance by patients and less intense patient management and follow-up requirements. The important difference between the aforementioned agents and insulin, however, is that insulin possesses an unlimited ability to lower A1C.

Glargine cannot be mixed with any other insulin. The pH of glargine is 4.0. If mixed with other insulin, it may cause precipitation and lead to deterioration in glucose control. The onset of insulin glargine occurs in 4-6 hours with no appreciable peak and duration of 24 hours in most patients.

Recent clinical treatment guidelines, such as those from the 2007 update to the American College of Endocrinology/American Association of Clinical Endocrinologists (ACE/AACE) treatment guidelines, suggest that these agents may be less effective as add-on therapy for patients with an A1c >9.5% and therefore recommend the initiation of insulin in all patients with an A1C > 10%.[4]

Although most newly diagnosed patients with type 2 diabetes will not present with an A1C > 10%, the early use of insulin is recommended in those patients experiencing limited benefit from oral therapies and in those at acute risk of glucotoxicity. Data show that intensive insulin therapy early in the course of type 2 diabetes can improve b-cell function by attenuating glucose toxicity.[5-7]

From my experience, in my own clinical practise, which has more than 3000 patients, on Glargine insulin, the ease of once daily administration, safer and longer shelf life (temperatures of 26-30 Celsius for 1 month), the minimal weight gain, lowering of HbA1c and the eating styles of our population in Pakistan, leading to reduced long term diabetic complication and a longer productive life, make this rather expensive insulin, a very feasible option for treatment of, both type1 and Type2 patients.

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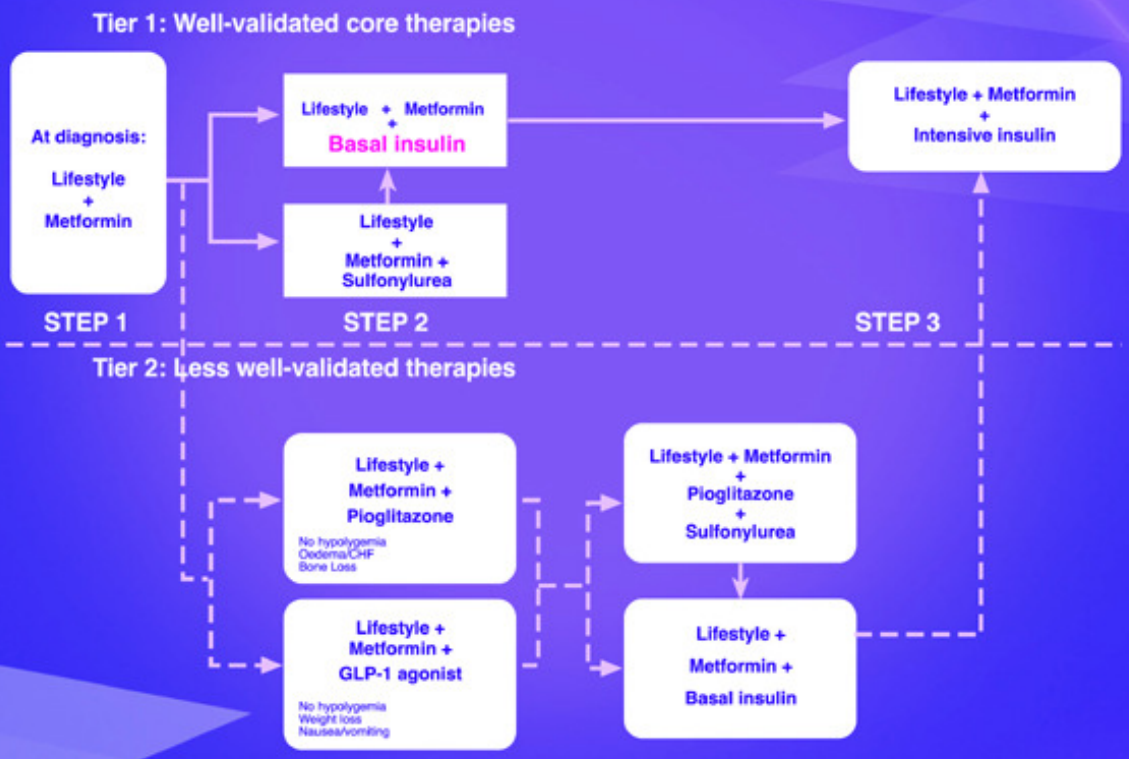
Algorithm for the metabolic management of Type 2 Diabetes

A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes



Diabetes Care, Volume 32, 193:203, Number 1, January 2009