Insulin Tactics in Type 2 Diabetes

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KEYWORDS

• Type 2 diabetes • Insulin secretion • Exogenous insulin profiles
• Insulin administration • Insulin adjustment • Noninsulin therapy

KEY POINTS

- Type 2 diabetes is a multifactorial disease comprising insulin resistance, relative insulin deficiency, increased hepatic glucose output, and increased renal glucose reabsorption, which together result in failure to maintain normal glucose homeostasis.
- Therapeutic interventions for Type 2 diabetes include lifestyle modifications, noninsulin drugs, and insulin therapy.
- Although insulin can be used as stand-alone therapy, it is more commonly used as add-on to other noninsulin agents.
- Insulin treatment in Type 2 diabetes is generally instituted with basal insulin alone and intensified to basal plus bolus insulin regimens if glycemic goals are not achieved.
- Self-monitored blood glucose (SMBG) testing is critical in guiding the titration of insulin treatment.
- The addition of newer noninsulin drugs to previous insulin treatment may allow for partial or complete reduction of the insulin.
- Patient education by a multidisciplinary treatment team that includes diabetes educators is helpful in maximizing efficacy and minimizing adverse events related to the use of insulin.

INTRODUCTION

Type 2 diabetes (T2D) is a heterogeneous disorder in which multiple pathophysiologic defects result in an imbalance between the rate of glucose production (which is increased) and its disposal (which is decreased) resulting in hyperglycemia (Fig. 1). Among the defects is insulin resistance, leading to decreased glucose uptake by peripheral tissues (predominantly the muscles) and an increase in hepatic glucose production (gluconeogenesis). Compounding this are defects in incretin hormones,

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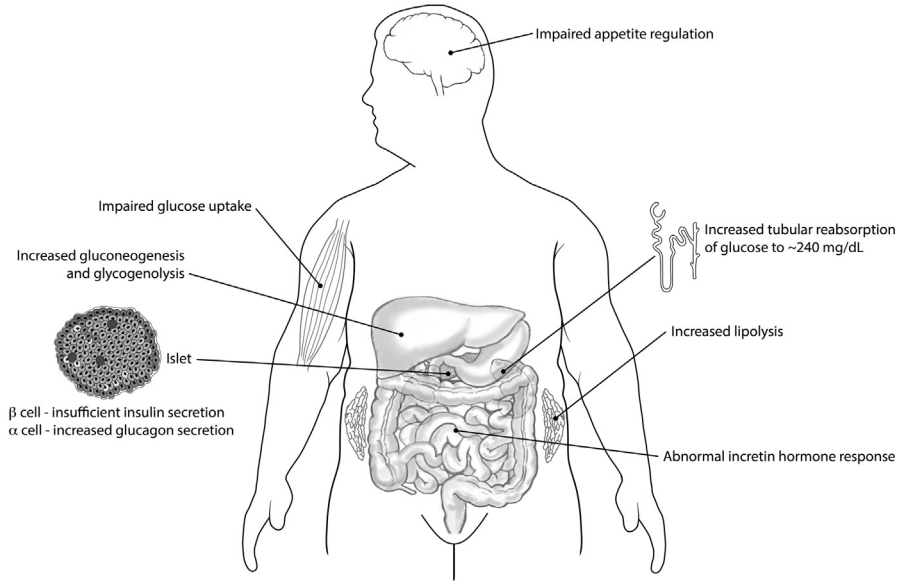

Fig. 1. Pathophysiologic defects in T2D.

resulting in decreased postprandial insulin release by the beta (β) cells accompanied by a failure to suppress glucagon by the alpha (α) cells, resulting in postprandial hyperglycemia and continued release of glucose from hepatic glycogen stores (glycogenolysis).[1] Furthermore, there is increased renal tubular reabsorption of glucose due to upregulation of sodium glucose co-transporters-2 (SGLTs-2) and a β-cell deficiency secondary to a decrease in its numbers, mass, and function.[1,2] All these factors together increase the workload of the β cell, which can, over time, lead to its exhaustion, implying that insulin therapy might be an inevitable consequence of longstanding T2D.[3–5]

Therapy with insulin, however, has challenges, because unlike most other drugs, it needs to be dosed in synergy with the peaks and troughs of glucose. Commercially available insulin, however, does not share the physiologic properties of endogenous insulin. It is therefore important to understand the pharmacokinetic properties of insulin preparations and to time the dose of the insulin to meet the needs of the patient. In this article, we discuss strategies of how to introduce insulin as a treatment option in patients with T2D and how to decrease it when other noninsulin drugs are added to the treatment.

Physiology of Insulin Production

Insulin secretion in the nondiabetic individual

Following an overnight fast, the liver of nondiabetic individuals produces glucose at a rate of approximately 2.0 mg/kg/min (**Fig. 2**).[1] The kidneys reabsorb most of this glucose, based on a physiologically set renal threshold of approximately 180 mg/dL, resulting in less than 0.5 g of glucose being excreted per day.[1,6] This glucose (referred to as basal glucose) is metabolized by a steady production of basal insulin by the β cell and euglycemia is maintained. With an oral load of glucose, such as during a meal, additional bolus (also referred to as prandial) insulin is secreted by the β cells (**Fig. 3**) to help in its metabolism.