After the initial bolus of normal saline or lactated Ringer's, replacement of the sodium and free water deficit is carried out over the next 24 h (fluid deficit is often 3–5 L). When hemodynamic stability and adequate urine output are achieved, IV fluids should be switched to 0.45% saline or lactated Ringer's depending on the calculated volume deficit. The change to 0.45% saline or using lactated Ringer's helps to reduce the trend toward hyperchloremia later in the course of DKA.

A bolus of IV (0.1 units/kg) short-acting regular insulin is usually administered immediately (Table 404-8), and subsequent treatment should provide continuous and adequate levels of circulating insulin. IV administration is usually preferred (0.1 units/kg of regular insulin per h) in patients with severe or complicated DKA because it ensures rapid distribution and allows adjustment of the infusion rate as the patient responds to therapy. Mild to moderate uncomplicated DKA can also be treated with SC short-acting insulin analogues. If chosen, IV regular insulin should be continued until the acidosis resolves and the patient is metabolically stable. As the acidosis and insulin resistance associated with DKA resolve, the insulin infusion rate can be decreased (to 0.02–0.1 units/kg per h). Long-acting insulin, in combination with SC short-acting insulin, should be administered as soon as the patient resumes eating, because this facilitates transition to an outpatient insulin regimen and reduces length of hospital stay. It is crucial to continue the insulin infusion or insulin SC until adequate insulin levels are achieved by administering long-acting insulin by the SC route. Even relatively brief periods of inadequate insulin administration in this transition phase may result in DKA relapse. In euglycemic DKA associated with SGLT2 inhibitors, the pharmacologic effect may persist for 10–14 days following discontinuation of SGLT2 inhibitor therapy as evidenced by ongoing glucosuria despite normoglycemia (glucose <180 mg/dL), during which time relapse of ketoacidosis is common if nutritional intake has not advanced (e.g., in the postoperative setting).

Hyperglycemia usually improves at a rate of 4.2–5.6 mmol/L (50–100 mg/dL) per h as a result of insulin-mediated glucose disposal, reduced hepatic glucose release, and rehydration.