6 Insulin Therapy

1. Indications for Insulin Therapy

- ● Patients with Type 1 diabetes, diabetic coma (diabetic ketoacidosis, hyperosmolar hyperglycemic syndrome) and pregnancy with pre-existing diabetes must be in insulin therapy. When diet therapy is not effective, insulin therapy is also recommended when patients are in severe infection and at the time of the surgical procedure with whole-body management is needed. (grade A; consensus)
- ○ Relative indications for insulin therapy include the following:
  ① If conspicuous hyperglycemia (e.g., a fasting glucose level of 250 mg/dL or higher or a casual glucose level of 350 mg/dL or higher) or a tendency toward ketosis (e.g., positive urine ketones) is noted.
  ② If favorable glycemic control is not obtained with glucose-lowering agents (e.g., primary or secondary sulfonylurea failure).
  ③ If adequate glycemic control is not achievable with diet therapy in patients with severe hepatic damage or renal failure.
- ● Insulin therapy is also used in type 2 diabetic patients when glycemic control is not obtained with diet/exercise therapy and glucose-lowering agents or when glucotoxicity needs to be resolved in these patients (grade A; consensus).

2. Risks Associated with Insulin Therapy

- ● Insulin therapy may generally be associated with hypoglycemia or aggravation of diabetic retinopathy or neuropathy in some patients.[1] Attention needs also to be given to weight gain as a potential risk associated with long-term insulin therapy.[2] (grade A)
- ○ Risk of intensive insulin therapy includes severe hypoglycemia, which is increased as glycemic control improves.[3] To prevent this, appropriate measures against potential hypoglycemia as well as patient education on effective prevention of hypoglycemia based on self-monitoring of blood glucose (SMBG) are required.
- ○ Drastic decline of glycemia may be associated with aggravation of diabetic retinopathy or neuropathy.[1]

3. Intensive Insulin Therapy for Type 1 Diabetes and its Complications

- ● In type 1 diabetes for which optimal glycemic control is being sought, multiple insulin injection therapy (3 to 4 injections/day) or continuous subcutaneous insulin infusion (CSII) is required.[3] (grade A)
- ● Intensive insulin therapy which combines the above modality with SMBG is shown to be effective in preventing the onset or progression of diabetic microangiopathy (retinopathy, nephropathy, and neuropathy)[3,4] as well as in preventing the progression of diabetic macroangiopathy (ischemic heart disease, cerebrovascular disease, peripheral vascular disease).[5,6] (grade A)

4. Type 2 Diabetes and Insulin Therapy

- ● Rigorous glycemic control is effective for preventing the onset or progression of diabetic microangiopathy in type 2 diabetic patients as well, thus providing the rationale for the use of insulin therapy in type 2 diabetic patients whose glycemic goal cannot be achieved with diet/exercise therapy and glucose-lowering agents.[2,7] (grade A)
- ● While favorable glycemic control may be achieved with once-daily injection of intermediate or long-acting soluble insulin or twice-daily injection of mixed insulin (morning/evening) in patients with mild diabetes, insulin therapy, including intensive insulin therapy with multiple insulin injections, should be used in patients with moderate or severe diabetes.[7,910] (grade A)

5. Combination Therapy with Insulin Preparations and Glucose-lowering Agents

- ● Combination therapy with insulin preparations and glucose-lowering agents (sulfonylureas,[11,12] biguanides,[13] α-glucosidase inhibitors,[14,15] thiazolidinediones[16,17]) is shown to improve glycemic control as well as to reduce the need for insulin. However, its long-term efficacy has not been adequately explored. (grade B)

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