In the case of diabetes mellitus, the primary therapeutic goal is to stabilize the concentration of glucose in the blood. Stabilization is accompanied by various forms of therapy, starting from simple dietary rules and leading to regular insulin injections. As a physician, it is very important to know all the therapeutic measures, and treat patients with an individual approach to protect them from fatal late complications of diabetes mellitus.

**Insulin Delivery Devices**

- Insulin syringe
- Insulin pen
- Jet injector
- Insulin pump

**Introduction**

Patients, who suffer from diabetes mellitus, need to be comprehensively examined and instructed by their physician. Only when the extent of the disease has been detected, late complications may be avoided, which, as a rule, lead to mortal cases in diabetes mellitus. The treatment of diabetes requires good compliance so that it can be successful.
Treatment of Diabetes Mellitus Type 1

As far as little amount or no insulin is provided in **diabetes mellitus type 1**, the body shall be supplied with **insulin from outside**. In fact, healthy diet and exercising can make a small contribution. However, the injection of insulin cannot be avoided.

In the case of **insulin therapy**, the need for insulin depends on the patient’s daily activities, as food, disease, and exercising affect insulin levels and must be considered in the dosage, so that it neither brings to hypo- or hyperglycemia. Every patient must be well-informed, which is very important, because he/she independently provides subcutaneous insulin administration, using an insulin pen. The greatest danger in insulin therapy is **hypoglycemia**. Insulin edema may also occur. Patients rarely produce allergies or antibodies to insulin.

For the treatment, there are different human insulin concentrations: U40 (40 IU/ml) and U100 (100 IU/ml):

- **Regular insulin**: Injection (10–30 min before meal), active for about 5 hours, corresponds to the body’s own insulin
- **Insulin analogues**: Injection (0–10 min before meal), active for about 3 hours, genetically modified
- Insulin analogues with a 24-hour action
- Insulin for insulin pumps
- **Long-acting insulin**: Active for about 10–12 hours by means of additives, such as zinc or protamine
- **Combination insulin**: Combination of regular and long-acting insulin, rapid
Intensified insulin therapy

Which insulin type is used depends on the patient. As a rule, the intensified insulin therapy is provided for patients with type 1 diabetes. In this case, regular as well as long-acting insulin is injected, in order to imitate the natural insulin level. Long-acting insulin constitutes 40–50 % of the total daily requirement and ensures a constantly low insulin level during the day and at night. A corresponding injection in the evening is usually sufficient. In rare cases, morning and evening injections are provided.

However, the regular insulin form, which accounts for the remaining 50–60 % of the total daily requirement, is administered before meals, in order to cover the corresponding insulin requirement. The bolus of regular insulin is previously determined by blood sugar levels, and it is based on the carbohydrate content of the meal and the corresponding activities. So, patients can individually adjust their insulin injection to their daily routines. However, such a therapy requires extensive training because patients need to often measure blood glucose level and obligatorily inject insulin. Therefore, an intensified insulin therapy is suitable only for the mentally fit type 1 diabetics.

Conventional insulin therapy

As elderly patients often have a regular daily routine, and they find it difficult to handle with an insulin pen, a conventional insulin therapy is advisable for them. Only in the morning and evening times, combination insulin must be injected before meals: in the morning, 2/3 of the total daily requirement is injected and in the evening, the remaining 1/3 is. The evening injection can also be replaced by long-acting insulin when a fasting blood glucose level is too high. In the conventional insulin therapy, it is important that the insulin injections should always occur at the same time, in order to avoid hypoglycemia.

Insulin pump therapy

Another alternative is the insulin pump therapy. It even allows a more individual daily routine and a better blood glucose control than the intensified insulin therapy. The insulin pump is mounted directly on the body and continuously injects regular insulin via catheter under the skin (continuous subcutaneous insulin infusion = CSII). Before meals, an administration of an extra bolus injection is provided on demand. The bolus can be adapted to the carbohydrate content of the diet. The insulin pump must be worn all day long. However, it is possible for you to take off the pump temporarily, but not for more than 1 to 2 hours.

The insulin pump therapy is especially suitable for patients with an irregular daily regime or those who suffer from the dawn phenomenon. In the latter case, patients may suffer from hypoglycemia which often occurs in the morning. It can be remedied by pumping programming as it may increase an insulin injection level during sleep. A disadvantage of the insulin pump is that the catheter may slip out of the subcutaneous fatty tissue, which leads to the rapid increase in blood sugar. Therefore, the insulin pump therapy is only suitable for the experienced type 1 diabetics.

Transplantation

Instead of injecting insulin several times a day, there is a possibility of pancreas or islet-cell transplantation. However, both the surgical procedures are carried out only
in rare cases. Pancreas transplantation is usually considered if young diabetics have already been suffering from a progressive renal insufficiency. The kidney will also be replaced in the surgery course. During their life, the patients should take immunosuppressive drugs in the case of pancreas or islet cell transplantation.

Dietary therapy

The type 1 diabetics may not influence the insulin production by keeping a diet, but they can control blood sugar levels. Patients should be fully informed about healthy eating, as they must coordinate food intake and insulin dosage parallel to each other. It should be noted that physical activity lowers the blood sugar level and must be considered in terms of insulin dosage.

In the therapy course with regular insulin, there should be six meals, divided into three main courses and three snacks. However, when the patient is treated with insulin analogues, three meals a day are sufficient. This norm avoids causing excessive blood sugar fluctuations, and blood glucose level remains relatively constant.

Treatment of Diabetes Mellitus Type 2

As the type 2 diabetics suffer from a relative insulin deficiency, the primary therapeutic goal is to stimulate the production of insulin by keeping a diet and exercising, in order to stabilize metabolism. 40–50 % of the type 2 diabetics get simultaneously obese and may reduce their diabetes risk in multiple times, trying to reach the body mass index (BMI) of 19–25. Nevertheless, it may be necessary to prescribe oral antidiabetics in the treatment process. If drug therapy is unsuccessful, the type 2 diabetics should be prescribed insulin. However, it is the last solution for this type of diabetes.

Dietary therapy

An appropriate diet in diabetes plays a more important role for the type 2 diabetics than type 1, because normoglycemia must be achieved. To achieve it, the following basic rules of healthy diet must be considered by every patient:

- The daily energy requirement should not be exceeded. (In light physical work: weight in kg × 32 = kcal);
- Food consumption must be divided into several small meals.
- 50–60 % carbohydrates (1 XE (bread unit) = 12 g carbohydrate equivalent), low in sugar and white flour (monosaccharides), high fiber
- 30 % fat (1/3 saturated fatty acids, 1/3 unsaturated fatty acids, 1/3 polyunsaturated fatty acids), cholesterol-poor
- 15 % protein (in renal failure correspondingly less)
- Refusal from sugary sodas and juices (cyclamate, aspartame, saccharin are allowed)
- Refusal from alcohol (it inhibits gluconeogenesis in the liver and leads to hypoglycemia)

Medical Nutrition Therapy (MNT)

- MNT is recommended for all patients with type 1 and type 2 diabetes mellitus
- The main goals of MNT can be summarized in the following:
  1. Achieve and maintain weight goals
  2. Achieve appropriate blood pressure, lipid, and glycemic goals
3. Delaying type 2 diabetes mellitus or preventing it

Physical Activity Per the American Diabetes Association Recommendations in 2016

- Exercise should be more than 150 minutes of moderate-intensity aerobic activity spread over three or more days per week
- Resistance training two or more times per week
- Do not sit without activity for more than 90 minutes

Type 2 Diabetics with Diabetic Complications and Physical Activity:

- Patients with retinopathy should avoid vigorous aerobic or resistance training
- Patients with autonomic neuropathy should undergo a full cardiac evaluation before starting intense aerobic exercise
- Patients with peripheral neuropathy should wear appropriate footwear and examine their feet daily after exercise

Oral drug therapy

Oral antidiabetic drugs may be prescribed if the dietary therapy and plenty of exercising are not sufficient to reduce blood sugar levels and stimulate the production of insulin. Currently, there are seven substance groups, including:

- **Alpha-glucosidase inhibitors** such as Acarbose and Miglitol (inhibit sugar-cleaving enzymes in the small intestine)
- **Biguanides** such as Metformin (delay the absorption of carbohydrates from the intestine, inhibit gluconeogenesis in the liver, promote glucose uptake into the muscles and curb appetite)
- **Glitazones** such as Pioglitazone may only be prescribed in exceptional cases (increase sensitivity of the peripheral cells to insulin, in combination with biguanides or sulphonylureas)
- **Glinides** such as Repaglinide (initiate short-term increase in the insulin secretion of beta cells)
- **Incretin analogues** such as Exenatide (imitate effects of natural incretins, regulate insulin secretion)
- **Incretin amplifiers** such as Linagliptin (prevent degradation of incretins by dipeptidyl peptidase-4 (DPP4); thereby, increase incretin concentration)
- **Sulfonylureas** such as Glyburide (stimulate insulin secretion of the pancreas, can be combined with insulin)

Insulin therapy

Frequently, the oral drug therapy is combined with insulin for type 2 diabetic patients. The oral combination therapy with biguanides (metformin) and sulfonylureas is the best way to be applied. Herewith, a single injection of insulin a day is sufficient. Either combination insulin in the morning, or long-term insulin in the evening, may be injected.

If the **combination therapy** is unsuccessful, the conventional insulin therapy can be effective. If it also brings no effect, the intensified insulin therapy is the next step to apply, in order to lower blood sugar level.
American Diabetes Association 2016 Guidelines for the Pharmacologic Therapy of Type 2 Diabetes

- Those who do not achieve and maintain glycemic control with lifestyle modifications alone should get metformin
- Those newly diagnosed with type 2 diabetes who have severe symptoms or a markedly elevated HbA1C at time of presentation should receive insulin therapy
- If oral hypoglycemic monotherapy does not achieve glycemic control over 3 months, add a second oral agent or consider GLP-1 receptor agonist or start basal insulin
- The following contraindications need to be addressed in any patient who is going to receive Metformin:
  1. Serum creatinine above or equal to 1.5 mg/dL in males and 1.4 mg/dL in females
  2. History of hypersensitivity to metformin
  3. Diabetic ketoacidosis
- When insulin therapy is needed, do not delay any further. Eventually, any type 2 diabetic will require insulin. Do not delay the inevitable.

Treatment of Gestational Diabetes

Women who develop diabetes during pregnancy are first recommended to decrease their blood sugar level by means of keeping the appropriate diet, performing physical exercises and controlling weight. Oral antidiabetic drugs are contraindicated during gestation. The insulin therapy is the last way to choose.

Review Questions

The correct answers can be found below the references.

1. After nocturnal unrecognized hypoglycemia, a type 1 diabetic always measures hyperglycemic values in the morning. How is this phenomenon called?
   A. Rebound hypoglycemia
B. Somogyi effect
C. Dawn phenomenon
D. Post-hypoglycemic hyperglycemia
E. Glucagon effect

2. What is not suitable for the treatment of gestational diabetes?

A. Short-acting insulin
B. Regular insulin
C. Nutrition adjustment
D. Metformin
E. Light sports

3. You are the practitioner of a 56-year-old type 2 diabetic who you had to switch to insulin several months ago. The HbA1c level, currently controlled by you, equals 12.3 %. You suspect that the patient is not always injected. What justifies your suspicions the most?

A. No bruises or injection sites on the abdominal skin
B. On checking, renewed HbA1c level is high for 12 weeks
C. In the patient’s diary, there are to a great extent too high, but also some too low blood sugar levels
D. Many injection sites on the fingertips
E. A 2×4 cm large site on the skin of the left abdominal part, where the subcutaneous fat tissue seems to be missing

References


Correct answers: 1B, 2D, 3A

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