Consequences of Diabetes Mellitus on the Nutritional Status

Module 21.2

Nutritional Support in Diabetes Type 1 and 2

Lubos Sobotka, MD, PhD
3rd Department of Medicine Metabolic Care & Gerontology
Medical Faculty Charles University in Prague
50005 Hradec Kralove - Czech Republic

Learning Objectives

- To know the basic metabolic differences between and consequences of type 1 and type 2 diabetes;
- To be able to prescribe nutrition support to patients type 1 diabetes mellitus;
- To know the methods of insulin administration during artificial nutrition in diabetic patients;
- To know the composition of artificial nutrition in patients with insulin resistance – type 2 diabetes;
- To know the role of insulin resistance in influencing nutrition support;
- To understand the concept of hypocaloric artificial nutrition in obese type 2 diabetic patients;
- To be able to understand the concept of glucose control in diabetic patients.

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Key Messages

- The prevalence of diabetes mellitus is high in hospitalized patients;
- Glucose tolerance is impaired in stress states and inflammatory processes;
- Glucose control is a crucial part of nutrition support in diabetic patients;
- There is an absolute deficit of insulin in type 1 diabetes mellitus;
- Type 2 diabetes mellitus is associated with insulin resistance and in some cases a degree of insulin deficiency;
- Oral antidiabetic drugs should be suspended in diabetic patients during acute illness;
- Continuous infusion is the preferred method for enteral or parenteral nutrition in diabetic patients;
- The choice of formulation of artificial feeds should depend on the underlying clinical state and not just on the presence of diabetes;
- In obese type 2 diabetic patients weight reduction can be useful;
- Good glucose control is recommended in diabetic patients, but glucose should nonetheless be higher than in non-diabetic patients requiring artificial nutrition in intensive care.

1. Introduction

Diabetes mellitus is widespread among hospitalised adult patients. Its prevalence in American hospitals was 12.45% in 2000 (1) and it is growing both in western and developing countries. Moreover, diabetes is a commonly encountered comorbid condition; it was shown recently that 18-26% of hospitalised adults had a secondary diagnosis of diabetes (2, 3). Type 1 diabetes is increasing in prevalence in some countries, being 0.3–0.4% of the population. However the prevalence of type 2 diabetes is increasing much more rapidly, largely due to the rising occurrence of obesity (BMI > 30) and also due to increased age (4). For instance, the prevalence of type 2 diabetes has risen from 6 to 20% in the UK since 1980. The same trend in increased prevalence of non-insulin dependent diabetes mellitus (NIDDM – type 2) is apparent in almost all European countries. It is therefore logical that diabetes is also becoming more frequent in patients who require nutritional support because of a wide range of other diseases.

2. Metabolic Consequences and Complications of Diabetes

Insulin is a hormone that controls metabolism of glucose and other substrates during the post-absorptive state and especially so after food intake. Glucose metabolism is fundamentally impaired in patients with diabetes. Principally, patients with diabetes have either decreased insulin secretion (type 1), decreased insulin effect (type 2) or both (later type 2). Pre- and postprandial hyperglycaemia is the usual consequence; this is due to increased hepatic glucose production and decreased glucose uptake in tissues with the insulin sensitive glucose transporter (GLUT 4) (5, 6).

However, insulin influences metabolism of all macronutrients. Besides carbohydrates, it also has an effect on the metabolism of proteins and lipids as well as many other metabolic effects. Many of these effects are dependent on the metabolic status of the entire organism. This should be kept in mind when nutrition support is provided to a diabetic patient.
The major metabolic functions of insulin can be summarised:

**Glucose metabolism**
- Inhibition of gluconeogenesis in the liver
- Stimulation of glycogen synthesis
- Stimulation of glucose transport to cells of insulin dependent tissues – muscle, adipose tissue (presence of GLUT 4)

**Lipid metabolism**
- Inhibition of lipolysis in adipose tissue
- Stimulation of fatty acids synthesis
- Suppression of ketone body production
- Activation of lipoprotein lipase in adipose
- Stimulation of lipogenesis

**Protein metabolism**
- Stimulation of protein synthesis
- Inhibition of protein catabolism

**Other**
- Stimulation of sodium reabsorption in the kidneys
- Stimulation of cell membrane Na,K-ATPase
- Cellular growth and division

Almost all of the effects mentioned before can to some extent influence the metabolism of energy substrates during nutritional support. However, glucose intolerance and high glucose levels in plasma are major consequences of diabetes mellitus (both type 1 and type 2). Moreover, the hyperglycaemia can itself lead to many adverse effects on several cellular and organ systems.

### 3. Consequences of Hyperglycaemia

Short-term hyperglycaemia can adversely affect:
- **Fluid balance**
  - glycosuria leads to free water loss (osmotic diuresis) and subsequent dehydration;
  - water loss due to osmotic diuresis can be accompanied by a loss of intracellular electrolytes (K, P, Mg).
- **Immune function**
  - Abnormalities in white cell function especially impaired granulocyte adhesion, chemotaxis, phagocytosis, respiratory burst, superoxide formation, and intracellular killing (7, 8);
  - Glucose, through complement glycation, has the potential to inhibit opsonization.
- **Inflammation**
  - Hyperglycaemia changes the inflammatory process and affects oxidative equilibration with subsequent augmentation of oxidative stress.
- **Clinical outcome**
  - Observational studies indicate that hyperglycaemia worsens the prognosis of patients following myocardial infarction and stroke (9).
Long-term hyperglycaemia usually leads to glycation of tissue proteins, which in turn leads to:
- polyneuropathy;
- microangiopathy (retinopathy);
- nephropathy (glomerular and tubular damage) with subsequent renal failure;
- atherosclerosis with ischaemic heart disease and peripheral vascular disease;
- skin defects (also due to micro- and macro-angiopathy) and subsequently impaired wound healing.

However, higher glucose turnover, increased insulin resistance and hyperglycaemia are consequences of many physiological and pathological situations. They are typically present in subjects suffering from stress and severe disease, and in patients with malignancies. Moreover, increased insulin resistance is also apparent during pregnancy, lactation or rapid growth (10, 11). The physiological consequences of insulin resistance in these situations are not fully elucidated.

Ten years ago it was generally recommended to keep plasma glucose level in the normal (healthy) range (12). However, the previously optimistic data were not confirmed in other studies and at the present time the criteria are not so strict. The plasma glucose level should be kept at normal levels both in non-diabetic and stable diabetic patients; in critically ill or septic patients the plasma glucose level must be controlled but it need not be in the range normal for healthy subjects. Instead, safer levels, which prevent development of hypoglycaemia, are recommended in critically ill patients as well in diabetic patients during nutritional support (13).

4. Nutritional Support in Diabetic Patients

4.1 Type 1 Diabetes Mellitus

In this type of diabetes, there is an absolute deficit of endogenous insulin. This is mostly due to the destruction of the islets of Langerhans in the pancreas (B cells) by an autoimmune mechanism; however, the lack of endogenous insulin can be also result of other destructive processes e.g. severe acute pancreatitis, pancreatic resection or haemochromatosis.

Type 1 diabetes can be also diagnosed according to low levels of plasma insulin and C peptide (the peptide fragment of proinsulin which is released from B cells during insulin secretion). In autoimmune type I diabetes specific antibodies are found in plasma (especially antibodies against glutamate decarboxylase).

4.1.1 Nutrition Support in Type 1 Diabetic Patients

The indication for nutritional support in patients with type 1 diabetes is predominantly due to intercurrent illness rather than to the diabetes. Therefore the composition of nutrition support is dependent on the goal of nutrition support (e.g. muscle mass gain, wound healing, growth in children). The use of special diabetic formulae is controversial, but in most cases, the design of feeds is determined by the intercurrent condition and is no different from that used in non-diabetics.
Energy should be prescribed according to energy needs and to achieve and maintain a desirable body weight (usually 30-35 kcal·kg⁻¹·day⁻¹) to maintain normal function and as far as possible to preserve lean body mass and desirable body weight. During acute illness it may only be possible to minimise rather than abolish loss of tissue, although during convalescence, when inflammation has subsided, it becomes possible to restore normal body composition. During long-term nutritional support for chronic conditions e.g. intestinal failure, it is possible, in most cases to maintain normal energy balance, proteosynthesis and nutritional status. In growing children or in patients recovering from muscle mass loss there should be an “anabolic” component to energy intake which is accordingly higher than energy expenditure. This is a necessary condition for growth, the healing process or increase of muscle mass.

- 55–60% of energy requirements should be covered by carbohydrates (glucose in PN and maltodextrin and starch in enteral nutrition). Complex carbohydrates and glucose are not only energy substrates. Glucose is also an important substrate for anaplerotic processes and for production of NADPH for synthetic, regenerative and antioxidant processes. Glucose replacement by sorbitol or fructose is not indicated in diabetic patients. This is because they do not improve the metabolic situation and can cause metabolic side-effects. Moreover the measurement of their plasma levels is not routine.

- Total fat energy should be 30-40% of total energy
  - 10-12% saturated
  - 14-19% monounsaturated
  - 6-9% polyunsaturated with increased ω-3 fatty acid

- Protein or amino acid intake is dependent on the clinical situation and the goals of nutritional support - 0.8-2.0 g·kg⁻¹·day⁻¹.

- Enteral nutrition should contain 20–30 g of fibre per day.

Type 1 patients have insulin deficiency and therefore need exogenous insulin to improve their metabolism towards normal. Dosage of insulin is then dependent on metabolic status and glycaemia. Both acute stress and severe inflammation lead to insulin resistance and the necessity to apply higher dosages of insulin. However, the presence of type 1 diabetes should not lead to suboptimal nutritional support, instead increased dosages of insulin should be administered.

### 4.1.2 Insulin Administration During Artificial Nutrition in Type 1 Diabetic Patients

The ways of administering insulin depend upon the clinical status and stability of the patient.

**Continual intravenous insulin infusion**

In unstable conditions, it is recommended to infuse insulin continually via a separate intravenous infusion during either enteral or parenteral nutrition. The rate of insulin infusion is adjusted according to frequent blood glucose monitoring. Normalisation of plasma glucose levels have been found to reduce catheter sepsis fivefold in diabetic patients (14). Other positive effects of intensive insulin treatment have been found in thoracic surgery (15), myocardial infarction (16) intensive care (13) and others. The dosage of insulin is regulated according to the plasma glucose level.
Levels of blood glucose should ideally be kept in the range 5-7 mmol/l, although this is not always possible to achieve without causing some episodes of hypoglycaemia. The level of blood glucose should be higher in critically ill diabetic patients (13). The method of intravenous insulin administration is shown in Fig. 1.

![Fig. 1 Insulin and glucose infusion during PN in unstable diabetic patient](image)

Table 1 provides an algorithm for intravenous management of patients in ward settings. In critical illness the glucose level control and insulin rate must be individualised. This is particularly important in critically ill diabetic patients, because in this group lack of insulin is combined with insulin resistance due to contraregulatory hormones (cortisol, catecholamines and glucagon) – see Topic 18- Nutrition in the ICU.

**Table 1**

Intravenous insulin infusion algorithm for ward settings (17)

<table>
<thead>
<tr>
<th>Plasma glucose level [mmol/l]</th>
<th>Insulin infusion rate [units/hr]</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;22.2</td>
<td>8</td>
</tr>
<tr>
<td>19.5 – 22.2</td>
<td>6</td>
</tr>
<tr>
<td>16.7 – 19.5</td>
<td>4</td>
</tr>
<tr>
<td>13.9 – 16.7</td>
<td>3</td>
</tr>
<tr>
<td>11.1 – 13.9</td>
<td>2.5</td>
</tr>
<tr>
<td>8.3 – 11.1</td>
<td>2</td>
</tr>
<tr>
<td>6.6 – 8.3</td>
<td>1.5</td>
</tr>
<tr>
<td>5.6 – 6.6</td>
<td>1</td>
</tr>
<tr>
<td>&lt; 5.5</td>
<td>0</td>
</tr>
</tbody>
</table>
Tony Woolfson showed many years ago, that this approach could lead to greater volatility of blood glucose with overshoot. He introduced a modified approach where the insulin infusion rate was adjusted not only according to the current blood glucose but took into account the direction of change since the last measurement:

### Table 2
**Method of insulin administration according to current blood glucose and the direction of change since last measurement (18).**

<table>
<thead>
<tr>
<th>Blood glucose (mmol/l)</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4.0</td>
<td>Reduce rate by 1.0 ml/hour</td>
</tr>
<tr>
<td>4.0 – 6.9</td>
<td>Reduce rate by 0.5 ml/hour</td>
</tr>
<tr>
<td>7.0 – 10.9*</td>
<td>Same rate</td>
</tr>
<tr>
<td>11.0 – 15.0</td>
<td>If lower than last test → same rate</td>
</tr>
<tr>
<td></td>
<td>If higher than last test → ↑ rate by 0.5 ml/hour</td>
</tr>
<tr>
<td>&gt; 15.0</td>
<td>If lower than last test → same rate</td>
</tr>
<tr>
<td></td>
<td>If higher than last test → ↑ rate by 1.0 ml/hour</td>
</tr>
</tbody>
</table>

If rate becomes 0.5 or 0 ml/hour → halve concentration (B) and restart at 0.5 ml/hour

If rate becomes 4.5 or 5 ml/hour → double concentration (B) and restart at 2.5 ml/hour

This method is superior in practice to the above and is described in the ESPEN Blue Book (4).

**Addition of insulin to parenteral nutrition mixture**

In diabetic patients and in patients who require insulin, insulin can be added to parenteral nutrition mixtures. Insulin is chemically stable in PN solutions, but adsorption to the plastic of the infusion set can cause decreased availability (19, 20). Surprisingly insulin availability in PN solutions is positively influenced by presence of micronutrients, especially trace elements (21). The insulin dosage should therefore be established not only for each patient but also for each AIO system.
This method is simple and easy to provide. Moreover, insulin is infused together with the nutrition mixture and risk of hypoglycaemia, if the feed is interrupted, is greatly reduced.

There are three important disadvantages of insulin application using this method:

- Mixing of insulin with artificial nutrition is only possible with parenteral nutrition;
- This method is inappropriate and potentially harmful in unstable conditions;
- Some portion of insulin is absorbed onto the material of the all-in-one bag. This amount is dependent not only on the materials used for the manufacture of the bag and giving set, but also on the PN composition and type of insulin used (19).

![Fig. 2](image_url)

**Fig. 2** Insulin concentration in parenteral nutrition mixtures with and without multivitamins and trace elements (MVITr) during infusion (21).

**Subcutaneous insulin application:**

Three basic methods of subcutaneous insulin application are described in this module.

I. Regular dosages of human short-acting insulin

This simple method can be used in unstable patients on general wards. The patient must receive nutrition (either enteral or parenteral) continuously and insulin is administered every 4-6 hours. Blood glucose is measured 30 minutes before the next insulin injection is due. The dosage of regular insulin can be given according to **Table 3**. This method allows correction of blood glucose levels over short periods, although it does not usually provide such tight control as the intravenous infusion method. It is easy to provide, however, and can also be used in subjects who are not very well compensated.
Table 3
Subcutaneous regular insulin supplementation in diabetic patients (17)
Insulin should be administered every 4 to 6 hours. For values in mg/dl multiply by 18.

<table>
<thead>
<tr>
<th>Plasma glucose level [mmol/l]</th>
<th>Subcutaneous insulin dose [units]</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.3 – 11.1</td>
<td>1 – 2</td>
</tr>
<tr>
<td>11.2 – 13.9</td>
<td>2 – 4</td>
</tr>
<tr>
<td>14.0 – 16.7</td>
<td>3 – 6</td>
</tr>
<tr>
<td>16.8 – 19.4</td>
<td>4 – 8</td>
</tr>
<tr>
<td>&gt; 19.4</td>
<td>5 – 10</td>
</tr>
</tbody>
</table>

II. Subcutaneous insulin pumps

Insulin pumps are small but exact devices used for subcutaneous insulin application in unstable diabetic subjects (22). They can be used for continuous or continual insulin administration, with rate adjustments according to blood glucose levels, or programmed to determine the rate of insulin infusion. They are useful especially in unstable type I diabetic patients and in patients who receive cyclic nutrition support. They are particularly suitable for the early stages of home artificial (especially parenteral) nutrition in diabetic patients.

Fig. 2 Subcutaneous insulin pumps

III. Long-acting insulin analogues

New insulin analogues have provided excellent practical results in the treatment of diabetic patients who are stable and receiving constant infusions of feed. This was shown in a publication where authors showed that a long-acting insulin analogue (glargine) was useful in diabetic patients receiving parenteral nutrition (23). Combinations of various insulin analogues (long- and short-acting) may be useful during cyclic home artificial nutrition.
4.2 Type 2 Diabetes Mellitus

Insulin resistance, usually due to obesity, is the primary mechanism in the development of type 2 diabetes mellitus, although many type 2 patients go on to develop insulin deficiency and require insulin treatment, particularly during undercurrent illness. Abdominal obesity with accumulation of visceral adipose tissue is the main risk factor and forms part of the "metabolic syndrome". Increased turnover of fatty acids and augmented liver glucose production are typical consequences of abdominal fat accumulation. Lipid storage in muscle tissue and hepatocytes is the next factor, which increases insulin resistance. It has been shown, that intramuscular steatosis decreases insulin-dependent glucose transport to skeletal muscle cells.

Glucose intolerance or frank type 2 diabetes is a component of the metabolic syndrome (see Module 21.1). Weight reduction and physical activity are the prime treatments of this type of diabetes, although most patients require drug treatment sooner or later. The mechanisms of actions of oral antidiabetic drugs differ substantially and their effectiveness is dependent on the clinical and metabolic situation. Moreover, oral antidiabetic drugs can influence metabolism adversely in critical illness. The main groups of oral antidiabetic drugs are shown in Table 4. The incretin, glucagon-like peptide 1 (GLP-1), which is now added to the table is not an oral drug (it is administered subcutaneously) but its effect is principally based on stimulation of endogenous insulin secretion.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Possible negative effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td>increase insulin secretion</td>
<td>hypoglycaemia</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>increase insulin secretion</td>
<td>hypoglycaemia</td>
</tr>
<tr>
<td>Biguanides</td>
<td>decrease liver glucose production</td>
<td>lactic acidosis due to decreased glucose production from lactate</td>
</tr>
<tr>
<td>Acarbose</td>
<td>decrease of glucose absorption</td>
<td>diarrhoea</td>
</tr>
<tr>
<td>Glitazones</td>
<td>PPARS agonists</td>
<td>fluid retention, weight increase, heart failure</td>
</tr>
<tr>
<td>Dipeptidyl peptidase-4 inhibitors</td>
<td>increase incretin levels</td>
<td>delayed gastric emptying, headache, nasopharyngitis,</td>
</tr>
<tr>
<td>SGLT-2 (Sodium-Glucose Co-Transporter 2) inhibitors</td>
<td>inhibition of reabsorption of glucose in renal tubules</td>
<td>loss of nutrients that are given for nutrition support, loss of water and electrolytes due to osmotic diuresis</td>
</tr>
<tr>
<td>Glucagon-like peptide-1 and analogues</td>
<td>Incretin _ stimulates endogenous insulin production</td>
<td>delayed gastric emptying, decreased gastric secretion, potential risk of pancreatitis and pancreatic cancer</td>
</tr>
</tbody>
</table>

It is generally accepted, that insufficient insulin secretion is the last stage leading from insulin resistance to manifest type 2 diabetes. Hence when production of endogenous insulin is decreased or diminished, treatment with exogenous insulin should be started. This is the rule in most critically ill patients, and in patients with severe acute (especially inflammatory) disease.
4.2.1 Nutrition Support in Type II Diabetic Patients

During acute illness or critical situations, the principles of nutritional support of the type 2 diabetic patients are not different from those in non-diabetic patients. The composition of macronutrients during artificial nutrition is also not different:

- **Energy** – usually 30-35 kcal·kg\(^{-1}\)·day\(^{-1}\)
  - 55–60% of energy as carbohydrates (glucose in PN and maltodextrin and starch in enteral nutrition)
  - 30–40% of energy as fat
    - 10-12% saturated fatty acids
    - 12-19% monounsaturated fatty acids
    - 6-9% polyunsaturated with increased \(\omega-3\) fatty acids
- **Protein or amino acids** 0.8–2.0 g·kg\(^{-1}\)·day\(^{-1}\) (dependent on clinical situation).
- **20–30 g** a day of fibre in the case of enteral nutrition

However, some specific metabolic problems must be taken into account in type 2 diabetes patients:

- Insulin sensitivity is decreased during acute illness due to contra-regulatory hormones and inflammatory cytokines. This, combined with the insulin resistance already present due to type 2 diabetes, necessitates higher insulin dosage in these patients.
- Both lactate and alanine production are increased during stress conditions (hypoxia, inflammation).
- Glucose production from lactate and alanine is increased during inflammation, hypoxia, hypovolaemia and other stress conditions.
- Biguanides inhibit glucose production (especially from lactate) and therefore can provoke development of lactic acidosis in severely ill patients.
- Absolute or relative lack of insulin can accelerate loss of muscle mass.
- Patients with metabolic syndrome (type 2 diabetes) are more susceptible to cardiovascular complications.

4.2.2 Insulin Application during Artificial Nutrition in Type 2 Diabetic Patients

Insulin application is frequently necessary in artificially fed patients with type 2 diabetes mellitus. This is due to the need to stop oral antidiabetic drugs and to the combination of insulin resistance and insufficient insulin secretion. During the acute phase of injury, when lactate production may be increased, biguanides, which inhibit gluconeogenesis may diminish lactate clearance through the Cori cycle and cause lactic acidosis. Additionally, accumulation of biguanides is a consequence of compromised renal function. As the effectiveness of oral antidiabetic drugs has not been studied in critically ill patients and because there are many potential negative effects (see Table 4) these drugs should therefore be stopped and insulin used to control the blood glucose. Hence, insulin administration is always indicated in type 2 diabetes patients who require artificial nutrition and who are suffering from critical illness. Moreover, insulin increases muscle protein synthesis and is therefore also useful as an anabolic agent. The methods of insulin application are the same as in type I diabetic subjects (see part 4.1.2).
In diabetic patient with severe lactic acidosis and history of recent ingestion of metformin (or other biguanides) immediate haemodialysis is indicated. This normalises acidosis, removes lactate and most importantly eliminates metformin.

4.2.3 Artificial Nutrition in Stable Obese Type 2 Diabetic Patients Who Need Weight Reduction

During acute intercurrent illness, the immediate need to preserve or restore lean mass with full nutritional support outweighs the longer-term aim of weight loss. However, in stable obese type II patients, who require nutritional support, the priority of weight loss to control diabetes and the metabolic syndrome returns and it is appropriate to reduce nutritional intake with that aim in mind (27). This is particularly the case in obese patients being prepared for elective procedures or those with gastrointestinal failure without significant inflammation.

The aims of artificial nutrition support in these patients are:
- Preserve or improve skeletal muscle quantity and function
- Improve wound healing
- Prevent further accumulation of subcutaneous and abdominal adipose tissue (which may complicate surgical procedures)
- Decrease extreme amounts of body fat

The patient must be in a stable situation without manifest inflammation. All possible inflammatory foci (abscesses, contaminated wounds etc.) must be cured before the commencement of this reduction regiments. Strict clinical and metabolic control is necessary during hypocaloric artificial nutrition. Especially regular control of glycaemia, muscle function and wound healing is necessary. Proper hydration is a necessary condition as well as haemodynamic stability.

Proteins and amino acids
The intake of proteins or amino acids should not be reduced. In some situations like wound healing this should be even increased to 1.5 – 2 g·kg⁻¹ of ideal body weight.

Carbohydrates
The amount of carbohydrate should cover the patient’s needs, although these may be difficult to define precisely. However according to the theoretical calculations (need for carbohydrate dependent tissues) the minimum requirement is approximately 180-220 g per day.

Lipid
Lipid intake should be reduced to that which is necessary to meet the requirement for essential fatty acids. Saturated fatty acids as well as medium chain fatty acids will be omitted. Usually 20 g of vegetable fat or LCT lipid emulsion is sufficient to cover the needs for essential fatty acids.
Table 5
Macronutrient composition during a hypocaloric diet for an obese diabetes type 2 patient

<table>
<thead>
<tr>
<th>Substrate</th>
<th>g.day⁻¹</th>
<th>kcal.day⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (amino acids)</td>
<td>80-160</td>
<td>320-640</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>150-220</td>
<td>600-880</td>
</tr>
<tr>
<td>Fat (lipid emulsion)</td>
<td>20</td>
<td>200</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1120-1720</td>
</tr>
</tbody>
</table>

This artificial nutrition formula facilitates weight reduction in most obese type II diabetic patients. When the blood glucose rises above 7 mmol/l, insulin treatment should be given - as described above.

It must be stressed that the nutrition effectiveness of the described hypocaloric artificial nutrition regimen is significantly lower in comparison with regimens which provide all energy needs. As emphasized above it should not be used during acute illness when nitrogen balance is the first priority, and it is useful only for those persons who profit from weight reduction (27).

5. Concept of Euglycaemia during Artificial Nutrition in Diabetic Patients

The consequence of chronic hyperglycaemia is glycosylation of various proteins, free radical production and adverse clinical outcomes (see part 2.1). Numerous studies have shown that hyperglycaemia is associated with increased morbidity and mortality in hospitalized patients. It is well known that hyperglycaemia in artificial nutrition patients is connected with poor outcomes (2, 28-30). It has been shown that in patients on parenteral nutrition the risk of any complication increased by a factor of 1.58 for each 1 mmol.l⁻¹ increase in blood glucose. Similar increases in risk with higher blood glucose levels were also seen with other outcome parameters (31) (see Table 6).

Table 6
Risk of complications in relation to increase of mean daily blood glucose level (31). For values in mg/dl multiply by 18

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any infection</td>
<td>1.40 (1.08–1.82)</td>
<td>0.01</td>
</tr>
<tr>
<td>Septicaemia</td>
<td>1.36 (1.00–1.86)</td>
<td>0.05</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>1.47 (1.00–2.17)</td>
<td>0.05</td>
</tr>
<tr>
<td>Cardiac complications</td>
<td>1.61 (1.09–2.37)</td>
<td>0.02</td>
</tr>
<tr>
<td>Death</td>
<td>1.77 (1.23–2.52)</td>
<td>0.01</td>
</tr>
<tr>
<td>Any complication</td>
<td>1.58 (1.20–2.07)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

The adverse effects of hyperglycaemia are greater in non-diabetic than diabetic hospitalized patients (32).

The metabolic response to stress and inflammation is mediated by catabolic hormones (glucagon, catecholamines and corticoids) as well as by cytokines, eicosanoids, oxygen radicals, and other local mediators (see topic: Nutrition in ICU). Hyperglycaemia and insulin
resistance are proportional to the severity of illness that is itself a risk factor for outcome (33). Insulin resistance appears designed to provide substrate to combat bacterial invasion, support immune responses, heal wounds, etc. This stress response is essential for survival in the short term in spite of the loss of body cell mass (especially muscle tissue). On the other hand, a serious loss of body cell mass can be critical to the development of later complications and for long-term survival. The stress response has evolved therefore as a balance between immediate and long term needs to give the individual the best chance of survival. Changes in insulin resistance and switching of substrate availability between tissues is part of this balance.

Intensive insulin therapy with the aim of normalising plasma glucose level (4.4 – 6.1 mmol/l) was shown to decrease ICU mortality by 47% and hospital mortality by 34% in critically ill surgical patients (12). This study was repeated by these authors in the medical ICU using the same protocol. Mortality was not significantly reduced in the intensive-treatment group, although several positive outcomes were seen such as a reduced duration of mechanical ventilation, and earlier discharge (34). The explanation of this favourable effect of insulin treatment is not entirely clear. It was suggested that high plasma glucose itself was responsible for detrimental effects. Mechanisms like mitochondrial injury, free radical production and protein glycation have been assumed as aetiological factors. Moreover, insulin is an anabolic hormone which prevents loss of body cell mass (especially muscle mass) and this could be one of its beneficial effects in acute illness. Addition of insulin to parenteral nutrition mixtures increased the rate at which the malnourished state was corrected (34).

However, other randomized trials as well as two meta-analyses, have failed to demonstrate an improvement in morbidity and mortality with tight glycaemic control, although they found significantly more hypoglycaemia (35-37). Moreover in the NICE-SUGAR study the intensive glucose control increased mortality. A blood glucose target of 10 mmol·l⁻¹ or less resulted in lower mortality than did a target of 4.5 to 6.0 mmol·l⁻¹ (38). The authors of the meta-analysis came to the conclusion that the intensive insulin therapy significantly increased the risk of hypoglycemia, but had no mortality benefit among critically ill patients. However, it may be beneficial to patients admitted to a surgical ICU (39).

At the present time it is recommended that insulin therapy should be initiated for treatment of persistent hyperglycaemia, starting at a threshold of no greater than 10.0 mmol·l⁻¹. Once insulin therapy has been started, a glucose range of 7.8 to 10.0 mmol·l⁻¹ is recommended for the majority of critically ill patients. For the majority of non-critically ill patients treated with insulin, the pre-meal blood glucose target should be lower than 7.8 mmol·l⁻¹ in conjunction with random values lower than 10.0 mmol·l⁻¹, provided that these targets can be safely achieved (40).

6. Summary

- The prevalence of diabetes mellitus among hospitalised adult patients can be as high as 20%. There are two basic types of diabetes mellitus – types 1 and 2. Type 1 is characterised by an absolute insulin deficit, while type 2 begins with insulin resistance with later development of partial insulin deficiency. Diabetic patients have more artificial nutrition related complications, which is mainly due to chronic hyperglycaemia and other factors including immune dysfunction, vascular disease, renal insufficiency etc. However their requirements for macro- and micro-nutrients do not differ substantially from those of non-diabetic patients.
- In type 1 diabetes insulin must be administered during nutritional support. The method of insulin administration is dependent on the clinical situation, presence of inflammation,
method of nutrition delivery (enteral or parenteral) and other conditions. Insulin can be given intravenously or subcutaneously using various devices like intravenous syringe insulin pumps, subcutaneous insulin pumps and subcutaneous insulin injections.

- In type 2 diabetic patients oral drug treatment should be stopped in stress conditions. Biguanides are particularly dangerous in conditions when lactate production is increased (hypoxia, inflammation, cardiac insufficiency). Obese type II diabetic patients often profit from hypocaloric nutrition, but only when they are stable and any acute inflammatory illness has passed. This may improve their condition before elective procedures. However strict monitoring of these patients is necessary to avoid reducing nutritional intake to the point where there is excessive loss of lean body mass.
- Acute illness and inflammation initiate insulin resistance, which further impairs insulin effectiveness in already insulin-resistant type 2 diabetic patients.
- Good control of glucose level improves effectiveness of nutrition support not only in diabetic patients but also in patients with insulin resistance.

7. References

15. Furnary AP, Zerr KJ, Grunkemeier GL, Starr A. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients


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