Consequences of diabetes on the nutritional status

Module 21.2.

Nutritional support in diabetes Type I and II

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Learning Objectives:

- To know the different approaches to patients with type I and type II diabetes;
- To be able to prescribe nutrition support to patients with insulin deficiency;
- 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 II diabetes;
- To know how insulin resistance influences nutrition support;
- To be familiar with the concept of hypocaloric artificial nutrition in obese type II diabetic patients;
- To be able to understand the concept of glucose control in diabetic patients.

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Key Messages:

- Incidence 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 nutritional support in diabetic patients;
- There is an absolute deficit of insulin in type I diabetes mellitus;
- Type II 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 of enteral or parenteral nutrition application in diabetic patients;

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• The formulation of artificial feeds should depend on the underlying clinical state and not just on the presence of diabetes;
• In obese type II diabetic patients weight reduction can be useful;
• Good glucose control is recommended in diabetic patients, but glucose should be higher than in non-diabetic patients requiring artificial nutrition during intensive care.
1. Introduction

Diabetes mellitus is widespread among hospitalised adult patients. Its prevalence in American hospitals was 12.45% in 2000 (1). Moreover it is a commonly encountered comorbid condition; it was shown recently that 18-26% of hospitalised adults had a secondary diagnosis of diabetes(2, 3, 4). Type I diabetes is increasing in prevalence in some countries, being 0.3–0.4% of the population. Type II diabetes is increasing much more rapidly, largely due to the rising prevalence of obesity (BMI > 30), e.g. from 6 to 20% since 1980 in the UK. In many European countries prevalence of non-insulin dependent diabetes mellitus (NIDDM – type II) is increasing with age (5). It is therefore logical, that diabetes is also becoming more frequent in patients who require nutritional support for various (other) diseases.

2. Aspects of nutritional support in diabetic patients

The homeostatic mechanisms that maintain euglycaemia in the postabsorptive state and which control postprandial glucose metabolism are impaired in patients with diabetes. Patients with diabetes have decreased insulin secretion (type I) or decreased insulin effect (type II) or both (later type II), causing pre- and postprandial hyperglycaemia due to increased hepatic glucose production and decreased glucose uptake in tissues with insulin sensitive glucose transporter (GLUT 4) (6, 7). However, insulin influences the metabolism of all macronutrients. Besides carbohydrates it has also 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 whole person. This should be kept in mind when nutritional support is provided to a diabetic patient.

Major metabolic functions of insulin:

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
- Stimulation of fatty acid synthesis
- Suppression of circulating ketone body concentrations
- Activation of adipose lipoprotein lipase
- Inhibition of lipolysis in adipose tissue
- Stimulation of lipogenesis

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

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

Almost all the effects mentioned before can to some extend influence metabolism of energy substrates during nutritional support. Glucose intolerance and high glucose levels in plasma are major consequences of diabetes mellitus (both type I and type II). Hyperglycaemia can itself lead to many adverse effects on several cellular and organ systems.

3. Influence of hyperglycaemia

Short-term hyperglycaemia can adversely affect:
- Fluid balance
Through glycosuria, along with loss of body water and subsequent dehydration

- Immune function
  - Abnormalities in white cell function especially impaired granulocyte adhesion, chemotaxis, phagocytosis, respiratory burst, superoxide formation, and intracellular killing (8, 9)
  - Glucose, through complement glycation, has the potential to inhibit opsonization.

- Inflammation
  - Hyperglycaemia changes inflammatory processes and affects oxidative equilibration

- Clinical outcome
  - Observational studies indicate that hyperglycaemia worsens the prognosis of patients following myocardial infarction and stroke (10).

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 diseases and in patients with malignancies. However increased insulin resistance is also apparent during pregnancy, lactation and rapid growth (11, 12).

The 2001 data led to a general recommendation to keep the plasma glucose level within the normal (healthy) range (13). However, at present the criteria are not so strict. The plasma glucose should be kept in the normal range in non-diabetic and stable patients; in critically ill or septic patients the plasma glucose must be controlled but it need not be in range normal for healthy subjects. Instead a safe level which prevents development of hypoglycaemia is recommended in critically ill patients as well in diabetic patients during nutritional support (14).

4. Nutritional support in diabetic patients

4.1. Type I diabetes mellitus

In this type of diabetes there is absolute deficit of endogenous insulin. This is due to the destruction of the islets of Langerhans in the pancreas (B cells) by an auto-immune mechanism, although it may be also result from other destructive processes, e.g. haemochromatosis, severe acute pancreatitis or pancreatic resection.

There are low plasma level of insulin and C peptide (a peptide fragment of proinsulin which is released from B cells during insulin secretion). In autoimmune type I diabetes specific antibodies are found in the plasma (especially antibodies against glutamate decarboxylase).

4.1.1. Nutrition support in type I diabetic patients

The indications for nutritional support in patients with type I diabetes are predominantly due to intercurrent illness rather than to the diabetes. 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 (usually 30-35 kcal·kg⁻¹·day⁻¹), and to achieve and maintain a desirable body weight, to maintain normal function and as far as possible to preserve lean body mass. 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 overall nutritional status. In growing children or in patients recovering from muscle mass loss the “anabolic” part of energy intake should be higher than energy expenditure. This is a necessary condition for growth, healing or increase in 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 reactions (such as the TCA/Krebs’ cycle) 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.

- Total fat energy should be 30-40%
  - 10% saturated
  - 12% monounsaturated
  - 6% polyunsaturated with increased ω-3 fatty acids (ω-3 PUFA should be 25-35% of PUFA)

- Preferred protein or amino acid intake is dependent on the clinical situation and the goal of nutritional support and will be in the range - 0.8-2.0 g·kg⁻¹·day⁻¹.
- Enteral nutrition should contain 20–30 g of fibre per day.

Type I patients have insulin deficiency and therefore need exogenous insulin to improve their metabolism towards normal. The optimal dosage of insulin depends on metabolic status and on glycaemia. Both acute stress and severe inflammation lead to insulin resistance and the need to use higher dosages of insulin. However, the presence of type I 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 I diabetic patients.

Depending upon the clinical status and stability of the patient there are several ways of administering insulin.

Continuous intravenous insulin infusion

In unstable conditions insulin should be given by continuous intravenous infusion during enteral or parenteral nutrition and adjusted according to frequent blood glucose monitoring. Normalisation of plasma glucose levels have been found to reduce catheter sepsis fivefold in diabetic patients (15). Other positive effects of intensive insulin treatment have been found in thoracic surgery, myocardial infarction (17) intensive care (13) and other contexts. The dosage of insulin is regulated according to the plasma glucose.

Levels of blood glucose should ideally be kept in the range 5-7 mmol/l (90-125 mg/dl), although this is not always possible to achieve without causing hypoglycaemia. The level of blood glucose should be higher in critically ill diabetic patients (14). The method of intravenous insulin administration is shown in Fig. 1.
Table 1 provides an algorithm for intravenous insulin for patients in the ward setting. 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 regulatory hormones (cortisol, catecholamines and glucagon) – see Topic 18 – Nutrition in the ICU.
Table 1. Intravenous insulin infusion algorithm for ward settings (18)

<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>

Multiply by 18 for mg/dl

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 also 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 (19).

<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 algorithm in Table 1 above and is described in more detail in the ESPEN Blue Book (4).
Addition of insulin to parenteral nutrition mixtures

In diabetic patients and in patients who require insulin, insulin can be added to parenteral nutrition mixtures. Insulin is chemically stable in PN, but adsorption to the plastic of the infusion set can cause decreased availability (20, 21). Surprisingly insulin availability in PN solutions is positively influenced by presence of micronutrients, especially trace elements (22). 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 the 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 useless 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 material used for the manufacture of the bag and giving set but also on the PN composition and the type of insulin used for the parenteral nutrition.

![Fig. 2. Stability of insulin expressed as insulin concentration (µU/ml) in parenteral nutrition mixtures with and without multivitamins and trace elements (MVITr) during infusion (22).](image)

**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, but 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 (18) Insulin should be administered every 4 to 6 hours.

<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>

Multiply by 18 for mg/dl

II. **Subcutaneous insulin pumps**

Insulin pumps are small exact devices used for subcutaneous insulin application in unstable diabetic subjects (23). They can be used for continual insulin administration with rate adjustments according to blood glucose levels or the rate of insulin infusion can be programmed. They are especially useful in unstable type I diabetic patients and in patients who receive cyclic nutritional support. They are particularly suitable for the early stages of home artificial (especially parenteral) nutrition in diabetic patients.

![Subcutaneous insulin pumps](image)

**Fig. 3.** 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, for example, in a publication where the authors showed that a long-acting insulin analogue (glargine) was useful in diabetic patients receiving parenteral nutrition (24). Combinations of various insulin analogues (long- and short-acting) may also be useful during cyclic home artificial nutrition.
4.2. Type II diabetes mellitus

Insulin resistance, usually due to obesity, is the primary mechanism in the development of type II diabetes mellitus, although many type II patients go on to develop insulin deficiency and require insulin treatment, particularly during undercurrent illness. Abdominal obesity with accumulation of visceral adipose tissue is a key 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 was shown that intramuscular steatosis decreases insulin-dependent glucose transport to skeletal muscle cells. Glucose intolerance or frank type II 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.

Table 4. Major groups of oral antidiabetic drugs.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism of action</th>
<th>Possible negative effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylureas</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 in 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>
</tbody>
</table>

It is generally accepted that insufficient insulin secretion is the last stage leading from insulin resistance to manifest type II diabetes. Hence when production of endogenous insulin is decreased or diminished, treatment with exogenous insulin should be started. This is the rule especially in critically ill patients, and in patients with 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 II diabetic patient are no different from those in non-diabetic patients. The composition of macronutrients during artificial nutrition is also no 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 in fat
  - 10% saturated fatty acids
- 12% monounsaturated fatty acids
- 6% polyunsaturated fatty acids with increased ω-3 fatty acids

- Protein or amino acids 0.8-2.0 g kg⁻¹ day⁻¹ (dependent on clinical situation).
- 20–30 g of fibre in the case of enteral nutrition

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

4.2.2. Insulin administration during artificial nutrition in type II diabetic patients.

Insulin application is frequently necessary in artificially fed patients with type II diabetes mellitus. This is due to the need to stop oral antidiabetic drugs and to a 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. These drugs should therefore be stopped and insulin used to control the blood glucose. Therefore, insulin administration is always indicated in type II diabetes patients who require artificial nutrition and who are suffering from critical illness. Moreover insulin increases muscle protein synthesis and therefore is also useful as anabolic agent. The methods of insulin administration are the same as in type I diabetic subjects (see part 4.1.2).

In the diabetic patient with severe lactic acidosis and a 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 II diabetic patients who need weight reduction

During acute intermittent illness, the immediate need to present 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 (25). 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 to:
- Preserve or improve skeletal muscle function and quantity
- 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 eliminated before the commencement of this reduction regimen. Strict clinical and metabolic control is necessary during hypocaloric artificial nutrition. Especially regular monitoring 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 theoretical calculations (the need of carbohydrate dependent tissues) the minimum requirement is approximately 180-220 g per day.

**Lipids**
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 must be omitted. Usually 20g of vegetable fat or LCT lipid emulsion is sufficient to cover the needs of essential fatty acids.

**Table 5.** Macronutrient composition of the hypocaloric diet for the obese patient with type II diabetes.

<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 blood glucose rises above 7 mmol/l (125 mg/dl), insulin treatment should be given - as described above.

It must be stressed that the nutritional effectiveness of the hypocaloric artificial nutrition regimen described is significantly lower in comparison with regimens which provides 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 will profit from weight reduction (25).

**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 outcome (3, 26, 27, 28). It was shown that in patients on total parenteral nutrition the risk of any complication increased by a factor of 1.58 for each 1 mmol·l⁻¹ (18mg/dl) increase in blood glucose. Similar increases in risk with higher blood glucose levels were also seen with other outcome parameters (29) (see Table 6).

**Table 6.** Risk of complications in relation to increase of mean daily blood glucose level (29)

<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 (30).

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 LLL topic on nutrition in ICU. Hyperglycaemia and insulin resistance are proportional to the severity of illness that is itself a risk factor for outcome (31). They appear 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 a critical factor in the development of later complications and in poor 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; 80-110mg/dl) was shown to decrease ICU mortality by 47% and hospital mortality by 34% in critically ill surgical patients13. This study was then repeated by the same 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 (32). The explanation of this favourable effect of insulin treatment is was 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 solutions increased the rate at which the malnourished state was corrected (33).

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 (33-36). Moreover in the NICE-SUGAR study intensive glucose control increased mortality. A blood glucose target of 10 mmol·l⁻¹ (180mg/dl) or less resulted in lower mortality than did a target of 4.5 to 6.0 mmol·l⁻¹ (80-110 mg/dl). The authors of the meta-analysis came to the conclusion that the intensive insulin therapy significantly increased the risk of hypoglycaemia, but
had no mortality benefit among critically ill patients. However, it may be beneficial to patients admitted to a surgical ICU (38). 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\(^{-1}\) (180mg/dl). Once insulin therapy has been started, a glucose range of 7.8 to 10.0 mmol·l\(^{-1}\) (140-180 mg/dl) 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\(^{-1}\) (140mg/dl) in conjunction with random values lower than 10.0 mmol·l\(^{-1}\) (180mg/dl) provided these targets can be safely achieved (39).

6. Summary

The prevalence of diabetes mellitus among hospitalised adult patients can be as high as 12%. There are two basic types of diabetes mellitus – types I and II. Type 1 is characterised by an absolute insulin deficit, while type II 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, with other factors including immune dysfunction, vascular disease, renal insufficiency, etc. However diabetic patients’ requirements for macro- and micro-nutrients do not differ substantially from those of non-diabetic patients.

In type I 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 methods including intravenous insulin syringe pumps, subcutaneous insulin pumps, and subcutaneous insulin injections. In type II 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


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