Obesity Diabetes and Ketoacidosis in Elderly

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Abstract

Diabetes can have significant health implications for life expectancy. The effect depends on various factors, such as how quickly a person gets diagnosed and treated, and how well they and their health care staff manage the situation.

Keywords: GMP-1; Insulin; Leptin; Treatment-Target

Abbreviations

FAD: Flavin Adenine Dinucleotide; FADH$_2$: Hydroxyquinone Form of FAD; AKA: Alcoholic Ketoacidosis; EABV: Effective Arterial Blood Volume; PAnion gap: Plasma Anion Gap; $P_{\text{Glucose}}$: Concentration of Glucose in Plasma; $PHCO_3^-$: Concentration of Bicarbonate ($HCO_3^-$) Ions in Plasma; $\beta$-HB: Beta Hydroxybutyrate Anion; AcAc: Acetoacetate Anion; ADP: Adenosine Diphosphate; ATP: Adenosine Triphosphate; NAD+: Nicotinamide Adenine Dinucleotide; NADH: H$^+$, reduced form of NAD$^+$; TG: Triglycerides; $P_{\text{Osmolal}}$ gap: Plasma Osmolal Gap

Figure 1: The obesity complications bring to mortality [1].

Introduction

Natural History of Obesity Leading to Diabetes Type 2: Complications of Onset of Diabetes Genetic Sensitivity Environmental Factors Nutrition Inactivity IGT Continuous Hyperglycemia Insulin Resistance Death Risk Disease Metabolic Syndrome Hyperglycemia Hypertension Nephropathy.

Overweight and diabetes, in particular, type 2 diabetes, are closely related. Obesity [2] is the major risk factor for type 2 diabetes, and the current increase in obesity in our society has led to a significant increase in the expression of this disease. Not only does weight, through the insulin resistance mechanism, exacerbate hyperglycemia. It also increases the risk of hypertension, hyperlipidemia and other conditions leading to cardiovascular disease [3].

Choosing drugs for people with diabetes involves examining several factors, including effects on weight [4]. Improvements in glucose control are most often associated with body-weight gain, and this does not have to be the only result of diabetes treatment. You may consider adding a drug that promotes weight loss, or it is neutral in weight to a drug that promotes weight gain and providing medical nutrition.

Although molecular approaches that alter mitochondrial content have suggested a direct link between mitochondrial bioenergy and insulin sensitivity, paradoxically, dietary intake of high fat (HF) increases mitochondrial content while causing insulin resistance. We hypothesized that, despite the migration of mitochondrial biogenesis, consumption of the HF diet would impair mitochondrial ADP sensitivity in mouse skeletal muscle and therefore be expressed in mitochondrial function in the presence of ADP concentrations suggestive of skeletal muscle biology. We found that HF intake increased mitochondrial protein expression; However, complete mitochondrial respiration and ADP sensitivity have been impaired in a variety of biologically relevant ADP concentrations. Also, HF intake reduced the ability of ADP to suppress mitochondrial \( H_2O_2 \) emission, further pointing to ADP sensitivity deficiencies. The abundance of ADP transport proteins was not altered, but the susceptibility to carboxy ester actyllose-mediated inhibition was attenuated after HF consumption, resulting in changes in ADP sensitivity of adenine nucleotide translocase (ANT) in these observations. Furthermore, palmitoyl-CoA is known to inhibit ANT, and modeled intramuscular palmitoyl-CoA concentrations that occur after HF consumption have exacerbated ADP sensitivity deficiency. Overall, these data suggest that HF nutrition triggers mitochondrial dysfunction secondary to a substantial impairment of palmitoyl-CoA-enhanced mitochondrial ADP sensitivity [5].

The current approach to treating type 1 and type 2 diabetes is to achieve the best glucose control. Previous clinical studies have shown that glycemia plays a crucial role in preventing both macro- and microvascular complications [6]. The current guidelines of the (ADA) indicate a glycemic target of having hemoglobin A1c (A1C) < 7%, but also stated that an A1C of ≤ 6% should be a target if this can be achieved without risk of complications [7]. Deficiency in glucose (fasting) (IFG), known as pre-diabetes, the risk of dramatically progressing to clinical diabetes [8] cardiovascular event cardiovascular disease and mortality in the third national health and nutrition survey (1988 to 1994) screened for 2000 pre-diabetes is very common, affecting nearly 12 million overweight people aged 45 to 74 years in the United States Weight loss and control are critical targets for people with diabetes. Weight loss improves insulin sensitivity to glycemic control [9] lipid profiles, blood pressure [10] mental health and health [11,12]; Moderate weight loss over time may be connected with mortality reduction [13,14]. Similarly, a large number of randomized controlled trials have shown that weight loss is also a considerable potential management strategy for overweight people with diabetes because it can delay or prevent progression. For type 2 diabetes is defined clinically. The position statement recommends that “people at high risk of developing diabetes should be aware of the benefits of some weight loss and regular exercise” [15].

The role of nutrition versus exercise interventions for Weight loss in people with pre-diabetes needs supplementation learning. Exercise interventions demonstrate benefits among people with diabetes, regardless of weight loss [16] and there is some data to support...
the positive effect of exercise on prevalence Diabetes regardless of weight loss [17]. The Role of Other Weight Loss Strategies (Isolated or Combined With nutritional, active or behavioral interventions) Such as medication [18] surgical interventions, or public health interventions (such as changes in The physical and social environment must still be determined). More research on weight control is needed obesity strategies and prevention. Small improvements in weight and other cardiovascular disease risk factors appear to be achievable in populations With abnormal glycemia. Another study is It is necessary to examine the impact of these interventions on Morbidity and mortality and their effectiveness in other High-risk populations. Work is needed to investigate Translation and implementation of these results in Community definition.

There is a high incidence of obesity [19] worldwide without many new drugs. Happy to take care of it. Therefore, a new view is urgently needed, Approaches to Obesity Treatment.

Bioactive peptides were used to treat metabolism Disorders - such as type 2 diabetes and obesity; While also having antioxidants, Anti-inflammatory, antimicrobial and antiviral properties. However, the development of These peptides occurred behind the scenes due to their size, reduced stability, poor delivery And bioavailability, rapid degradation rate, etc. But with the advent of newer Multifunctional peptide techniques, mimetics, peptide analogs, and aptamers, where Is a sudden revival in this therapeutic field. Increased attention is needed Development of the natural peptides from food and from aquatic sources that may mimic The role of mediators involved in weight management to prevent obesity. Here, The search for obese peptide structures was carried out in order Establish the potential for future drug development. Search extensively Current state of endogenous peptides, seafood, and novel Interesting experimental approaches based on peptidomimetics for obesity control, Presented. Apolipoprotein A-I (apoA-1), melanocortin-4 receptor (MC4R) Agonist, GLP-1 double and triple agonists, neuropeptides and prolactin release peptidomimetics have been specifically tested for their role in obesity. New peptides, mimetics, and synthesis interventions occur and may offer safer alternatives to another case It is almost impossible to obtain a safe anti-Brit drug. A deeper understanding of peptides and whole Chemistry using peptide engineering can be useful to overcome Disadvantages and choose the best mimics and analogs for future care.

Figure 2: GLP-1 synthesis, release, metabolism and effects of GLP-1 on body organs: Stimulate secretion of GLP-1 from intestinal L-cell after meal ingestion and activated GPR-119 receptors through cAMP. GLP-1 and GIP rapidly converts inactive metabolites by DPP-4 enzyme. Inhibition of DPP-4 enzyme activity by specificDPP-4 enzyme inhibitors and prevents GLP-1 and GIP degradation. GLP-1 actions in peripheral body tissue. Mostly GLP-1 action by specific GLP-1 receptors present on specific body tissues such as pancreas, GLP-1 increase insulin biosynthesis, secretion from beta cells and inhibits glucagon secretion from alpha cells in pancreas. However, the indirect action of GLP-1 in another body tissue liver (reduces hepatic gluconeogenesis), brain (Increase Neuroprotection) etc [20].
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The role of ghrelin and leptin in weight gain [21-24]

Obesity is a complex metabolic and behavioral disorder associated with increased health risk, including coronary artery disease, heart failure and sudden cardiac death. Effective obesity prevention and treatment strategies are needed. This unmet need for effective and safe anti-biscuit drugs has resulted in many new treatments at various stages of development. Obesity has become one of the most intensively studied diseases due to the availability of appropriate animal and cell culture models for adipocyte differentiation and appetite regulation.

Opiates as appetite suppressant

Contrave® is a combination therapy of naltrexone and bupropion and is currently undergoing phase III clinical trials by Orexigen Therapeutics. Bupropion was used to treat depression and addiction to smoking, while naltrexone was used independently to treat the withdrawal of opiate addiction. It has been argued that the combination of these two drugs, naltrexone and bupropion, synergistically increases the firing of neurons and reduces food intake through satiety. One of these two components, naltrexone, is known as an opioid receptor antagonist and competitively linked to the same binding site as morphine, which is a natural opioid analgesic compound isolated from the plant poppy. Naltrexone can be synthetically described as a substitute oxymorphone and an oxymorphone is a semi-morphine derivative with a stronger analgesic effect than morphine itself. Based on the concept of the relationship between structure and activity in medical chemistry, molecules with structural similarity tend to act similar biologically, especially in the case of enzymatic activities. However, because of the complexity of biological systems, little disruption of structural elements can result in precisely opposite biological actions. As shown in figure 3, oxymorphone and morphine are opioid receptor agonists, whereas naltrexone acts as an antagonist, despite their structural similarities [25,26].

Figure 3: Appetite suppressors [24,25,27].

The hunger games

Simply put, the ghrelin makes you feel hungry. Why is perceived hunger so important? Because research has highlighted hunger as a complex cause of many diets failing.

Studies have repeatedly shown an increase in ghrelin levels following low-calorie weight loss diets. One study published in the New England Journal of Medicine showed a 24 percent increase in ghrelin after a six-month weight loss diet. Preparation phase and witnessed a 40 percent increase in ghrelin levels after six months of diet! [28].

If you are dieting continuously or have been dieting several times before, your starting ghrelin levels are likely to be high. This can be bad news if you want to stay lean all year or diet again in the future.

Intestinal peptides play many roles in gastrointestinal function and initiation. The plasma levels of these peptides are affected differently by the presence of gastrointestinal nutrients and peptide release patterns are both compatible feeding stimulating and inhibitory actions. Several of these peptide systems have been tested as potential targets for the development of anti-disease drug. Progress has progressed in development long-acting peptide analogues and in some cases non-peptide agonists and antagonists. It remains to be shown whether any individual approach will have significant long-term effectiveness.

**Figure 4:** Approaches targeting multiple systems may ensure the highest promise.

**Lixisenatide (Lyxumia)**

Lixisenatide is a synthetic analogue of human GLP-1 which acts as a GLP-1 receptor agonist. Lixisenatide is a peptide containing 44 amino acids, which is amidated at the C-terminal amino acid (position 44). The order of the amino acids is given in the figure below. Its molecular weight is 4858.5, and the empirical formula is $\text{C}_{215}\text{H}_{347}\text{N}_{61}\text{O}_{65}\text{S}$ with the following chemical structure:

**Figure 5:** Lyxumia.
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Mechanism linking diabetes mellitus and obesity

The body mass index has a strong relationship to diabetes and insulin resistance [30]. Inside Obese people, the amount of unapproved fatty acids, glycerol, hormones, cytokines, Pre-inflammatory markers and other substances involved in insulin development resistance, increased. The pathogenesis of diabetes development is based on the fact because β-cells of the pancreas are damaged and cause a lack of blood glucose control. Diabetes development becomes inevitable if the failure of pancreatic islet cells. Together with insulin resistance.

Weight gain and body mass are the fundamentals of the work and an increase in type 1 diabetes and type 2. This literature review will demonstrate the Facts linking obesity with insulin resistance and β-cell function. In conclusion, New approaches to managing and preventing diabetes should be studied in obese people Questioned based on the facts.

Obesity treatment will treat type 2 diabetes [31]

Weight loss is an essential target for people who are overweight or obese, especially those with type 2 diabetes. A diet, exercise, and behavior change program can successfully treat obesity but may justify medication and/or surgery.

Diet

Weight loss occurs when energy expenditure exceeds energy consumption. Creating an energy deficit of 500-1,000 calories a day will result in a weight loss of two pounds per week. Food registration, portion size, and calorie count increase awareness and provide objective evidence of caloric intake.

For effective weight loss, calories are the ones that do not count the percentage of fat, carbohydrate or protein. However, when people lose weight, they must adhere to a diet similar to that recommended in the 2005 American Dietary Guidelines: Fat 20 - 35 percent of calories; Carbohydrate 45 - 65 percent; Protein 10 - 35 percent.

For a patient affected by obesity with diabetes or insulin resistance, restricting complex carbohydrate doses may be helpful. These foods include bread, rice, pasta, potatoes, cereals, peas and sweet potatoes. Complex carbohydrates can raise blood sugar more than other foods, causing the body to produce and use more insulin. With insulin resistance, these increased amounts of insulin can promote weight gain.

Increasing the amount of fiber in this diet may be beneficial for both diabetes and obesity. High intake of dietary fiber, especially of the soluble type, can improve glycemic control, reduce hyperinsulinemia and decrease plasma lipid concentrations in patients with type 2 diabetes. Demand for more chewing and taking longer to eat, providing less calories per serving, creating a gut feeling and improving fullness between meals.

Exercise

Regular exercise helps maintain weight loss and prevent a recurrence. It improves insulin sensitivity and glycemic control, may reduce the risk of developing diabetes and reduce diabetes mortality.

A target for 30 to 45 minutes of moderate training must be carried out five times a week. The exercise does not have to take place in one session to benefit. Using the activity into multiple and short episodes yields similar benefits and can improve compliance. Using a pedometer can help determine objective training goals. To increase the number of steps per day, with a goal of 8,000 steps, is ideal. Any increase in activity along the baseline will help balance the equation of fewer calories in the face and more calories to promote weight loss.

Medicines

There are several drugs designed to treat diabetes, insulin resistance, and obesity. A full review of these drugs is not an area of this article. However, metformin is one drug that has been shown to be beneficial in lowering the risk of type 2 diabetes in patients with insulin resistance. Metformin has reduced the rate of diabetes progression in obese people with impaired glucose tolerance.

Metformin-treated men who had major obesity and other metabolic syndromes (insulin resistance, hypertension, hyperlipidemia) suffered slightly more weight loss and fasted blood glucose levels lower than those receiving placebo.

Bariatric surgery

According to the National Institutes of Health (NIH), bariatric surgery should be considered by anyone with BMI greater than 40, or who have a BMI of 35 - 39.9 and medical problems like diabetes, heart disease or sleep apnea.

Bariatric surgery changes the normal digestive process. There are three types of surgery: restrictive, malabsorptive and combined limiter/malabsorptive. The NIH website provides an overview of the procedures and how they produce weight loss.

Studies continue to show that diabetes can be cured in many patients using bariatric surgery. These clinical improvements occur not only because of the significant weight loss, but because of hormonal changes that occur when food bypasses the stomach.

Patients and physicians should consider the risk of bariatric surgery compared to the risk of obesity and related medical problems. When other weight loss methods have failed, bariatric surgery may cause significant and sustained decline.

Prevention

Prevention and treatment of obesity will help prevent and treat diabetes. Promoting a healthy lifestyle among children and adolescents will help them reduce their risk of diabetes and its complications. Helping high-risk adults with diabetes change their diet and lifestyle may prevent them from developing diabetes.

Late stages diabetes 2

Diabetes (DM) is a group of diseases characterized by high blood glucose levels that result from defects in insulin generation, insulin action or both. The term diabetes describes a multiple etiologic metabolic disorder characterized by chronic hyperglycemia with carbohydrate, fat, and protein metabolism, as a result of impaired insulin secretion, insulin action, or both. The effects of diabetes include long-term damage, dysfunction and failure of various organs.

Figure 6: Types of diabetes [32].
Type 2 diabetes is related to old age, obesity, family history of diabetes, history of diabetes, poor glucose metabolism, physical inactivity and gender/ethnicity. African Americans, Hispanic/Latin Americans, American Indians and some Asian Americans, Native Hawaiians or other Pacific native Islanders are particularly at risk for type 2 diabetes.

**What is measurable at home in diabetes, glucometer [33]**

A glucometer, also known as a glucose meter or blood glucose monitoring device, is a home measurement system you can use to test the amount of glucose (sugar) in your blood.

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**Prevention or delay of diabetes:**

**Life style modification**

- Research studies have found that lifestyle changes can prevent or delay the onset of type 2 diabetes among high-risk adults.
- These studies included people with IGT and other high-risk characteristics for developing diabetes.
- Lifestyle interventions included diet and moderate-intensity physical activity (such as walking for 2 1/2 hours each week).
- In the Diabetes Prevention Program, a large prevention study of people at high risk for diabetes, the development of diabetes was reduced 58% over 3 years.

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**Values of Diagnosis of Diabetes Mellitus**

<table>
<thead>
<tr>
<th>Glucometer parameter</th>
<th>Venous</th>
<th>Capillary</th>
<th>Venous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>2.6 (110)</td>
<td>2.6 (110)</td>
<td>2.7 (240)</td>
</tr>
<tr>
<td>or 2 h post glucose</td>
<td>2.1 (110)</td>
<td>2.1 (220)</td>
<td>2.1 (220)</td>
</tr>
<tr>
<td>or fasted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impaired Glucose Tolerance (IGT): Fasting (measured)</td>
<td>&lt; 6.1 (110)</td>
<td>&lt; 6.1 (110)</td>
<td>&lt; 7.0 (120)</td>
</tr>
<tr>
<td>Impaired Glucose Tolerance (IGT): Fasting (measured) and 2 h post glucose</td>
<td>&lt; 8.3 (110) and &lt; 9.2 (110)</td>
<td>&lt; 7.8 (140) and &lt; 9.2 (120)</td>
<td>&lt; 7.8 (120) and &lt; 9.2 (120)</td>
</tr>
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**DMT at the advanced stages is a deadly disease**

Diabetes is one of the 10 major threats to human health in the 21st century [34]. Diabetes is metabolic disorder or chronic condition in which high blood sugar levels. Diabetes is long term complications that affect almost every part of the body and often lead to blindness, blood vessels and blood vessels. Brain stroke, kidney failure, amputations and nerve damage. Also, it has to do with significantly accelerated rates of Some debilitating microvascular complications such as nephropathy, retinopathy and neuropathy and macrovascular Complications such as atherosclerosis and stroke. In the present article we discussed the resistance of Insulin and its consequences in diabetics. Insulin resistance causes various disorders. Metabolic syndrome is she envisioned becoming a major public health problem in many of the developed and developing countries.

Of the 56.9 million deaths worldwide in 2016, more than half (54%) resulted from the top 10 causes. Ischemic heart disease and stroke are the world’s most giant killers, accounting for 15.2 million deaths in 2016. These diseases remain the leading cause of death worldwide in the last 15 years [35].

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Diabetic Ketoacidosis (1)

Warning signs: Check your ketones when 240 mg per generation you have Symptoms of high blood Sugar, like dry in the mouth, Feeling really thirsty, either Pissing a lot. you can check Your levels with urine test strip. A few meters of glucose Ketones are also measured. Try for Bring your blood sugar Below and check yours Ketones again at 30 subtlety. Call your doctor or go to the doctor Immediately sorted If it doesn’t work, if you do There are some symptoms Down and your ketones Are invalid, or if you have More than one symptom [36].

DKA is characterised by the triad of hyperglycaemia, metabolic acidosis and increased total body ketone concentration. DKA results from absolute or relative deficiency of circulating insulin and the effects of increased levels of counter-regulatory hormones [37].
Diabetic ketoacidosis (DKA) is an accumulation of blood acids. This can happen when your blood sugar level is too high over time. It can be life-threatening, but it usually takes many hours to be serious. You can handle it and prevent it too.

What causes OKA?

This usually happens because your body does not have enough insulin. Your cells cannot use your blood sugar for energy, so they use fat instead of fuel. Fat burning produces acids called ketones, and if the process takes some time, they can build up in your blood. This excess can replace the chemical balance of your blood and throw away your entire system. People with type 1 diabetes are at risk for ketoacidosis, as their bodies do not produce insulin. Your ketones can also rise when you miss a meal, are you sick or stressed.

Advanced Diabetes - Ketoacidosis (2)

Glucose tolerance [38,39] and insulin responses were tested over extended periods in obese but healthy subjects. Three significant points emerge from this study. First, it has been shown that obese subjects, supposedly lactose-resistant, may deteriorate for a short period from a proper glucose clearance and adequate or increased insulin responses to insulin-free diabetes, peaking in ketoacidosis. Exceptionally high glucose levels that complicate ketoacidosis in two patients indicate hypo-scholarly obesity and an additional risk factor in severe diabetic patients. It seems that after years of obesity and years of hyper-insulinemia, a large weight gain as a result of prolonged overeating may place an excessive challenge on marginalized islet cells. Such an event in itself or pressure presented or both may result in acute insulin deficiency and/or insulin resistance leading to diabetic ketoacidosis. Overweight may worsen obesity upon stopping food intake due to large losses of salt and water. Second, many symptoms and manifestations of hyperphagic obesity are similar to the early functional abnormalities of decomposed diabetes. The onset of the critical stage of uncontrolled diabetes, therefore, fails to frighten the obese patient and may escape the recognition of time by the physician. Third, technical and mechanical difficulties due to severe obesity may cause critical delays in treatment. These factors, when added to coexistence hyperosmolarity and ketoacidosis, probably account for the high mortality in these patients.

Standard definition of DKA ID?

Many definitions of DKA are found in the literature, most of which are ancient. According to Canadian DKA guidelines, “There are no absolute criteria for diagnosing DKA” [40].

My favorite setting: every patient in diabetes plus a significantly elevated serum beta-hydroxy-butyrate level (above 2 - 3 mM/L) [41,42].

Please note the following:

- DKA patients can get regular glucose (DKA euglycemic, more on that later).
- DKA patients can have normal pH and normal bicarbonate. This usually occurs because of a combination of ketoacidosis plus metabolic alkalosis from vomiting.
- That’s right: DKA patients may suffer from ABG normal cold stone.

Approximately 30.3 million people (9.4%) in the United States suffer from diabetes, of which about 1.5 million suffer from type 1 diabetes and most others have type 2 diabetes. These include the monogenic defects of B cell function or insulin action, primary exocrine pancreatic disease, endocrinopathy, and drug-induced diabetes. Updated information on diabetes incidence in the United States is available at the Centers for Disease Control and Prevention [43-45].

Although DKA can appear in patients with type 2 diabetes, it is developing mainly in people with type 1 diabetes who need insulin for their condition. If people do not get insulin, they will develop DKA.
If there is a deficiency of insulin, the body is unable to use blood glucose for energy and instead fats break down in the liver. When these fats are decomposed, acidic compounds called ketones are produced as a byproduct. These ketones accumulate in the body and eventually cause ketosis. Apart from missed or inadequate insulin doses, another common cause of DKA is infection or illness as it can raise the level of hormones that counteract the effects of insulin. In addition, dehydration caused by significant injury or surgery can raise these hormone levels.

The physiological significance of dual forms of endogenous fat transport mode of energy supply (FFA and KB) has been the subject of much speculation. It is known that the major physiological role of ketone bodies is to serve as a fat-derived substrate that can serve as the brain’s non-FFA-containing organ. Thus, under conditions of carbohydrate deprivation, KB will limit the removal of glucose in the brain and allow the retention of proteins that would otherwise be exaggerated in glucose synthesis. Though KB represents primarily a cerebral substrate. They can be used by a number of other tissues such as the heart, skeletal muscle, bowel and kidney. KB must exist in the entire organism’s mechanisms or the KB flow between organs while maintaining a particular priority to the brain. Another potential benefit of supplying KB as a second form of fat enriched fuel is that it may be used to reduce the need for transporting FFA which are poorly soluble in body fluids and may be toxic at high concentrations. The benefit of water-solubility mechanisms can keep plasma at normal levels. Physiological conditions can therefore be observed. Appropriate regulatory processes will keep tonemia below this level.

**NEFA and treatment in Ketosis**

![Figure 10](image)

Blood metabolite changes were measured in six clinical legume cows after four 40g oral nicotinic acid doses administered at two-hour intervals. Subclinical ketosis was characterized by hyperketonemia, unverified fatty acid (NEFA) and acetate, and suppressed triglycerides, cholesterol and phospholipids. Clinically cortical cows showed hypoxia, hypophagia, hypoglycemia, hypertonnia, increased NEFA and acetate, and other lipid depression. The use of glucose and triglycerides in the mammary gland is not likely to be impaired during ketosis, although NEFA uptake may be cost-effective on triglyceride fatty acids. The appetite returned within 18 hours after treatment. At 48 hours after treatment, NEFA and ketone bodies were further increased and appetite was again suppressed. Blood metabolites and appetites began to return to normal immediately after the rebound phase. Glucose was back to normal as early as day 7, while ketone body concentrations were normal by day 14. By day 21, all blood metabolites were within acceptable ranges [46].
Symptoms of DKA

- In the early stages of DKA, the affected individual appears flushed and breathes rapidly and deeply. This is called hyperventilation.
- As the condition progresses, the skin may turn pale, cool and clammy, dehydration may begin to set in and the heart rate may become rapid and breathing shallow.
- Nausea, vomiting and severe abdominal cramps.
- Blurred vision.
- Fruity or pungent smelling breath due to the presence of acetone and ketones in the breath.

**Stage I (appearance):** Initial treatment of DKA patient with alarming acidosis Let’s start with examining a patient who is experiencing severe DKA with alarming acidosis. This is not uncommon. Features that may be of concern include the following:

a. Bicarbonate < 7 mc/L
b. pH < 7 (if measured; there is usually little benefit to measuring pH)
c. Clinically ill appearance (e.g. apnea, cosmol-marked breathing) These patients usually suffer from severe metabolic acidosis with respiratory compensation. This raises two concerns:
   1. If the metabolic missed is aggravated, it may fall apart.
2. The patient depends on breathing compensation to maintain his or her acidity level. If they had to get tired and lose the ability to hypnotize, their acidity would drop. It is important to reverse the missed procedure before the patient may become tired or develop respiratory failure (for example due to inhalation or pulmonary edema). There are several steps that may be used to stabilize and improve these patients.

There are several measures that may be used to stabilize and improve these patients.

1. Give an adequate dose of insulin
2. Avoid normal saline
3. Consider high-flow nasal cannula
4. Bicarbonate is a distraction here.

**Figure 12**

**Antiobesity drugs [48,63]**

Lorcaserin, currently marketed under the trade name Belviq and previously Lorqess during development, is a weight-loss drug developed by Arena Pharmaceuticals. It reduces appetite by activating a type of serotonin receptor known as the 5-HT2C receptor in a region of the brain called the hypothalamus, which is known to control appetite.

**Diagnosis and treatment**

Blood examinations are carried out to check the sugar levels and blood pH, which is classified as acidic if it is below the usual 7.3. Unlike non-ketotic hyperosmolar coma, in DKA the blood and urine levels of ketones are high and the blood osmolarity is low.

Treatment involves rehydrating the patient with isotonic fluids and replacing lost electrolytes with supplements such as potassium, magnesium and phosphates. Insulin is administered intravenously to reduce blood levels of glucose and reverse ketoacidosis.

**Insulin infusion: Getting started [49]**

Unless the patient is hypokalemic, insulin infusion should be started immediately.
For hypokalemia, hold insulin until the potassium level rises. The maximum potassium infusion rate is often considered to be 20 mc/h, however, in DKA hypokalemia, a reasonable 40 mc/hr is followed at strict monitoring. To prevent arterial injury this can be given through a central or multiple peripheral line (E.g. 20 mph per hour simultaneously through the two fourth peripheral cases).

Insulin bolus (10 IV units) should be considered if the transfusion setting is > 30 minutes. The main benefit of insulin bolus is that it can usually be given immediately (most units have a 10-unit vial of insulin available immediately, whereas insulin mixing should be involved in a pharmacy). Insulin infusion usually starts at 0.1 U/kg/hour (up to a maximum of 15 units/hour in morbid obesity). However, for patients with severe acidosis (e.g. bicarbonate < 5 mcal/liter) or marked insulin resistance (with high chronic insulin requirements), higher doses (e.g. 0.2 - 0.3 U/kg/hour) are usually required.

Insulin infusion should be adjusted as needed to lower glucose by 50 - 70 mg/dL (2.8 - 3.9 mm) per hour.

**Adult diabetic ketoacidosis (3)**

In 2009 [50], there were 140,000 hospitalizations for diabetic ketoacidosis with an average duration of 3.4 days [51]. The direct and indirect annual cost of DKA hospitalizations is US $ 2.4 billion. Insulin omission is the most common sediment in DKA [52,53] infections, acute medical diseases involving the cardiovascular system (myocardial infarction, stroke) and digestive tract (bleeding, pancreatitis), endocrine disease (acromegaly, Cushing’s syndrome), And stress of recent surgical operations can contribute to the development of DKA by causing dehydration, an increase in insulin-resistant hormones, and a worsening of peripheral insulin anticonvulsants may affect carbohydrate metabolism and volume, and may therefore precipitate DKA. Other causes that may contribute to DKA include psychological problems, eating disorders, insulin pump function, and illicit substance use [54,55]. It is common knowledge that type 2 diabetes that started with DKA [56]. These patients are obese, mostly African American or Hispanic, and resistant Very insulin in presentation [57].

**Pathology**

Insulin deficiency, increased insulin resistance hormones (cortisol, glucagon, growth hormone and catecholamine) and peripheral insulin resistance cause hyperglycemia, dehydration, ketosis and electrolyte imbalances, which underlie DKA’s pathophysiology, due to an increase in lipohypophyseal lipsuction due to increased Ketone: ß-hydroxybutyrate (ß-OHB) and acetoacetate. Hyperglycemia-induced osmotic urine, if not accompanied by an adequate amount of oral fluids, leads to dehydration, hyperosmolarity, electrolyte loss, and subsequent decline in glomerular filtration rate. With renal function decline, glycosuria decreases and hyperglycemia worsens. With impaired insulin and hyper-glucagon activity, potassium uptake by skeletal muscle must be greatly reduced; Hyperosmolarity can also cause potassium flux from the cells. The result is intracellular potassium depletion and subsequent loss of potassium through osmotic diarrhea, causing total body potassium to decrease on average 3 - 5 mm/kg of body weight. However, DKA patients can display a wide range of serum potassium concentrations. Plasma levels of “normal” potassium still indicate that overall potassium stores in the body are severely diminished, and an institution for insulin therapy and hyperglycemia repair will cause hypokalemia. On average, patients with DKA may suffer from the following deficit of water and key electrolytes per kilogram of body weight: free water 100 ml/kg; sodium 7 - 10 mcg/kg; potassium 3 - 5 mcg/Kg; chloride 3-5 mm/kg; and phosphorus 1 mm/kg.

Diabetic ketoacidosis (DKA), is a rare but in potential fatal hyperglycemic crisis that can occur in individuals with type 1 and type 2 diabetes because of its increasing prevalence and its economic impact related to treatment and comorbidities, effective management and prevention are key. Management components include making appropriate diagnosis using up-to-date laboratory tools and clinical criteria and coordinating fluid resuscitation, insulin therapy, F and electrolyte replacement through patient feedback from timely follow-up and knowledge of resolution criteria. In addition, awareness of special populations such as kidney disease patients appearing in DKA is important. During DKA treatment, complications may arise and appropriate strategies are needed to prevent these complications. DKA prevention strategies that include educating patients and essential providers [50].

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Obesity Diabetes and Ketoacidosis in Elderly

Treatment options for metabolic obesity

Other Names: Overweight; weight gain Health Reference Guide for Medical Computers List of FAQs About Obesity: More than 50% of the US population is overweight. But obesity is different from being overweight. Is considered morbid obesity.

Obesity drugs

Obesity is also defined as BMI (body mass index) above 30 kg/sqm. Patients with BMI between 25 and 29.9 are considered overweight, but are not obese. See also diet and calories [58].

Antiobesity agents [59]

Obesity is an extremely complex disease caused by the interaction of a myriad of genetic, nutritional, lifestyle and environmental factors, which favor a chronically positive energy balance, leading to an increase in body fat mass [60]. The occurrence of obesity is rising at an alarming rate and is becoming a significant public health concern with indescribable social costs. Indeed, obesity allows the development of metabolic disorders such as diabetes, hypertension and cardiovascular disease in which comes addition to chronic diseases such as stroke, osteoarthritis, sleep apnea, some cancers, and inflammation-based pathologies.

Recent studies have demonstrated the potential of natural obesity prevention products. Multiple natural product combinations may result in synergistic activity that increases their bioavailability and action on multiple molecular targets and offers advantages over chemical treatments. In this review, we discuss the potential for obesity of natural products and analyze their mechanisms.

Anti-obesity agents derived from natural products

Orlistat (Xenical® from Roche), known as tetrahydrolipstatin, has been one of the few long-term obesity drugs since it was launched in 1998. Orlistat's behavior is to reduce energy consumption by preventing fat absorption. Through irreversible inhibition of gastrointestinal lipase activity. As shown in Figure orlistat is a synthetic derivative of lipstatin, a potent and is easy to synthesize compared to its parent, lipstatin [61,62]. Hadváry and co-workers in Hoffman-La Rocha wonderfully illustrated the Orlistat lipase inhibition mechanism: Orlistat's lactone fraction varies covalently with the Ser152 hydroxyl group at the active lipase Hariri site, which inhibits its hydrolysis and its uptake. Of dietary triacylglycerol [63]. and is easy to synthesize compared to its parent, lipstatin [57,58,64]. Hadváry and co-workers in Hoffman-La Rocha wonderfully illustrated the Orlistat, lipase inhibition mechanism: Orlistat's lactone fraction varies covalently with the Ser152 hydroxyl group at the active lipase Hariri site, which inhibits its hydrolysis and its uptake. Of dietary triacylglycerol. Natural inhibitor of pancreatic lipases, isolated from Streptomyces toxytricini. Orlistat was synthesized as one of the lipstatin analogs and recognized as an antiseptic agent by the selective inhibition of pancreatic lipase activity. It has the added benefits of physical stability and is easy to synthesize compared to its parent, lipstatin [57,58]. Hadváry and co-workers in Hoffman-La Rocha wonderfully illustrated the Orlistat lipase inhibition mechanism: Orlistat's lactone fraction varies covalently with the Ser152 hydroxyl group at the active lipase Hariri site, which inhibits its hydrolysis and its uptake. Of dietary triacylglycerol.

**Figure 15**

Conclusion

Diabetes and obesity [65] are chronic disorders that are present in the environment to rise worldwide. Body mass index has a strong relationship. For diabetes and insulin resistance. In obese people, the Amount of NEFA [66], glycerol, hormones, cytokines, pro-inflamm-
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Inflammatory, and other substances involved. The development of increased insulin resistance. Insulin Resistance with β-cell dysfunction leads to Diabetes development. Weight gain in early life is associated with the development of type 1 diabetes. NEFA It is a cornerstone of the development of insulin resistance Impaired β-cell function. New approaches b Management and prevention of diabetes in obese people. These facts should be studied and investigated.

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Fatty acids are straight-chain carboxylic acids (either saturated or unsaturated). They are derived from the hydrolysis of fats or can be synthesized from two carbon units (acetyl- or malonyl-CoA) in the liver, mammary gland and, to some extent adipose tissue. Nearly all have an even number of carbon atoms. Individual fatty acids, free fatty acids (FFA), or the non-esterified fatty acids (NEFA), circulate primarily in association with albumin. They are an important metabolic fuel. Fatty acids play a central role in providing energy to tissues, particularly during fasting. The liver, kidneys, myocardium, and skeletal muscles, but not the brain. The major storage form of fatty acids is in triglycerides (large amounts are also esterified to cholesterol or in phospholipids), and the enzymes lipoprotein lipase and hepatic lipase hydrolyze the triglycerides to fatty acids and glycerol, thereby releasing them as energy sources for the various tissues. FFA that have been released from triglyceride by the actions of lipoprotein lipase and hepatic lipase are elevated in blood of subjects with central obesity, insulin resistance and type II diabetes.