Hypoglycemia in a Patient with Type 1 Diabetes Mellitus with Recurrent Ketoacidosis

Feriadi Suwarna, Rio Anggoro,* Sarwono Waspadji***

ABSTRACT

Hypoglycemia is a reduction in blood glucose level below 60 mg%. Epidemiologic data report a 0.02/1000 patient/year mortality rate due to hypoglycemia in patients using insulin in the United Kingdom. Reports from Indonesia are still quite rare. Parto Atmojo (1993) reported the incidence rate of hypoglycemia in diabetic patients hospitalized at Sardjito Hospital, Yogyakarta. Conditions are quite different than in Western nations, perhaps due to a smaller population of patients with type 1 diabetes mellitus in Indonesia.

INTRODUCTION

Recurrent ketoacidosis is an acute complication of diabetes mellitus, manifested in the form of hyperglycemia, ketosis, and academia. This condition occurs due to a relative or absolute insulin hormone deficiency. If the condition is not well managed, ketoacidosis may end in death.[1,2,3,14,15]

Symptoms and signs of ketoacidosis may be divided in two: those due to hyperglycemia, and those due to ketosis. Insulin deficiency also increases glucagon hormones and increases lypolysis in fat tissues as well as ketogenesis in the liver. Such lypolysis results in increased free fatty acid supply to the liver. In the liver mitochondria, free fatty acids are transformed into ketons, and finally oxidized into CO_2 or triglycerides. This process of ketosis produces beta-hydroxybutirate acids and aceto-acetic acid and causes acidosis.[1] According to Roswita (2000), the mortality rate due to recurrent ketoacidosis at the Emergency Ward of Cipto Mangunkusumo Hospital within the first 24 hours is 30%.[14]

CLINICAL SYMPTOMS

Clinical symptoms that occur in patients are in accordance with the pathophysiology of ketoacidosis, consisting of rapid and deep breathing (kussmaul), various degrees of dehydration, sometimes hypovolemia, even to the point shock. Ketoacidosis is often preceded by symptoms of polyuria and polydipsia, insulin termination, fever, or the presence of infection. Abdominal discomfort is usually related with gastroparesis. The patient may be in a degree of consciousness ranging from fully conscious to comatose.

The diagnostic criteria of ketoacidosis are as follows: glucose level of > 250 mg%; pH level of less than 7.35; low HCO3-; large anion gap; and positive serum keton.

TRIGGER FACTOR OF KETOACIDOSIS

Ketoacidosis may be triggered by various conditions such as infection, myocardial infarct, termination of insulin, pregnancy, stroke, drugs, alcohol, and pancreatitis, as well as various other gastrointestinal disturbances.[1,2,3,4,8,13,14]

MANAGEMENT

The aim of ketoacidosis management is the correction of circulation volume and tissue perfusion, reduction of serum glucose, elimination of serum and urinary ketons to safe limits, and correction of electrolyte imbalance.[1,3,13,14]

* *Department of Internal Medicine, Faculty of Medicine of The University of Indonesia/Cipto Mangunkusumo Hospital, Jakarta, Indonesia*

** *Division of Metabolism and Endocrinology, Department of Internal Medicine, Faculty of Medicine of The University of Indonesia/Dr.Cipto Mangunkusumo General Central National Hospital, Jakarta, Indonesia*

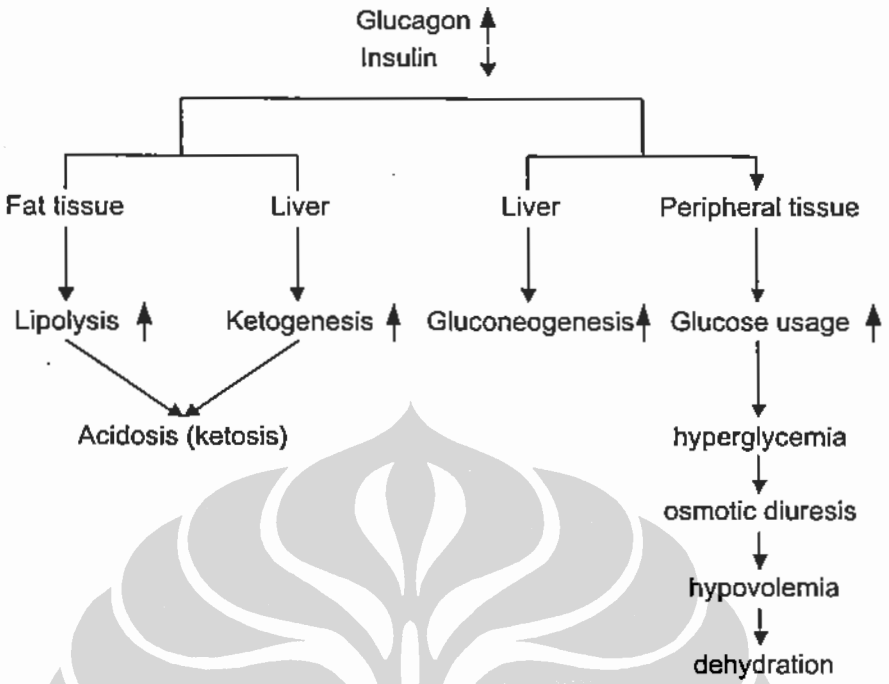


Figure 1. The Pathophysiology of Ketoacidosis

The Principles of Management [3,8,13,14]

1. Replacement of loss of fluids and electrolytes
2. Suppression of lypolysis and gluconeogenesis with the administration of insulin
3. Management of the triggers of ketoacidosis
4. Restoration of normal physiology

HYPOGLYCEMIA IN PATIENTS WITH DIABETES MELLITUS

Definition

The lowest limit of fasting blood glucose (true glucose) is 60 mg%. Based on this limit, the condition where blood glucose drops below 60 mg% is called hypoglycemia.

Epidemiology

Death due to hypoglycemia in insulin users in the United Kingdom is 0.2/1000 patients/year. There have not been many reports from Indonesia. Parto Atmojo (1993) reported the incidence of hypoglycemia in diabetic patients hospitalized at Sardjito Hospital, Yogyakarta. His findings were still very much different from that in Western Nations, possibly due to a lower number of patients with type 1 diabetes mellitus in Indoensia.[7]

Pathogenesis

To understand the pathogenesis of hypoglycemia, we must understand body glucose and energy homeostasis. During meals (absorption) there is adequate energy absorbed from the intestines. Excess energy will be stored in the form of macromolecules, thus rendering the phase as the anabolic phase. The hormone in charge is insulin.

Digestion and absorption of proteins causes an increase in amino acid in the blood, which with the help of insulin, will be stored in the liver and muscles as fat and protein.

After meals (post-absorption) or after 5-6 hours of fasting, the blood glucose level starts to fall, causing a subsequent reduction in insulin secretion, but with increase contra-regulator hormones, glucagons, epinephrine, cortisone, and growth hormones. The reverse condition, known as catabolism, occurs, where synthesis of glycogen, protein, and triglycerides falls, while their breakdown increases. A sudden drop in blood glucose is caused by glucagons and epinephrine. The two hormones initiate glycogenolysis and gluconeogenesis as well as proteolysis in the muscles and lypolysis in fat tissues. Thus, materials for gluconeogenesis, consisting of amino acids, particularly alanine, lactic acid, piruvic acid, and glycerols, are thus available. In short, we can say that during post-absorbtion, there is a reduction of insulin and an

Table 1. Phases of Blood Glucose Reduction and Symptoms That Occur

Phase	Blood glucose Level	Hormonal/mental state changes	Symptoms that occur
Sublimation phase	75% - 50mg%	Insulin secretion falls & glucagon secretion increases	• absence of clinical symptoms • can be determined using auditory evoked potential
Activation phase	50mg% - 20mg%	• activation of autonomic center at the hypothalamus • secretion of glucagon & epinephrine is further increased	• adrenergic symptoms: palpitation, excessive sweating, tremor, fear, hunger, nausea, etc.
Neurological phase	< 20mg%	Disturbance in brain function	Headache, blurry vision, reduced mental acuity, loss of fine motor skills, loss of consciousness, convulsions, coma

Table 2. The Etiology of Hypoglycemia in Diabetes Mellitus

1. Hypoglycemia in early stages of diabetes mellitus
2. Hypoglycemia due to treatment of diabetes mellitus
   a. Use of insulin
   b. Use of sulphonilurea
   c. Babies born from diabetic mothers
3. Hypoglycemia related to diabetes mellitus
   a. Post-gastrectomy alimentary hyper-insulinism
   b. Insulinoma
   c. Severe liver disease
   d. Extra-pancreatic tumor: vibrosarcoma, renal carcinoma
   e. Hypopituitarism

increase in contra-regulatory hormones.

Hypoglycemia occurs due to inability of the liver to produce glucose. This is caused by a reduction in glucose components, liver disease, or hormonal imbalance. Increased glucose use in peripheral tissues does not cause hypoglycemia, as long as the liver is still able to maintain balance by increasing glucose production.

Symptoms of Hypoglycemia

Symptoms that occur due to glycemia belong to two phases. The first phase consists of symptoms that occur due to activation of the autonomic center at the hypothalamus, which causes release of epinephrine. Symptoms comprise of palpitation, sweating, tremor, fear, hunger, and nausea. The second phase consists of symptoms that occur due to disturbance in brain function, and is thus called neurological symptoms. Symptoms consist of headache, blurry vision, reduced mental acuity, loss of fine motor skills, loss of consciousness, convulsions, and coma.

Several factors that facilitate the incidence of hypoglycemia in patients with diabetes mellitus receiving insulin/sulphonilurea are delayed or reduced food intake, incorrect drug dosage, excessive physical exercise, change in site of insulin injection (from the arm to the abdominal wall), reduced requirement for insulin and sulphonilurea (neuropathy, liver disease, labor, healing from infection/stress, hypothyroidism), administration of other hypoglycemic agents, and diabetic gastroparesis.

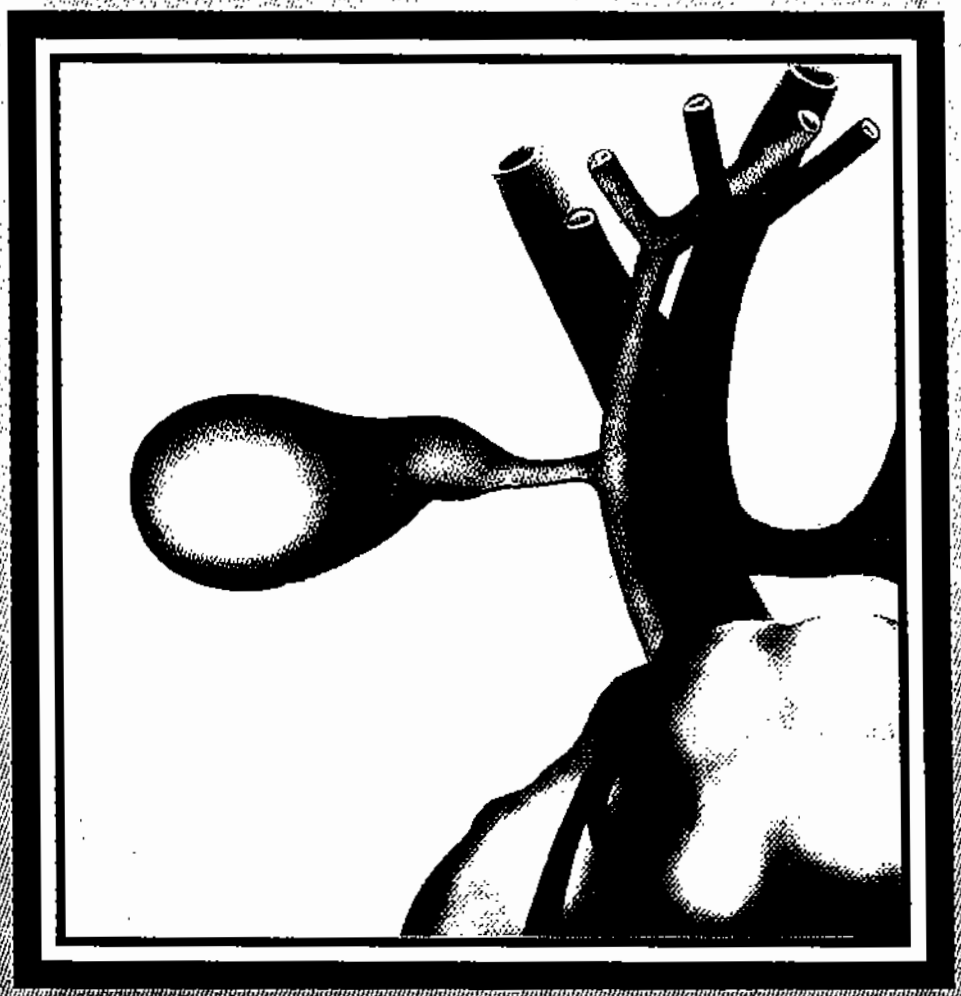
Malingering in patients with diabetes mellitus may occur with the aim of receiving attention from the family, physician, or nearby spectators by injecting water instead of insulin, increasing/reducing the dose of insulin, or not injecting insulin at all in the hope of diabetic ketoacidosis, and subsequent public attention (Briethel Diabetic).

Insulin

There are 2 important events that may occur when insulin is administered, the Somogyi effect and the Dawn effect.[12] These two phenomena cause hyperglycemia in the mornings. The Somogyi effect pertains to hypergly-

BEBAS :

Batu empedu kolestrol....



Memperbaiki fungsi liver secara nyata
(Penurunan SGPT, SGOT, dll)

ESTAZOR®

www.fahrenheit.co.id

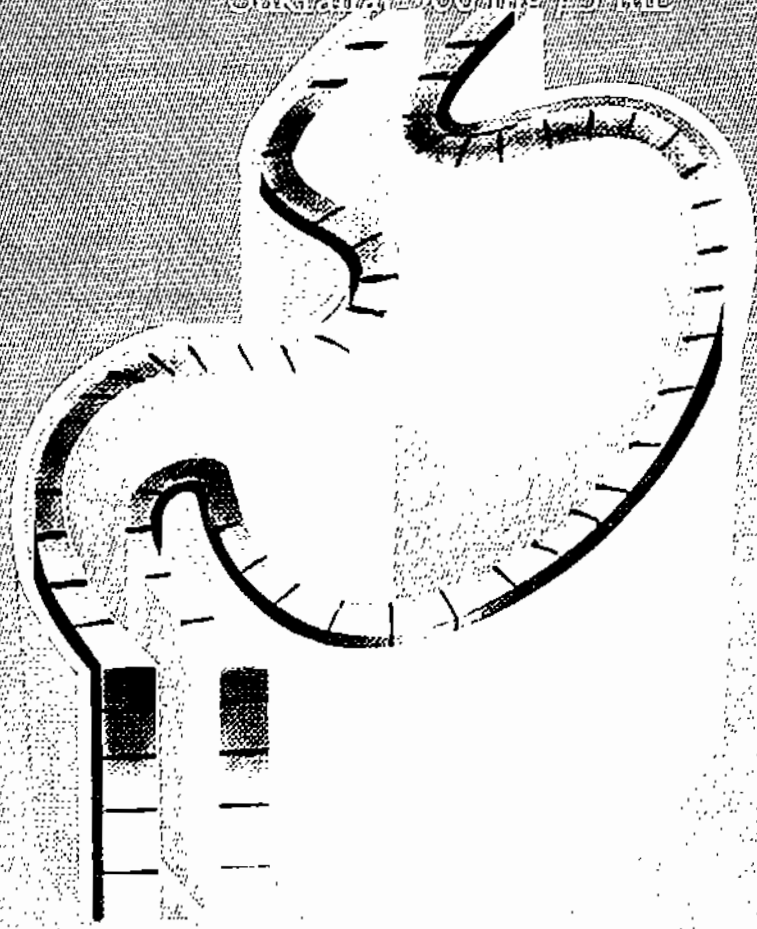
FAHRENHEIT

quality for better health

INPEPSA®

SUSPENSI

Sukralfat 500 mg / 5 mL



Proteksi & terapi secara global

- Secara klinis **Inpepsa®** suspensi (Sukralfat) terbukti efektif terhadap :
  - Tukak duodenal
  - Tukak lambung
  - Stres ulkus
  - Pencegahan tukak lambung yang kambuh
  - Pencegahan & pengobtan dari ulkus yang disebabkan oleh NSAIDs
- Secara klinis **Inpepsa®** suspensi terbukti aman dan efek samping minimal sekali

www.fahrenheit.co.id.

FAHRENHEIT

Quality for better health

Table 3. Predisposing Factors of Hypoglycemia in Patients Receiving Insulin/ Sulphonilurea

1. Factors associated with the patient
   - Reduced or delayed food intake
   - Excessive physical exercise
   - Change in site of insulin injection
   - Reduced insulin requirement
     - Healing from illness
     - Diabetic nephropathy
     - Addison's disease
     - Hypopituitarism
   - First days of labor
   - Severe liver disease
   - Diabetic gastroparesis
   - Malingering (pretending)
2. Factors associated with the physician
   - Close control of blood glucose
   - Administration of drugs that have the potential to induce hypoglycemia
   - Change in type of insulin

cemia in the morning after hypoglycemia (rebound effect). Due to excessive insulin administration, hypoglycemia occurs at night (from 2 to 3 a.m.). Thus, the body's effort to manage hypoglycemia causes hyperglycemia. While in the dawn effect, hyperglycemia occurs in the morning due to the action of anti-insulin hormones (glycogenic hormones). The action of these anti-insulin hormones is a physiologic process. These two events require different management. The Somogyi effect is controlled by reducing night-time dose of insulin or adding a bed-time snack. While for the dawn effect, the dose of insulin is increased to prevent hyperglycemia in the morning.

CASE REPORT

Mr. S, 37-year-old, was hospitalized on the fourth floor of the B in-patient ward of Dr. Cipto Mangunkusumo General Central National Hospital from the 23rd of August to the 8th of September 2000, with a chief complaint of general weakness since 2 days prior to admission.

Two days prior to admission, the patient suffered from moderate fever, a general sick feeling and weakness. The patient had a cough with white sputum, and felt pain when swallowing. He also had a headache. He denied any sore throat. The patient lost his appetite, and his body weight fell 1 kg in 2 months. He denied any night sweats. He felt nauseated and vomited after meals. The vomit contained food remnants. He denied any bloody vomiting or black defecation. He urinated frequently, over 12 times/day, clear yellow in color, unaccompanied by burning or painful sensations. His eyes were blurry, but the patient has not used glasses, since he felt they were expensive. He denied fainting or difficulty breathing at home.

The patient had visited the Metabolic-Endocrine outpatient clinic since 1997, and was diagnosed with diabetes and was given insulin injection (Mixtard, dose 12-0-14). However, two days prior to hospitalization, the patient did not inject insulin due to fear that his blood glucose will fall, causing a loss of consciousness that he had experienced the previous 8 months. The patient had been hospitalized twice in Dr. Cipto Mangunkusumo General Central National Hospital, the first incidence in August 1997, and the second in January 2000, with similar complaints as this incidence (previous hospital records stated recurrent diabetic ketoacidosis with low compliance). The patient also refused to inject insulin when he had a fever or a cold, and admitted to have frequently forgotten to inject insulin in the mornings, having to rush to work early in the morning. History of intake of oral hypoglycemic drugs was denied. No one in the patient's family suffered from diabetes. Parasthesia and long-standing wound was denied.

The only history of illness that the patient admitted was diabetes mellitus since 1997. The patient denied any history of hypertension, hepatitis, heart disease, lung disease, renal or urinary tract disease. He had no drug or food allergies. He belonged to the low social-economic class. He worked as a cleaning service personnel at an office building in Rasuna Said with a monthly salary of Rp.40,000. He has a wife and two children, 17-year old son in the first grade of elementary school, and one 14-

month old daughter. His wife and two children are currently living in his parents' home in Cirebon because he is unable to support the family from the last 8 months. The patient lives in a shack in Pasar Rumput with his sister's family. His medical bills are shared by his sister, neighbors, and office friends. He is introverted in nature, and easily stressed out. Pertaining to his illness, he only knows that he has diabetes mellitus, and has to inject insulin, but in not discipline with his diet.

During physical examination at admission to the inpatient ward (August 23rd, 2000), the patient was found to be severely ill, somnolent, with sufficient nutrition (height 150 cm, weight 45 kg). His blood pressure was 130/70 mmHg, his pulse rate 72 times/minute, his respiratory rate 20 times/minute, and his body temperature 38.4° Celsius. His conjunctiva were not pale and his sclera had no signs of jaundice. Both his eyes demonstrated immature cataract. His tonsils were hyperemic, but not enlarged. His pharynx was hyperemic, his tongue dry. His jugular venous pressure was 5-2 cmH2O. He had no meningeal signs. His chest movements were symmetrical, the left and right fremitus were equal, lung percussion was sonor, lung auscultation findings were vesicular, without rales or prolonged expiration. Cardiac findings were as follows: ictus cordis was not observable, palpable below the fourth rib on the left mid-clavicular line, the heart was not enlarged, first and second heart sounds were pure, without murmur or gallop. The patient's abdomen was not distended, with adequate turgor. His liver and spleen were not palpable, ballottement was negative, bowel sounds normal. His extremities were warm, there was no edema, no palmary erithema, no clubbed fingers. His lymph nodes were not palpable. A fowley catheter and nasogastric tube had been inserted at the emergency ward of Dr. Cipto Mangunkusumo General Central National Hospital.

Laboratory findings were as follows: Hemoglobin level: 15.3 mg/dL, Leukocyte count: 30,000/ul, Hematocryte: 45 vol%, Platelet count: 380,000/ul, Erythrocyte count: 5.07 million/mL, Cito blood sugar 462 lmg/dL, blood aceton ++, Ureum level 87 mg/dl, Creatinine level 3.5 mg/dl. Urinalysis findings were as follows: density 1.025; yellow, protein + 1; glucose + 3; keton + 3; billirubin -; urobillin 0.1; leukocyte 3/large microscopic view, erythrocyte 12-13/large microscopic view. Blood gas analysis results were as follows: pH: 6.96; pCO2: 9; pO2: 124; HCO3: 3; BE: -27.5, Sat O2: 99; Na: 133 mEq/l; K: 6.9 mEq/l; Ca: 0.8 mg/dl; Na: 145 mEq/l, K: 3.5 mEq/l, Ca: 0.6 mg/dl. Chest x-ray demonstrated no infiltrates, and a Cardio-thoracic ratio of 49%. Electrocardiography demonstrated sinus rhythm, a QRS rate of 75 times/minute, normal axis, un-lengthened PR segment, absence of elevated T, inverted T, ST elevation, ST depression, and no signs of left or right ventricular hypertrophy (LVH and RVH), left or right bundle branch block (LBBB and RBBB).

The following problems were established: diabetic ketoacidosis (3rd incidence), type 1 diabetes mellitus with adequate bodyweight, uncontrolled blood sugar, acute tonsillo-pharyngitis, and microhematuria.

The problem of ketoacidosis was established based on the presence of nausea, reduced consciousness, excessive thirst, frequent urinations, fever, weakness, dry tongue, and history of diabetes since 3 years, failure to inject insulin, a cito blood glucose level of 462, blood acetone +2, metabolic acidosis, and large anion gap. The trigger was suspected to be throat infection and refusal to inject insulin. The diagnostic plan was as follows: observation of vital signs and consciousness, hourly fluid-intake-urine measurement-monitoring, blood gas and electrolyte analysis, and plan of treatment in accordance with the protocol of ketoacidosis: if the patient's blood glucose stabilizes within 12 hours (200-300 mg/dL), sliding scale + drip of 1 unit of regular insulin /hour. Plan for education: explain to the patient's sister about the patient's condition and possible complications during hospitalization, the dangers of prolonged immobilization in diabetic patients, which can result in hard-to-heal wounds in the back or the bottom. It is recommended that the patient be positioned to his left and right side every morning and afternoon.

The problem of type 1 diabetes mellitus, normal weight, with uncontrolled blood sugar was established based on a history of diabetes, a height of 150 cm and a bodyweight of 45 kg, and a cito blood sugar of 462 mg/dl. The diagnostic plan was to check the patient's blood sugar curve daily, to search for the patient's old status, to check C-peptide, to check the patients HbA1c, and to consult the eye department. Plan for treatment consisted of fluid diabetic diet of 1900 calories, reached gradually starting with 6 x 250 cc via the nasogastric tube. Educational plan was as follows: to explain the importance of maintaining the patient's health, both during hospitalization and at home, and to explain the importance of regularly injecting insulin, and coming for regular visits to the metabolic-endocrine polyclinic.

The problem of acute tonsilo-pharingitis was established based on pain when swallowing, moderate fever, cough with whitish sputum 2 days prior to admission, an un-enlarged, hyperemic tonsil, hyperemic pharynx, a tem-

perature of 38.4° Celsius, absence of rales, and a leukocyte count of 30,000/ul. The diagnostic plan was to take a throat swab for culture and antibiotic sensitivity testing, and repeat peripheral blood check. The plan for treatment was 3 times 1 tablespoon of potio nigra, and 2 times 1 g of intravenous ceftriaxone. The educational plan was to explain to the family that there was infection of the respiratory tract, and that refusal to inject insulin was the cause of diabetic ketoacidosis in the patient.

Microhematuria was established based on urinary erythrocyte count of 12-13/large microscopic view, absence of pain during urination, no history of trauma. Hematuria was thought to be due to trauma during catheter insertion at the emergency ward, with the differential diagnosis of urinary tract stone. The diagnostic plan was for repeat urinalysis, culture and antibiotic sensitivity testing of the urine.

The patient's condition was under control within 24 hours. The patient was then initiated on a six-hour sliding scale of 1 unit drip of insulin per hour. From the sliding scale, we achieved an insulin dose of 44 units/24 hours, achieved from a sliding scale from 20 units/24 hours plus 1 unit of insulin drip every hour (24 units/24 hours). Based on this, the patient received a constant dose of 3 x 10 units of insulin (administered gradually to avoid hypoglycemia), and daily blood sugar curve was taken twice a week. From the daily blood sugar curve, the patient's morning blood sugar was 399, 499 during the day, and the afternoon test was not conducted. Thus, the gradual dose was increased to 3 x 15 units.

During the second day of care (25th of August 2000), the patient's condition improved, characterized by full consciousness, almost normal temperature, a leukocyte count of 8600/ul, and negative blood acetone. The patient was found with compensated CAD based on electrocardiography. The patient had a nasogastric tube in place, with a greenish gastric fluid production. The patient complained of nausea and pain when fed with fluid foods. The patient was thought to have suffered from acute pancreatitis. Amylase and lipase evaluation were 151 S.Somogyi and 48 S.Cherry Crandall respectively. Urine production fell to 800 cc/24 hours compared to the previous 3000 cc/24 hours. The patient's ureum level was 87 mg/dl, and his creatinine level 3.5 mg/dl, and his calculated creatinine clearance was 18.39%. The patient was thus thought to have suffered from acute renal failure. Quantitative protein was 1008 mg/24 hours with a urine volume of 1400 cc. The patient underwent fluid balance for suspected diabetic nephropathy.

During the fourth day of treatment (Sunday, 27th of August 2000), the patient had difficulty breathing, occasional cough, and reduced consciousness (somnolence). There were soft rales on the back lungs, and the patient's blood acetone was +3. The problems of diabetic ketoacidosis (fourth incidence) and hospital acquired pneumonia were established. The protocol for diabetic ketoacidosis was reapplied with sliding scale. There was an increased need for insulin to 79 units/24 hours plus insulin drip of 1 unit/hour (or 24 units in 24 hours). The antibiotic was switched to cefoperazone, administered intravenously at a dose of 2 times 1 gram. Urinalysis demonstrated normal leukocyte and erythrocyte, thus the problem of microhematuria was proclaimed to have been resolved. The problem of tonsilo-pharyngitis was also considered resolved, since the patient's tonsils and pharynx were no longer hyperemic.

On the fifth to seventh day of treatment the patient's clinical condition improved. The patient became fully conscious, his hemodynamic state stable, his blood acetone negative. The patient's intravenous line was disconnected, his oxygen line removed, and the catheter removed. The patient began to sit actively and gradually learned to stand and walk. The patient was treated with 3 times 25 units of regular insulin. The patient was given 1900 calories of solid diabetic diet, which the patient was able to finish. Results of the first consultation to the eye department (August 30th, 2000) were as follows: grade I diabetic retinopathy with vitreal opacity of the left and right eyes, and was advised to undergo repeat consultation at the vitreo-retinal polyclinic. The patient received education on the importance of regular injection of insulin, and the patient was reeducated on the proper technique of insulin injection, determining of the proper dose, acute complications of diabetes mellitus, avoiding stress, which can trigger diabetic ketoacidosis, as well as proper physical exercise and diet for diabetic patients. The patient and family requested to be released on Friday, September 1st, 2000, but was denied due to a high cito blood glucose level (402 mg/dL). The cause of re-increase in blood glucose was thought to be incorrect administration of insulin, refusal to stick to diet, or other factors such as hidden infection. We tried to prevent recurrent ketoacidosis both in the ward and at home.

On the ninth day of treatment (Sunday, September 9th, 2000, at 09.00), the patient again suffered from difficulty breathing. His blood pressure was 150/90 mmHg. His pulse rate was 136 times/minute, his temperature was normal, his respiratory rate 40 times/minute (rapid and deep). There were no rales. Cito blood sugar level

was 411 mg/dL. Blood gas analysis findings were as follows: pH: 7.097; pCO2: 8.9; pO2: 127.2; BE: -26; $HCO3^-$: 2.6; O2 Sat: 96.8. Na: 129 mEq/l, K: 5.5 mEq/l. Blood acetone was: +3. The patient was placed on the ketoacidosis protocol once again by the physician in duty. The following problems were established: diabetic ketoacidosis (fifth case), severe metabolic acidosis, hyponatremia, improved clinical manifestations of pneumonia. The patient was treated with 100 meq of bicarbonate. The patient was placed on a larger fixed dose insulin of 103 units/24 hours based on an insulin drip 2 units/hour (48 units/24 hours) and a sliding scale of 55 units/24 hours. The condition of hyponatremia was corrected using 3 times 250 mg oral NaCl for 3 days. On Monday, September 4th, 2000, the patient received a fixed dose of insulin starting gradually from 4 x 20 units, resulting in a daily blood sugar curve of 411, 425, and 190. There was no trigger such as infection. There was nausea and vomiting, and greenish fluid came from the nasogastric tube once more. The suspicion of acute pancreatitis re-emerged. The physician on duty ordered re-evaluation of amylase and lipase levels, resulting in 156 S.Somogyi (N: <120 S.Somogyi) and 176 S.Cherry Crandall (N: <190 S.Cherry Crandall), respectively. Insulin was gradually increased to 4 x 25 units on Thursday, September the 7th, 2000, with a daily blood sugar curve of 138 mg/dL at 6 a.m., 178 mg/dL at 11 a.m., and 183 mg/dL at 4 p.m.

The insulin drip was thus terminated, while other means of treatment continued, with close observation of vital signs and consciousness. Follow up on the fourteenth day of treatment (Friday, September 8th, 2000, at 06.45 a.m.) demonstrated clinical improvement in diabetic ketoacidosis; type 1 diabetes mellitus, normal weight, controlled blood sugar; diabetic nephropathy and hypernatremia (Na: 151 mEq/dl). The patient felt thirsty, did not suffer from nausea or vomiting, was moderately ill, somnolent, with a blood pressure of 125/85 mmHg, pulse rate of 80 times/minute, respiratory rate of 20 times/minute, and had no fever. Cito blood sugar was 115, Sodium level 151. There was trace level of blood acetone September 5th, 2000, 9 a.m. The diagnostic plan was as follows: repeat electrolyte, repeat blood acetone, consultation with the department of nutrition, and the division of metabolic-endocrinology. The patient was treated with intravenous Marthose 12 hour/500 cc and NaCl 0,9% for emergencies, a diabetic liquid diet DM via nasogastric tube of 1900 calories divided into 4 large doses of 350 cc each and 2 small portions of 250 cc each, at 7 a.m., 8 a.m., 11 a.m, 3 p.m., 4 p.m., and 7 p.m., 4 x 25 units of Insulin at 7 a.m., 11 a.m, 3 p.m., and 7 p.m. prior to administration of liquid diet via nasogastric tube.

On Friday afternoon, at 3 p.m., the patient's consciousness was apathetic-somnolent. His blood pressure was 100/60 mmHg, his pulse rate 100 times/minute, his respiration rate 20 times/minute, body temperature 38°C, and cito blood sugar 87 mg/dL. At 5 p.m. the patient was somnolent, blood pressure 90/60 mmHg, pulse rate 108 mg/dL, respiratory rate 20 times per minute, body temperature 36.8°C, blood sugar 24 mg/dL. The patient received a bolus of 4 vials of 40% dextrose which was available after 40 minutes, an infusion of 5% Dextrose 12 hours/500 cc, continuation of diet, hourly cito blood sugar evaluation. The patient was placed on the special control list. At 5.45 p.m. the patient suffered from respiratory arrest. Heart and lung resuscitation was conducted for 5 minutes, and was declared to have failed. The patient's blood pressure could not be obtained, there was no respiration, negative light reflex and flat electrocardiography (Friday, September 8th 2000, 5.50 p.m.). The patient was pronounced dead due to hypoglycemia in type 1 diabetes mellitus with a history of recurrent diabetic ketoacidosis, with a differential diagnosis of a long-standing process/abnormality in the brain.

DISCUSSION

Ketoacidosis is a frequent complication in type 1 diabetes mellitus. Triggers of ketoacidosis include termination of insulin injection, infection, myocardial infarction, stroke, stress, and 20% due to unknown causes.[1,7,8] In this patient, there were symptoms of fever, nausea, vomiting, dry tongue, history of diabetes mellitus, termination of insulin treatment and high blood sugar accompanied by metabolic acidosis, positive blood acetone, large anion gap, and hyperosmolar serum. Treatment was administered according to the protocol for ketoacidosis. The triggers were respiratory tract infection and termination of insulin injection due to the patient's fear of a drop in glucose resulting in loss of consciousness.

Two important factors in this patient is the cause of recurrent ketoacidosis in the ward and the cause of his death. For the first problem, it is believed the causes of diabetic ketoacidosis were as follows: infection, be it mild; inaccuracy in the measurement of insulin fixed dose; cardiac ischemia; improper storage of insulin in a cooler or use of expired insulin; lack of instruction from the nurse or lack of comprehension on the part of the nurse on duty; food that was not eaten by the patient; or the patient eating foods that could increase blood sugar due to boredom of hospital foods. Psychological factors in-

cluded inability of the patient to pay his hospital bills, and stress that his wife and children did not visit him during his illness. The last possibility is that ketoacidosis was due to unknown etiology (less than 20%).[8,14]

The mortality due to ketoacidosis has dropped from year to year with more rapid and accurate management of ketoacidosis according to hospital protocols.[8,14]

The cause of death in this patient is still under debate, whether it is truly due to hypoglycemic shock or pure hypoglycemia, or both problems occurring side by side.

The cause of hypoglycemia itself was suspected to be due to: no intake of food after the last insulin injection, reduced insulin requirement due to infection or psychological problems. Considering the increase in insulin requirement during hospitalization, there is a possibility that the doctor was not careful in calculating the fixed dose of insulin, or that there was truly an increased requirement (the last being 103 units/24 hours).

Based on the insulin mapping, it is observed that there is a lack of awareness from both the ward doctor as well as the physician on duty on the patient's state of consciousness, which became apathetic-somnolent from 3 p.m., where the blood glucose level had already seem to drop. Dextrose 40% bolus should have been administered immediately. Blood acetone should have been evaluated, and if it had been positive, the patient should have undergone the protocol for ketoacidosis. Rapid and accurate management would have minimized the morbidity and mortality risks in patients with hypoglycemia and recurrent ketoacidosis.

The cause of recurrent ketoacidosis should have been explored, and treatment administered even though the cause remained unknown. If the blood glucose increased without a known trigger, suspect the possibility of expired Actrapid. After inspection, the Actrapid was not expired, but the nurse had refused to administer the dose of insulin according to instruction due to fear of the patient entering hypoglycemia phase.

The possibility of the patient being a Briethell diabetic should be evaluated through ICA and anti-GAD evaluation (was too expensive to be conducted).

REFERENCES

1. Supartondo, Noer HM Sjaifullah et al. Ketoasidosis. In: Buku ajar ilmu penyakit dalam. 1st vol, 3rd ed, Jakarta: Balai Penerbit FKUI; 1996. p.622-6.
2. Lebovitz HE. Diabetic ketoacidosis. The Lancet 1995;345:767-71.
3. Kitabchi AE, Wall BM. Diabetic ketoacidosis. J Med Clin of North Am 1995;79(Pt 1):9-33.
4. Musey VC, Lee JK, Crowford R, Klatka MA, Adam DM, Philips LS. Diabetes in urban African-Americans: Cessation of insulin therapy is major precipitating cause of diabetic ketoacidosis. Diabetes Care 1995;18(Pt 4):483-9.
5. Kitabchi AE, Fischer JN, Murphy MB, Rumbak MJ. Diabetic ketoacidosis and hyperglycemic: Hyperosmolar nonketotic state in Joslin's diabetes melitus. In: Kahn CR at al eds. 13th ed. 1994. p.738 –70.
6. Foster DW. Diabetes melitus In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, et al editors. Harrisons's principle of internal medicine.14th ed. New York: Mc-Graw Hill; 1997. p.2060-80.
7. Wiyono P. Hipoglikemia pada pasien diabetes mellitus. In: Buku ajar ilmu penyakit dalam. 1st vol. 3rd ed. Jakarta: Balai Penerbit FKUI; 1996. p.616-21.
8. Soewondo P. Ketoasidosis diabetik. In: Naskah lengkap pertemuan ilmiah tahunan ilmu penyakit dalam. Jakarta: Pusat Informasi dan Penerbitan Bagian IPD FKUI/RSUPNCM; 1997. p.181-8.
9. Perkumpulan Endokrinologi Indonesia. Konsensus pengelolaan diabetes mellitus di Indonesia. Jakarta: 1998. p.3-7.
10. Boedisantoso R. Komplikasi akut diabetes mellitus. In: Penatalaksanaan diabetes mellitus terpadu. Jakarta: Pusat Diabetes dan Lipid RSUP Nasional Dr. Cipto Mangunkusumo Fakultas Kedokteran Universitas Indonesia; 1999. p.133-7.
11. Soegondo S. Penyuluhan dan edukasi diabetes melitus. In: Buku ajar ilmu penyakit dalam. 1st vol. 3rd ed. Jakarta: Balai Penerbit FKUI; 1996. p.665-70.
12. Ikatan Dokter Anak Indonesia dan Perkumpulan Endokrinologi Indonesia. Konsensus nasional pengelolaan diabetes mellitus tipe I di Indonesia. April 2000. p.5-48.
13. Soewondo P. Penatalaksanaan kedaruratan di bidang ilmu penyakit dalam. In: Makalah ketoasidosis diabetik. Jakarta: Pusat Informasi dan Penerbitan Bagian IPD FKUI; 2000. p.89-96.
14. Noor R. Penelitian pasien ketoasidosis berulang di IGD RSCM [Final Paper]. Jakarta: Indonesia Univ.; 2000.
15. Fleckman AM. Diabetic ketoacidosis. Endocrinology and metabolism J Clin of North Am 1993;22(Pt 2):181-204.