Chapter 4

Diabetic Coma: Diabetic Ketoacidosis, Hyperglycemic Hyperosmolar State and Hypoglycaemia

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Introduction

The management of Diabetic Coma in the first three hours becomes a medical emergency. A known diabetic presenting with coma may have Diabetic Ketoacidoses, Hyperglycemic Hyperosmolar state or Hypoglycemia. Early recognition and prompt management are imperative for reducing the mortality associated with these conditions. With the advent of insulin, the most common cause of diabetic coma is drug-induced hypoglycemia. The clinical differentiation shown in Table 1 is of utmost importance because the line of management of these conditions are diagonally opposite.

Table 1

	Hypoglycemic Coma	Coma with ketosis
History	No food; too much insulin; Unaccustomed exercise.	Too little or no insulin; an infection; digestive disturbances
Onset	In good previous health; related to last medication	III-health for several days.
Symptoms	Hypoglycemia; occasional vomiting.	Of glycosuria and dehydration, pain in abdomen and vomiting
Signs	Moist skin and tongue; full pulse; Normal or raised systolic BP; shallow or normal breathing; brisk re exes.	Dry skin and tongue; weak pulse; low BP; air hunger; diminished re exes
Urine	No ketonuria; No glycosuria	Ketonuria; Glycosuria.
Blood	Hypoglycemia; Normal plasma bicarbonate.	Hyperglycaemia; reduced plasma bicarbonate.

Diabetic ketoacidosis should be differentiated from other causes of metabolic acidosis with high anion gap like lactic acidosis, uraemia alcoholic and starvation ketoacidosis.

Diabetic coma can also present itself in a diabetic patient due to precipitating conditions like septicaemia, acute myocardial infarction, stroke, acute liver injury and other hypoxic states. It would be essential to treat the underlying cause aggressively. Detailed management of Diabetic Ketoacidosis, Hyperglycemic Hyperosmolar state and Hypoglycaemia are discussed.

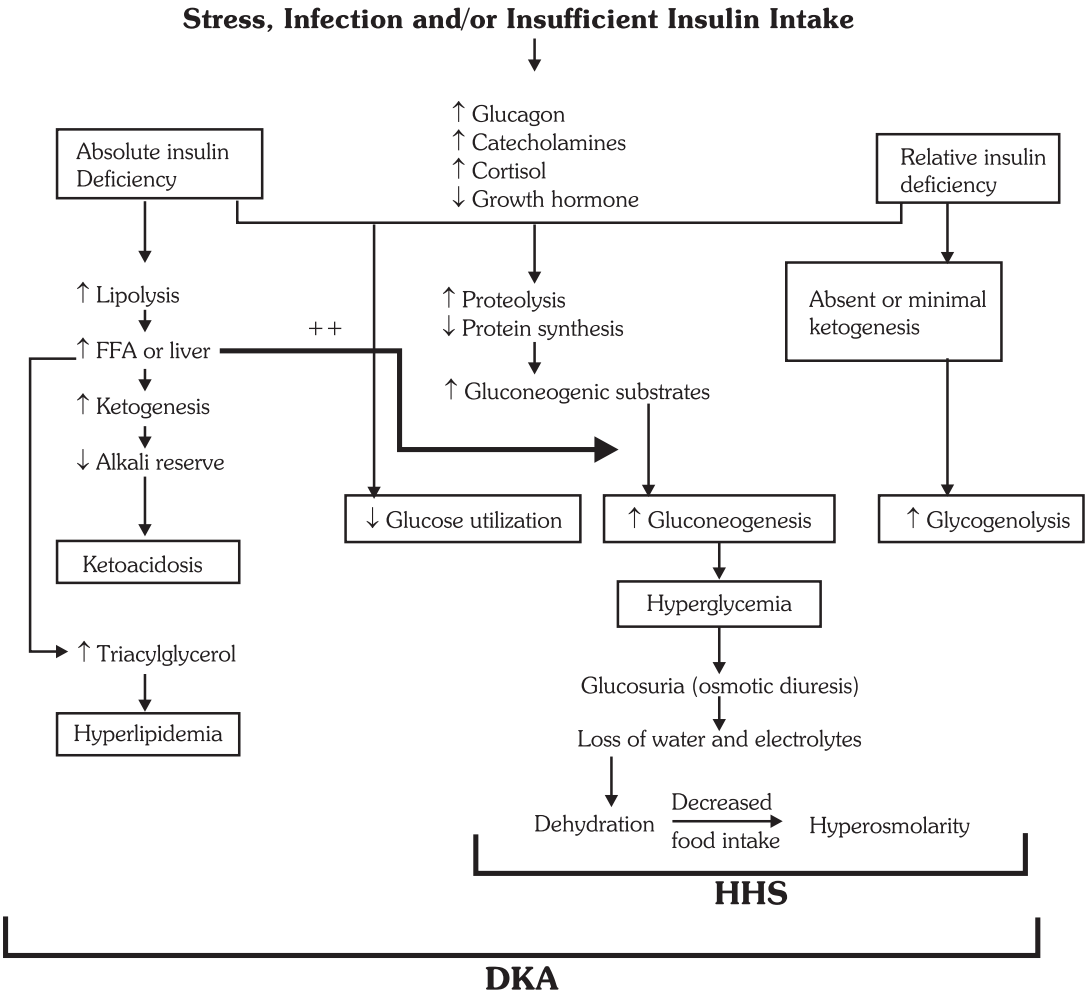


Fig. 1 : Pathogenesis of DKA and HHS

Diabetic Ketoacidosis

Definition

Diabetic Ketoacidosis (DKA) is a metabolic disorder consisting of three major abnormalities: elevated blood glucose level, high ketone bodies, and metabolic acidosis with an elevated anion gap. Dehydration and hyperosmolarity are usually present. All patients may not meet all the above criteria.

When considering the precipitating factors for the development of DKA, it is important to remember that DKA develops due to either an absolute or a relative absence of insulin. In Type 2 diabetes, it is usually a relative lack of insulin unlike that seen in Type 1 diabetics who usually manifest an absolute absence of insuluin (Table 2).

Pathogenesis of DKA and HHS (See Figure 1)

Clinical Features

The common clinical features are enlisted in Table 3.

Table 2

A. Absolute Lack of Insulin
   - Type 1 diabetes

B. Relative Lack of Insulin
   i. Acute Illness
      - Infection or other in ammatory process
      - Myocardial infarction
      - Stroke
      - Trauma
   ii. Endocrinopathies: Anti Insulin Hormone Excess
   iii. Drugs
      - Steroids
      - Calcium channel blockers
      - Pentamidine
      - Beta-blocking agents
      - Dilantin
      - Alcohol
      - HCTZ

Table 3 : Signs and symptoms of DKA

Symptoms	Signs
Polyuria	Hyperpnoea
Polydipsia	Hypothermia
Weakness	Acetone breath
Lethargy	Acidotic breathing
Myalgia	Dyspnea
Headache	Acute abdomen
Anorexia	Dehydration
Nausea	Hypore exia
Vomiting	Hypotonia
Abdominal pain	Stupor/coma
Breathlessness	

Diagnosis

Diagnosis requires the demonstration of hyperglycemia, hyperketonemia, and metabolic acidosis. However, a presumptive bedside diagnosis is justified if the patient's urine or blood is strongly positive for glucose and ketones. A thorough search for a treatable infection must be made.

Laboratory Abnormalities

In general, the laboratory diagnosis of DKA is based on an elevated blood glucose (usually above 250 mg/dl), a low serum bicarbonate level (usually below 15 mEq/L), and elevated anion gap with demonstrable ketonemia. Individually, all of these values may vary considerably, but taken together they help make the diagnosis of DKA. In addition to the above, there are several calculations that are important in the evaluation and therapy of the patient with DKA.

Serum Osmolality: Mental status changes can occur in DKA and may be the result of DKA, or some underlying process that may have caused the patient to develop DKA. It has been well documented that mental status changes in DKA correlate with the effective serum osmolality. The effective serum osmolality is calculated as follows:

Table 4 : Clinical Features of Diabetic Coma

	Starvation or high intake	DKA	Lactic acidosis	Uremic acidosis	Alcoholic Ketosis (starvation)	Salicylate intoxication	Methanol or ethylene glycol intoxication	Hyperosmolar coma	Hypoglycemic coma	Rhabdomyolysis
pH	Normal	↓	↓	Mild↓	↓↑	↓↑	↓	Normal	Normal	Mild↓
Plasma glucose	Normal	↑	Normal	Normal	↓ or normal	Normal or ↑	Normal	↑↑ >500 mg/dl	↓↓ <30 mg/dl	Normal
Glycosuria	Negative	++	Negative	Negative	Negative	Negative	Negative	++	Negative	Negative
Total Plasma Ketones#	Slight↑	↑↑	Normal	Normal	Slight to moderate↑	Normal↑	Normal	Normal or slight	Normal↑	Normal
Anion gap	Slight↑	↑	↑	Slight↑	↑	↑	↑	Normal	Negative or Slight ↑	↑↑
Osmolality	Normal	↑	Normal	↑	Normal	Normal	↑↑	↑↑ >330 mOsm/kg	Normal	Negative or Slight↑
Uric acid	Mild (starvation)	↑	Normal	Normal	↑	Normal	Normal	Normal	Normal	↑
Miscellaneous	--	May give false-positive for ethylene glycols	Serum lactate >7 mmol/L	BUN >200 mg/dl	--	Serum salicylate positive	Serum levels positive	--	--	Myoglobinuria Hemoglobinuria

+, positive, - negative #Acetest and Ketostix measure acetoacetic acid only, thus, misleading low values may be obtained because the majority of 'ketone bodies' are β-hydroxybutyrate; #may get false-positive or false-negative urinary glucose caused by the presence of salicylate or its metabolites. From Morris and Kitabchi.

$$\text{Serum Osmolality} = 2\,(Na^+) + \text{Glu}/18 + \text{BUN}/2.8$$

Calculated total osmolalities of greater than 340 mOsm/kg are associated with stupor and coma. Calculated values below this level would not explain a patient with coma and an additional cause such as meningitis, or stroke should be considered.

Corrected Serum Sodium Levels: Despite volume depletion, serum sodium may be low, normal or elevated. This variation has several causes. When trying to determine the degree of dehydration in a patient it is best to use corrected serum sodium level. This can be calculated using the following formula:

$$\text{Corrected } Na^+ = [Na^+] + 1.6 \times [\text{glu in mg/dl}] - 100$$

Often, the initial serum sodium appears low, but when the above calculation in performed, the final value is elevated. This indicates a marked intracellular dehydration.

Anion Gap: The ketoacids produced during DKA are buffered by the serum bicarbonate and then excreted in the urine. This causes a loss of bicarbonate which is a measured anion. As the bicarbonate is lost, the anion gap increases.

The three ketone bodies are beta-hydroxybutyrate, acetoacetate, and acetone. Only acetoacetate and acetone are measured in the nitroprusside reaction, but the formation of these ketones bodies favors the development of beta-hydroxybutyrate. Thus, the test for ketone bodies may be only weakly positive even when large amounts of total ketones are present. Acetone does not contribute to the anion gap but it is measured in the nitroprusside reaction and is a precursor for the regeneration of bicarbonate.

It is not uncommon for the patient to be improving clinically, but to have the nitroprusside test become more strongly positive since acetone is being produced. At this point, the anion gap should be narrowing, even as the nitroprusside test is getting stronger.

Additional Laboratory Evaluation: When the patient arrives in the emergency department some initial labs should be sent. Many of these common tests will give the data needed to do the above important calculations. A tube should be sent for exact glucose determination, but a bedside test can be used to determine gross blood sugar levels. To determine the degree of acidosis and bicarbonate loss, an ABG should be sent early in the evaluation of a patient considered to have DKA.

The complete blood count often shows an elevation of the white blood cells. This may be, in part, due to hemoconcentration secondary to dehydration. Thus, WBC counts to 20,000 occur commonly. Those patients with WBC's greater than 30,000 who have a bandemia on peripheral smear should be assumed to have an infectious process.

Additional evaluation should take into considering the best tests to help determine the potential cause of the patient's decompensation into DKA. Urinalysis, chest radiograph, and electrocardiogram should be done on most patients.

Treatment

Algorithm (Fig. 2)

Initial Evaluation (perform immediately)

- History and physical examination
- Laboratory tests: arterial blood gases, complete blood count with differential urinalysis, blood glucose, blood urea nitrogen, creatinine, electrolytes
- Electrocardiogram
- Chest radiograph and cultures as needed
- Start IV uid: 1 L of 0.9% sodium chloride per hour initially (15-20 ml/kg/hour)

Diagnostic Criteria for Diabetic Ketoacidosis (Table 5)

- Blood glucose level >250 mg/dl (13.9 mmol/L)
- Arterial pH <7.3
- Serum bicarbonate level <15 mEql/L
- Moderate Ketonuria and Ketonemia

The treatment goals of the patient with DKA are as follows:

1. improve hypovolemia and tissue perfusion,
2. decrease the serum glucose,
3. reverse ketonemia and acidaemia at a steady rate,
4. correct electrolyte losses and imbalances,
5. find and treat the underlying cause of the patient's DKA.

Hydration Therapy: Patients with DKA are invariably dehydrated and foremost in the treatment of DKA is restoration of the intravascular volume. Estimates of uid deficits in the decompensated diabetic is 4-10 litres (usually 5-6 liters). Enough uid should be given to approximate this amount (Table 6).

Initially, one to two liters of normal saline is given within the first hour followed by 1 L/hour for the next several hours. This initial management should be guided by the patient's general condition and response, with more or less uid as indicated. After the first 3-4 hours, as the clinical condition of the patient improves, with stable blood pressure and good urine output, uids should be changed to ½ normal saline at 250-500 cc an hour for 3-4 hours. Ongoing reassessment is critical. When dehydration does not appear severe, rehydration rates one-half as fast as the above regimens have been studied with good results and less electrolyte disturbance. This may be considered in those patients who appear only minimally dehydrated.

Insulin: Insulin has several actions in managing DKA. These include decreasing glucagon release from the pancreas and limiting glucagon's effect on the liver. This decreases gluconeogenesis and ketogenesis

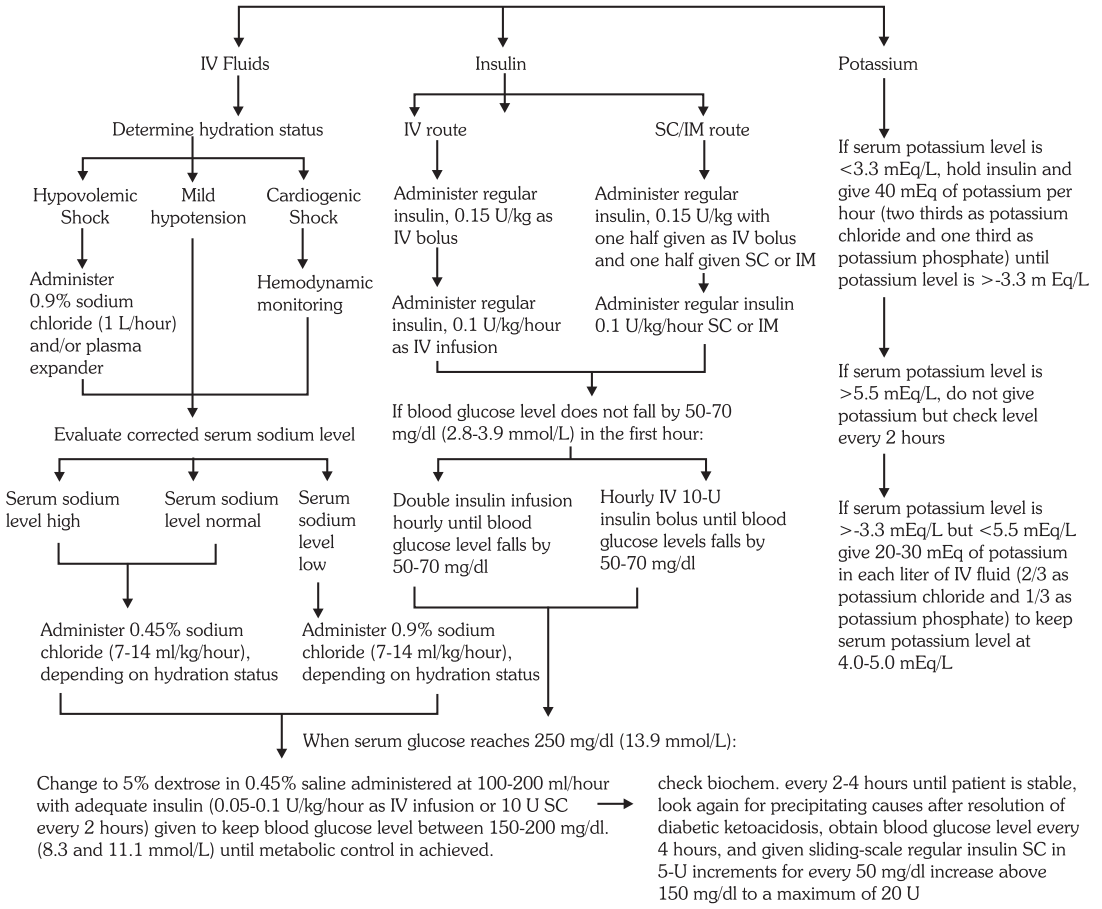


Fig. 2: Algorithm for treatment of DKA

in the liver. Additionally, the insulin allows glucose uptake and utilization by peripheral tissues.

Current recommendations for insulin therapy include an initial intravenous insulin bolus of 0.1-0.4 U/kg body weight followed by a continuous intravenous infusion of 0.1 U/kg/hour. This usually amounts to 5-10 U/hour in the typical adult. The goal of treatment should be to lower the serum glucose of the patient by 75-100 mg/dl/hour. The rate can be doubled every hour if this rate is not achieved. Ongoing difficulty in controlling the glucose levels may indicate the presence of a severe underlying infection.

The ketosis and acidaemia in DKA takes longer to resolve than the elevation of glucose. For this reason, the insulin therapy must be continued even when the blood glucose levels have improved to near normal levels. When the glucose levels begin to approach 250 mg/dl, insulin infusions are continued, but the uid composition is changed to include 5-10% dextrose in water to avoid hypoglycemia.

Potassium: Regardless of the serum potassium level at the initiation of therapy, during treatment of DKA there is usually a rapid decline in the potassium concentration in the patient with normal kidney function.

General recommendations for potassium replacement are as follows. If the patient does not have marked elevation of potassium, is not in renal failure, the ECG does not show evidence of hyperkalemia beyond peaked T-waves, potassium therapy is initiated once good urine output has been established. Potassium is usually added to the intravenous uids and should not exceed 40 mEq per liter of

intravenous uids. Some authors recommend splitting the potassium replacement as KCL and KPO_4. The potassium level should be checked every one to two hours initially since this is when the greatest shift occurs. After the patient has stabilized the potassium can be checked every 6-8 hours.

Bicarbonate Therapy: The use of bicarbonate in the treatment of DKA is highly controversial. Current recommendations for bicarbonate therapy are as follows. Use of bicarbonate is considered unnecessary when the blood pH is greater than 7.1. For those patients with pH between 6.9 and 7.1 there are no clear guidelines. If the patient is elderly or very debilitated there may be some benefit to give bicarbonate in this range. If it is given it should be given with the intravenous uids and not as IV push. For those patients with pH below 6.9 bicarbonate should be added to the intravenous uids. One ampuole of bicarbonate has 44 mEq of sodium bicarbonate. Attempts should be made to create an isotonic uid with the bicarbonate being added to either one-half normal saline or D5W.

Phosphate: Phosphate is normally an intracellular substance that is dragged out of the cell during DKA. Similarly like potassium, at presentation the serum levels may be normal, high, or low while the total body supply is depleted. Despite this depletion, replacement of phosphate has not been shown to affect patient outcome and routine replacement is not recommended.

Antibiotics

In most instances, it may be necessary to start treatment with a broad spectrum antibiotic without waiting for specific proof of the presence of an infection and a culture and sensitivity test.

Frequency of Monitoring in DKA

- In severely ill patients, electrolytes including potassium, pH and serum creatinine should be monitored hourly for the first 4 hours then at 4 hourly intervals, over the next 12 hours.
- Vital signs (e.g., pulse, temperature, respiration, blood pressure and mental status) should be monitored with similar frequency.
- Once the glucose is <15 mmol/L, the pH is near normal and the patient is eating and drinking well, the frequency of laboratory blood tests can be reduced further. At this stage, start checking the urine for ketones to ascertain whether these are clearing.

Laboratory Evaluation of DKA vs HHS

	DKA	HHS
Plasma Glucose	elevated	very high
pH	below 7.3	above 7.3
Bicarbonate	<15 mEq/l	>20 mEq/L
Serum Ketones	present	negative
Ketonuria	present	negative
Osmolarity	varies	very high
Insulin Levels	very low	can be normal

Flow Sheet for Monitoring Treatment

Suggested DKA/HHS Flowsheet

Date Hour	ER												
Weight (daily)													
Mental Status*													
Temperature													
Pulse													
Respiration/Depth**													
Blood pressure													
Serum glucose (mg/dl)													
Serum ketones													
Urine ketones													
Electrolytes													
Serum Na (mEq/L)													
Serum K (mEq/L)													
Serum Cl (mEq/L)													
Serum HCO_3^- (mEq/l)													
Serum BUN (mg/dl)													
Effective Osmolality													
pH Venous (V) Arterial (A)													
pO_2													
pCO_2													
O_2SAT													
Units Past Hour													
Route													
0.45% NaCl (ml) Past hour													
0.9% NaCl (ml) Past Hour													
5% Dextrose (ml) Past Hour													
KCl (mEq) Past Hour													
PO_4 (mMoles) Past Hour													
Urine Output (ml)													
*A – Alert; D – Drowsy; S – Stuporous; C – Comatose; **D – Deep; S – Shallow; N - Normal													

Complications of DKA Therapy

Brain Edema: Clinical brain edema occurs in less than one percent of the pediatric population and even less frequently in adults. When it does occur the mortality rate is high. It is probably prudent to prevent over vigorous correction of severe hyperosmolarity and hypernatremia.

When this complication does develop, it typically has a rapid onset of severe headache and depression of the mental status. CT scan will show characteristic changes. Treatment must be started rapidly with intravenous mannitol and intubation as indicated.

Adult Respiratory Distress Syndrome: This complication usually occurs during therapy with uids, insulin and electrolyte replacement.

Table 5: Diagnostic Criteria for DKA and HHS

	DKA			HHS
	Mild	Moderate	Severe	
Plasma glucose (md/dl)	>250	>250	>250	>600
Arterial pH	7.25-7.30	7.00-<7.24	<7.00	>7.30
Serum bicarbonate (mEq/l)	15-18	10-<15	<10	>15
Urine ketones*	Positive	Positive	Positive	Small
Serum ketones*	Positive	Positive	Positive	Small
Effective serum osmolality (mOsm)⊥	Variable	Variable	Variable	>320
Anion gapΨ	>10	>12	>12	<12
Alteration in sensorium	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

* Nitroprusside reaction method; ⊥ calculation: 2 [measured Na (mEq/l)] + glucose (mg/dl)/18; + BUN/2.8
Ψ anion gap calculation: $(Na^+) - (Cl^- + HCO_3^-)$ (mEq/l)

Table 6 : Typical Total Body Deficits of Water and Electrolytes in DKA and HHS

	DKA	HHS
Total water (liters)	6	9
Water (ml/kg)	100	100-200
Na^* (mEq/kg)	7-10	5-13
Cl^- (mEq/kg)	3-5	5-15
K^+ (mEq/kg)	3-5	4-6
PO_4 (mmol/kg)	5.7	3-7
Mg^{++} (mEq/kg)	1-2	1-2
Ca^{++} (mEq/kg)	1-2	1-2

Hyperchloremic Acidosis: This complication can be recognized by a low bicarbonate level, low to normal pH, normal anion gap, and an increased serum chloride level. The cause of this condition is multifactorial. It may be minimized by switching to hypotonic uids during therapy and by using smaller amounts of chloride during therapy (KPhos rather than KCl).

Hypokalemia: As the patient is being treated for DKA, the volume expansion, and insulin therapy can rapidly lower potassium. To avoid sudden decompensation due to severe hypokalemia, it is prudent to recheck serum potassium following each liter of uid. If large doses of insulin are required to control the patients blood glucose, the potassium level will need to be checked more frequently.

Hypoglycemia: As discussed previously, during DKA therapy, the serum glucose typically normalizes before the ketotic state has been corrected. To reverse this state it is necessary to continue insulin therapy after the glucose levels have improved. Without close monitoring, this can result in life-threatening hypoglycemia. To help avoid this, glucose measurements should be done frequently, and as the glucose level nears 250 mg/dl, the insulin infusion rate should be slowed, and glucose infusion with 5% dextrose should be started.

Hyperglycemic Hyperosmolar State (HHS)

Hyperglycemic hyperosmolar state (HHS) was first described by Sament and Schwartz in 1957. It is defined by extreme hyperglycemia, increased serum osmolality, and severe dehydration without significant ketosis or acidosis. HHS is one of the most serious acute complications of diabetes and is an important cause of morbidity among patients with diabetes. The incidence of HHS is difficult to state with certainty due to the lack of population based studies and the comorbidity that is usually found

Table 7 : Predisposing or Precipitating Factors for HHS

Acute illness	Drugs/therapy
Acute infection (32-60%)	Drugs
Pneumonia	β-Adrenergic blockers
Urinary tract infection	Calcium channel blockers
Sepsis	Chlorpromazine
Cerebral vascular accident	Cimetidine
Myocardial infarction	Diazoxide
Acute pancreatitis	Diuretics
Acute pulmonary edema	Encainide
Intestinal obstruction	Ethacrynic acid
Dialysis, peritoneal	Immunosuppressive agents
Mesenteric thrombosis	L-asparaginase
Renal failure	Loxapine
Heat stroke	Phenytoin
Hypothermia	Propranolol
Subdural hematoma	Steroids
Severe burns	Total parenteral nutrition
Endocrine:	Previously undiagnosed diabetes
Acromegaly	
Thyrotoxicosis	
Cushing's syndrome	

with the condition. However, it is estimated that the rate of hospital admission due to HHS is much lower than DKA and accounts for less than 1% of all primary diagnosed diabetic admissions. While the mortality rate has been stated to be less than 5% in DKA, it is much greater for HHS (15%), which increases with age and the presence of comorbid conditions, such as hypotension and deterioration of consciousness. Based on the recent ADA guidelines, DKA differs from HHS by the serum glucose concentration, arterial pH, serum bicarbonate, urine ketone, anion gap, and degree of mental obtundation. These differences are depicted in Table 5. The formulae for calculation of osmolality and anion gaps are also presented in this table. Table 6 depicts water and electrolyte deficits in DKA and HHS.

Precipitating and Predisposing Factors

In general, patients with HHS have a longer history of symptoms of diabetes and present to the emergency room in an obtunded or comatose state. Such precipitating factors as infection, steroid usage, thrombosis, renal disease, peritoneal dialysis, hyperalimentation, and myocardial infarction are some of the major contributing factors to the development of HHS. These factors and drugs are listed in Table 7. Typically, such individuals have type 2 diabetes, whose diagnosis has been delayed or missed, have severe infection of gram negative type or acute viral illnesses. The delayed diagnosis of diabetes leads to hyperglycemia and severe dehydration. These patients are frequently nursing home residents aged 57-69 years.

Pathogenesis

The basic underlying pathogenic mechanism for HHS is reduction in the net effective concentration of circulating insulin and concomitant elevation of counterregulatory or stress hormones, such as

Table 8: Biochemical Data in Patients with HHS or DKA

Parameters Measured	HHS	DKA
Glucose (mg/dl)	930 ± 83	616 ± 36
Na^+ (mEq/l)	149 ± 3.2	134 ± 1.0
K^+ (mEq/l)	3.9 ± 0.2	4.5 ± 0.13
BUN (mg/dl)	61 ± 11	32 ± 3
Creatinine (mg/dl)	1.4 ± 0.1	1.1 ± 0.1
pH	7.3 ± 0.03	7.12 ± 0.04
Bicarbonate (mEq/l)	18 ± 1.1	9.4 ± 1.4
3-β-hydroxybutyrate (mmol/l)	1.0 ± 0.2	9.1 ± 0.85
Total osmolality	380 ± 5.7	323 ± 2.5
Insulin (nmol/l)	0.08 ± 0.01	0.07 ± 0.01
C-peptide (nmol/l)	1.14 ± 0.1	0.21 ± 0.03
FFA (nmol/l)	1.5 ± 0.19	1.6 ± 0.16
Human growth hormone (ng/ml)	1.9 ± 0.2	6.1 ± 1.2
Cortisol (ng/ml)	570 ± 49	500 ± 61
Insulin (nmol/l) (stimulated)	0.27 ± 0.05	0.09 ± 0.01
C-peptide (nmol/l) (stimulated)	1.75 ± 0.23	0.25 ± 0.05
ΔGap (anion gap-12) (mEq/l)	11	17

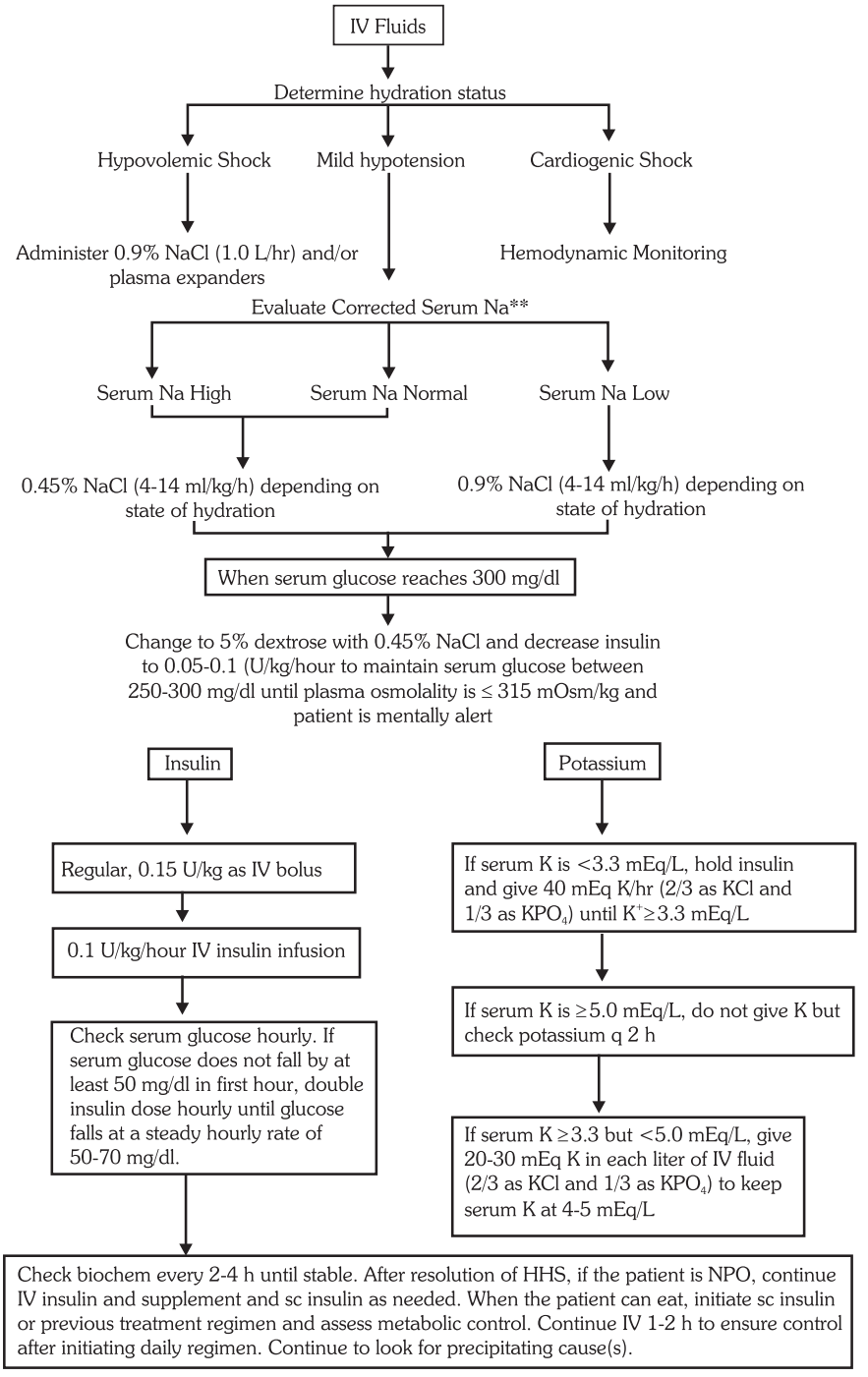
glucagons, catecholamines, cortisol, and growth hormone in association with severe dehydration. DKA and HHS represent opposite ends of a spectrum of hyperglycemia with or without ketosis. However 'mixed' mild ketotic hyperosmolar conditions may exist. In certain studies, approximately one-third of DKA patients were also hyperosmolar. There have been many hypotheses proposed for the lack of severe ketoacidosis in HHS. These include lower levels of counterregulatory hormones, decreased level of lipolysis secondary to hyperosmolar state, and lower circulating levels of insulin in HHS. Table 8 compares the admission biochemical data between DKA and HHS. In these studies, both baseline and stimulated C-peptide were significantly lower in DKA than in HHS, with comparable levels of free fatty acids. Thus, the consensus for the lack of ketoacidosis in HHS seems to be a greater level of pancreatic insulin in HHS than in DKA, which would be adequate to inhibit ketogenesis but not adequate to control hyperglycemia. Figure 1 depicts the pathogenic pathway for DKA and HHS in regard to carbohydrate, lipid, and protein metabolism. As can be seen in this figure, the major difference between the two conditions is the absence of ketogenesis in HHS and a more severe dehydration, which results in hyperosmolarity and moderate to severe obtundation.

Diagnosis

The laboratory criteria for diagnosis of hyperosmolar state are defined in Table 5 and consists of blood glucose >600 mg/dl, pH >7.3, bicarbonate >15, and mild ketonemia and effective osmolality >320 mOsm/kg, with variable level of mental obtundation. Approximately 50% of HHS patients have increased anion gap, secondary to mild acidosis or increased lactate.

Treatment Strategies

The therapeutic goal for HHS is to improve circulatory volume and tissue perfusion by uid and electrolyte replacement, to decrease serum glucose and hyperosmolarity by a gradual decrease in blood glucose with the use of low dose insulin (see Figure 3). Hydration in an important aspect of initial therapy. The initial uid should consist of normal saline and the subsequent hydration should be based on serum electrolyte levels. Patients should not be started on insulin until the initial serum potassium



** Serum Na should be corrected for hyperglycemia: For each 100 mg/dl glucose >100 mg/dl, add1.6 mEq to sodium for corrected serum value.

Fig. 3 : Protocol for Management of Adult Patients with Hyperglycemic Hyperosmolar State (HHS)*
* This protocol is for patients admitted with mental changes or severe dehydration who require admission to an intensive care unit.

level has been established. The second bottle of IV uid should have 20-40 mEq of potassium chloride added as replacement therapy. It is important to point out that the initial diagnosis, which usually occurs in the emergency room, should be prompt, looking for all the possible precipitating factors, and prompt management of infection and other contributing factors. Patients with HHS are most often obtunded and infected; therefore, they should be initially treated in the emergency room and then followed in the ICU since the mortality rate is higher than in DKA.

Prevention

As the care of patients with HHS is of paramount importance, so is the prevention of subsequent hyperglycemia crises. The most important aspect of prevention is education of the patients and better evaluation of patients in the hospital or nursing homes, since a considerable number of such patients with HHS have undiagnosed hyperglycemia. Recent studies, both in a surgical ICU as well as in general hospital admissions demonstrated that unrecognized hyperglycemia is a marker for increased hospital mortality. Therefore it is important that nursing home residents be frequently monitored for blood glucose as well as for signs of dehydration, with frequent offering of water, to these individuals, some of whom may not be able to recognize the need for water. Of particular importance is the prevention of hyperosmolar state in those who experience the precipitating conditions itemized in Table 7. Provision of a ow sheet to record laboratory values and the clinical status of patients will enhance follow-up and care of such patients. Thorough assessment of precipitating events will improve mortality rate and foster early resolution of DHA or HHS.

Complications

While adult respiratory distress syndrome (ARDS), hypercholemic acidosis, and cerebral edema may be observed in DKA, these conditions are very rare in HHS patients. The only significant complication in HHS may be thromboembolic events and possible disseminated intravascular coagulation as well as pulmonary aspiration in the presence of obtunded state. Use of heparin may be an important adjunct to therapy or prevention of thromboembolic events in HHS.

Hypoglycemia

The term hypoglycemia refers to the clinical condition resulting from an abnormally low plasma glucose levels (<40 mg/dl). Clinically it is characterized by varying degree of neurological dysfunction and is responsive to the administration of glucose.

The predisposing factors are Delayed or skipped meals, Decreased carbohydrate intake, increase in the dose of insulin or oral antidiabetic drugs, decrease in insulin requirements (after delivery, or with the elimination of stress or control of infection, renal or hepatic insufficiency), sick days, unexpected physical strain after taking insulin or oral hypoglycemic drugs, alcohol consumption etc. Hypoglycemia needs to be treated promptly. While it is useful to document the degree of hypoglycemia, this should not delay treatment, and the general advice is “If in doubt, treat”.

Clinical Features

Rapid fall of blood glucose (as with insulin) leads to manifestations of the activation of the sympathetic nervous system while a gradual fall (as seen with OHAs) lead to the symptoms due to decreased cerebral function (Table 9).

Persistence of hypoglycemia for over six hours may lead to permanent brain damage. Recurrent attacks may also contribute to mental changes in cognitive function.

Table 9 : Symptoms of hypoglycemia

Neuroglycopenic	Adrenergic
Fainting	Hunger
Yawning	Perspiration
Weakness	Rise in BP
Tingling in the fingers	Tremors
Diplopia	Headache
Hysterical behaviour	Palpitation
Disorientation	Anxiety and nervousness
Mental confusion	Weakness
Convulsions and coma	

Management of Hypoglycemia

a) The Conscious Patient

The treatment involves immediate intake of 10-20 gms of glucose or a rapidly digestible form of carbohydrate orally, followed by a snack of a more slowly digestible form of carbohydrate (equivalent to one slice or bread) to maintain normoglycemia until the next meal. If the patient is on acarbose also, then treat it with glucose.

b) The Unconscious Patient

A severe hypoglycemic episode can only be treated by intravenous glucose (50-100 ml of 25%/50% dextrose). In unresponsive patients, parenteral glucagon (0.5-1 mg IM) should be administered. In these patients carbohydrates should be given orally as soon as the patient regains consciousness. The patient must regain consciousness within half an hour. Parenteral dexamethasone is also recommended in unresponsive patients.

It is important to follow glucose level for at least 24-48 hours in patients where hypoglycemia is induced by long acting sulphonylureas (chlorpropamide/glibenclamide) or long acting insulin (Lente/NPH). A long term glucose infusion may be necessary and the patient should be hospitalized. Occasional patient may take longer time to recover.

c) Prevention of Hypoglycemia

Education of patient and family members is a must. Education of the health care providers in terms of diagnosing diabetes, its management and also diagnosing hypoglycemic episodes early is important.

Suggested further readings:

1. Fishbein HA, Palumbo PJ: Acute metabolic complications in diabetes. In Diabetes in America. National Diabetes Data Group, National Institutes of Health, 1995;p.283-291 (NIH publ. No.95-1468).
2. Kitabchi AE et al. Management of hyperglycemic crises in patients with diabetes. Diabetes Care 2001;24: 241-269.