

X. DIABETES CARE IN THE HOSPITAL

A. Guidelines for Hospitalization

The decision to hospitalize a patient for diabetes must be individualized. The following criteria serve as general indications for hospitalizing patients for reasons related to diabetes:

- Life-threatening, acute metabolic complications of diabetes (diabetic ketoacidosis, hyperglycemic hyperosmolar state, or hypoglycemia with neuroglycopenia).
- Newly diagnosed diabetes in children and adolescents.
- Substantial and chronic poor metabolic control that necessitates close monitoring of the patient to determine the etiology of the control problem, with subsequent modification of therapy.
- Severe chronic complications of diabetes that require intensive treatment or other severe conditions unrelated to diabetes that significantly affect its control or are complicated by diabetes.

Glycemic Goals for Hospitalized Patients

Inpatient diabetes management has been the focus of attention in the past few years and several highly-acclaimed studies have demonstrated important benefits in tighter glycemic control in hospital patients. These benefits are more apparent in acutely ill patients in the ICU settings. In August 2006, the American College of Endocrinology and the American Diabetes Association published a consensus report on inpatient diabetes and glycemic control. However, the optimal glycemic goals in non-critical patients are not well established. The following glycemic goals present generally recommended targets for hospitalized patients:

Glycemic goals in the intensive care setting:

- 80-110 mg/dL (4.4-6.1 mmol/l) all the time.

Glycemic goals in the non-critical setting:

- <110 mg/dL (6.1 mmol/l) pre-prandial
- <180 mg/dL (10.0 mmol/l) maximal.

Values above 180 mg/dL (10 mmol/l) are an indication to monitor glucose levels more frequently to determine the direction of any glucose trend and the need for more intensive intervention. Achieving these targets may require consultation with a diabetes specialist.

The occurrence of significant hyperglycemia in the hospital requires close follow-up after discharge. In those with previously diagnosed diabetes and an elevated A1c on hospital admission, revision of the pre-admission diabetes therapy is required to establish glycemic control. In those without previously diagnosed diabetes, the differentiation between hospital-related hyperglycemia and undiagnosed diabetes requires follow-up testing (Fasting BG*, 2-hour OGTT) once metabolically stable.

Glycemic Goals for Pregnant Inpatients

Separate upper-limit targets (Table 30) have been developed to address the increased risk of poor outcomes caused by hyperglycemia in pregnancy.

* BG throughout these Recommendations means plasma or serum glucose. For a discussion on the ways of measuring glucose in the blood and their differences, see the Appendix, page 93.

TABLE 30
Glycemic Goals for Pregnant Inpatients

ADA			AACE		
Prenatal			Prenatal		
≤ 100 mg/dL	(5.6 mmol/l)	preprandial	60-90 mg/dL	(3.3-5.0 mmol/l)	preprandial
≤ 120 mg/dL	(6.7 mmol/l)	1 hr postprandial	<120 mg/dL	(6.7 mmol/l)	1 hr postprandial
Labor and Delivery			Labor and Delivery		
≤ 100 mg/dL	(5.6 mmol/l)	---	70-90 mg/dL	(3.9-5.0 mmol/l)	---

Again, if these targets are unable to be achieved, then consultation with a diabetes specialist should be considered.

B. Hospital Barriers to Excellent Glycemic Control

There are several reasons why patients with diabetes often do not have excellent glycemic control when hospitalized:

- Infection, fevers, glucocorticoid therapy, surgical trauma, and general medical stress may make diabetes control challenging.
- Decreased physical activity (especially in a previously active patient) can result in worsening hyperglycemia.
- Subcutaneous insulin absorption may be erratic in acutely ill patients.
- Patients often lose individual control of their diabetes and are unable to utilize self-management techniques when the responsibility is taken over by the health care team.
- Interruptions in meals and medication doses due to hospital diagnostic and therapeutic procedures.

C. Common Errors in Inpatient Glucose Management

- **Admission Orders:** All too frequently no change in a patient's diabetes regimen is made or it is stopped completely upon hospitalization. Modification of the outpatient diabetes treatment is generally necessary after hospitalization.
- **Use of "Sliding Scales:"** Frequently patients will be managed on a nonphysiologic sliding scale, without scheduled basal and pre-meal insulin, resulting in wide glycemic excursions.
- **Under utilization of insulin drip:** IV insulin is an effective tool in attaining excellent glycemic control and should be considered in the majority of inpatient diabetes cases.

Recommendations

Diet: Diet should always be individualized based on a patient's medical status and concurrent illness. Consultation by a dietitian or diabetes educator while an inpatient should be considered.

Glucose monitoring: Patients should have blood glucose testing at least four times a day upon admission. This may be continued or reduced depending on the glycemic control and medical status of the individual patient. More frequent testing (every 1 or 2 hours) is indicated for more seriously ill patients and/or those on IV insulin.

Glycemic control: Poor glycemic control can result in many complications such as infection and poor wound healing. Glycemic goals should be individualized for each patient.

D. Inpatient Pharmacotherapeutic and Insulin Recommendations

General Recommendations

- Inpatient diabetes regimens should be reassessed frequently.
- Patients with type 1 diabetes will require some insulin at all times, even when fasting, to prevent ketoacidosis.
- The use of sliding scales should be minimized. The use of sliding scale insulin alone should be completely avoided in all type 1 and in many insulin-requiring type 2 patients. These patients are better managed with scheduled dose basal and prandial insulin. A supplementation/correction scale may then be added at the discretion of the clinician to address hyperglycemia.
- If optimal glycemic control is not attained, consultation with diabetes specialist should be considered.

Specific Recommendations

Type 2 patient usually treated with oral medications who IS NOT eating:

- Consider stopping insulin secretagogues (sulfonylureas, etc.) to avoid hypoglycemia. Addition of long-acting insulin can be considered in those patients with glycemic excursions or persistent hyperglycemia on short acting insulin alone.
- Metformin is frequently recommended to be stopped upon hospitalization because of concerns about altered renal function in an acutely ill patient. It should definitely be held in patients who are perioperative, scheduled to have radiocontrast studies, have evidence of or are at high risk for renal, hepatic, or cardiac dysfunction or dehydration.
- Thiazolidinediones may be continued for a short time, unless there are cardiac (acute CHF) or hepatic problems.

Type 2 patient usually treated with oral medications who IS eating:

- Insulin secretagogues (sulfonylureas, etc.) may be continued but attention should be paid to increased risks of hypoglycemia in a hospital patient with decreased oral intake or gastrointestinal absorption.
- Metformin should be held for same reasons as outlined above.
- Thiazolidinediones may be continued unless there are cardiac (acute CHF) or hepatic problems.
- Always consider adding insulin for those unable to attain optimal glycemic control on oral medications alone.

Type 1 or insulin-requiring type 2 patient:

- Strongly consider using an intravenous insulin infusion.
- Another less desirable option can be subcutaneous long-acting insulin with a scheduled rapid-acting insulin for meals and supplemental insulin for hyperglycemia.
- IV 5% dextrose should be utilized to prevent hypoglycemia.
- Blood glucose should be checked no less frequently than every 6 hours.
- Insulin-requiring type 2 patients who are fasting can sometimes be managed with correction scales of short/rapid-acting insulin alone, but addition of scheduled long-acting insulin to this regimen should always be considered in those with glycemic excursions or persistent hyperglycemia.

1. Sample Intravenous Insulin Infusion Orders (not intended for management of DKA)

General Guidelines

- Discontinue all subcutaneous insulin and/or oral anti-diabetes medications.
- Standard drip: 50 units of Regular insulin in 50 mL of 0.9% NaCl.
- Insulin infusion should be stopped 2-3 hours after subcutaneous insulin has been resumed. Contact physician for orders.
- Surgical patients who have received oral anti-diabetes medication within the previous 24 hours should start the infusion when BG is above 120 mg/dL. Post-operative patients require hourly BG monitoring until the infusion protocol is initiated.
- All other patients should start when BG is above 70 mg/dL.
- Most patients require 5-10 gm of glucose per hour (D5 @ 100-200 mL/hr) or equivalent continuous TPN or enteral feeding.
 - D5NS + _____ mEq Kcl/L at _____ mL/hr
 - D5½NS + _____ mEq Kcl/L at _____ mL/hr _____ at _____ mL/hr

Initiating the Infusion

Blood glucose (BG) Goal Range = 80-180* mg/dL or _____. No patient should be initiated on Algorithm 3 or 4 unless discussed with physician.

- Algorithm 1: Start here for MOST patients.
- Algorithm 2: Start here for patients receiving above 80 units/day of insulin as an outpatient. Move to this one for patients not controlled with Algorithm 1 or patients on glucocorticoids.
- Algorithm 3: Move to this one for patients not controlled with Algorithm 2.
- Algorithm 4: Move to this one for patients not controlled with Algorithm 3.

↳ Move up one algorithm: If the patient is above goal range AND the BG does not decrease by at least 60 mg/dL within 1 hour.

↳ Move down one algorithm: When BG is under 70 mg/dL for 2 consecutive checks.

↳ Move down one algorithm: If nutritional therapy (TPN or tube feedings) is discontinued or reduced by 50% or more.

↳ Move down one algorithm: If BG decreases greater than 80 mg/dL within 1 hour.

* Maintain drip rate when goal is obtained

Algorithm 1		Algorithm 2		Algorithm 3		Algorithm 4	
BG	Units/Hr	BG	Units/Hr	BG	Units/Hr	BG	Units/Hr
Under 60 = See next page for treatment							
Under 70	Off	Under 70	Off	Under 70	Off	Under 70	Off
70-109	0.2	70-109	0.5	70-109	1	70-109	1.5
110-119	0.5	110-119	1	110-119	2	110-119	3
120-149	1	120-149	1.5	120-149	3	120-149	5
150-179	1.5	150-179	2	150-179	4	150-179	7
180-209	2	180-209	3	180-209	5	180-209	9
210-239	2	210-239	4	210-239	6	210-239	12
240-269	3	240-269	5	240-269	8	240-269	16
270-299	3	270-299	6	270-299	10	270-299	20
300-329	4	300-329	7	300-329	12	300-329	24
330-359	4	330-359	8	330-359	14	330-359	28
≥360	6	≥360	12	≥360	16	<i>continued on next page</i>	

1. Sample Intravenous Insulin Infusion Orders - Continued

Patient Monitoring

- Check BG every hour until it is within goal range for 4 consecutive hours, then decrease to every 2 hours for 4 hours. If the BG remains within the goal range, decrease monitoring to every 4 hours.
- If the patient is eating, hourly BG monitoring is necessary for at least 3 hours after a meal.
- Hourly monitoring may be needed for critically ill or perioperative patients even if the BG is stable and within the goal range.
- Monitor every 30 minutes for BG between 60-70 mg/dL.

Treatment of Hypoglycemia (BG under 60 mg/dL)

- Stop insulin drip AND:
 - If awake and taking PO, give 4 ounces of juice or non-diet soda. If not taking PO, give 25 mL (1/2 amp) D₅₀ IV push.
 - If NOT awake, give 50 mL (1 amp) of D₅₀ IV push.
- Recheck BG every 20 minutes and repeat 25 mL of D₅₀ IV until BG is above 60 mg/dL.
- Restart insulin drip one Algorithm lower once BG is above 70 mg/dL on 2 consecutive checks.

When to Notify the Physician

- For any BG decrease more than 50% in 1 hour.
- For any BG increase greater than 100 mg/dL in 1 hour.
- For any BG above 360 mg/dL.
- For hypoglycemia that has not resolved within 20 minutes of giving 50 mL of D₅₀ (make sure insulin drip is stopped).

Patients usually on an insulin pump as an outpatient:

- Patients who are hospitalized for minor procedures and who will be awake and alert for the entire hospitalization may be permitted to continue to self manage their diabetes and use their insulin pump while in the hospital.
- Patients who are acutely ill, not awake and alert, or otherwise unable or unwilling to self manage their insulin pumps during hospitalization should be converted to IV insulin.
- Also, if glycemic goals are not being reached during hospitalization, then the pump should be discontinued and alternative insulin regimen begun. Consultation with a diabetes educator or certified pump trainer should be considered to troubleshoot the pump.

Perioperative Recommendations:

- Blood glucose should be checked every 1 to 2 hours before, during and after surgery or procedure.
- Sliding scales alone should be avoided because of greater risk of glycemic excursions.

Perioperative type 1 diabetes:

- Preferred: Begin IV insulin drip.
- A less desirable option is to give a long-acting insulin with supplemental doses of rapid-acting insulin.

Perioperative type 2 diabetes:

- Hold oral hypoglycemic agents the day of procedure and resume when the patient is eating again.
- Metformin should be held for 48 hours until normal renal function is assured.
- Thiazolidinediones may be continued (except for the other reasons noted above); however, missing a few doses in a patient who must be kept NPO would not negatively affect blood glucose control.
- Insulin-requiring type 2 patients may be treated similarly to type 1 patients.

Intravenous Insulin Infusion Recommendations:

- The use of intravenous insulin therapy is strongly recommended in the following groups of patients:
 - Critical illness
 - Prolonged NPO status
 - Perioperative period
 - After organ transplant
 - Total parenteral nutrition therapy
 - Blood glucose exacerbated by high-dose glucocorticoid therapy
 - Stroke
 - Labor and delivery
 - As a dose-finding strategy prior to conversion to subcutaneous insulin therapy
 - Other illnesses requiring prompt glucose control

Intravenous insulin therapy should always be used in certain settings such as diabetic ketoacidosis and hyperglycemic hyperosmolar state.

E: Hypoglycemia: Treatment of Adults and Children Older than 1 Year of Age

Recognition of hypoglycemia in the patient with diabetes:

- Patient has a diagnosis of diabetes.
- Patient is on a medication that can cause hypoglycemia (insulin or insulin secretagogues).
- One or more symptoms of hypoglycemia are present: shakiness, hunger, irritability, altered level of consciousness, headache, sweats, and cool skin.
- A stat bedside blood glucose should be done (patient may perform his/her own bedside blood glucose).
- Hypoglycemic treatment should begin when bedside blood glucose is lower than 70 mg/dL.

Treatment of the CONSCIOUS patient with hypoglycemia:

- 15/15 rule: Give a 15 gm carbohydrate oral feeding of one of the following:
 - 8 oz of low fat/nonfat milk
 - 4 oz of any juice WITHOUT ADDED SUGAR
 - 4 oz of regular soda pop
 - 1 tube of glucose gel
 - 3 glucose tablets.
- Wait 15 minutes. Recheck bedside blood glucose. If still less than 70 mg/dL, feed a second 15 gm carbohydrate feeding.
- Wait 15 minutes. Recheck bedside blood glucose. Notify physician of event if not resolved after 30 gm of carbohydrate.
- If meal is not to be served for over an hour, give patient a snack of 30-45 gm carbohydrate. Consider sandwich, cheese and crackers, or other snack that incorporates carbohydrates with fat and protein.
- Troubleshoot for cause. Too much medication, extra activity, medication taken/given at wrong time or delay in meal are common reasons for hypoglycemic events. Prevent reoccurrence and educate patient as needed.

Treatment of the UNCONSCIOUS patient with hypoglycemia:

- Call for bedside glucose in the patient with known diabetes.
- Stop IV insulin if present.
- Treat hypoglycemia and call physician.
- Consider IV placement if one not present.

- 1/2 to 1 ampule of Dextrose 50% solution IV per orders, or 1 amp of glucagon IM per orders. Glucagon takes 20 minutes to raise blood glucose and for patient to regain consciousness. Nausea and vomiting are common side effects of glucagon.
- Recheck blood glucose. If glucagon was given, the possibility of continued hypoglycemia is present for 24 hours and the patient may need extra carbohydrate intake. Test blood glucose every four hours and feed as necessary to keep blood glucose readings greater than 80 mg/dL.
- Troubleshoot for cause.

Prevention of Hypoglycemia

Prevention of hypoglycemia requires diligent monitoring of blood glucose, proper dosing of medications, regular meal planning and close monitoring during and after exercise. Sick day management includes increased fluid intake and frequent blood glucose monitoring with meals and at bedtime. Monitoring urine for ketones (if on insulin) is an essential tool of diabetes management.

Education: Hospital admission should be viewed as an opportunity to reassess a patient's self-management and other skills. Patients who have never received diabetes education, who lack knowledge of these skills or who need a review of diabetes self-management, should be considered for consultation by the diabetes education team or specialist prior to being discharged from the hospital.

Discharge Planning: Ideally, the outpatient regimen should be begun prior to the patient being discharged. Patients should be made aware of any changes in this regimen. Appropriate follow-up should be arranged and patients should be instructed on how to proceed if there are any diabetes related issues or problems that arise after discharge.

F. Diabetic Ketoacidosis (DKA)

Definition

- Absolute or relative insulin deficiency with consequent hyperglycemia and accumulation of ketones in the blood resulting in a metabolic acidosis of the anion gap type.
- Criteria: glucose >250 mg/dL; arterial pH <7.35; bicarbonate <15; positive serum ketones; anion gap >10.

Pathogenesis

- Reduction in the net effective action of circulating insulin.
- Elevation of counter-regulatory hormones: glucagon, catecholamines, cortisol and growth hormone.
- Increased hepatic and renal glucose production and impaired glucose utilization in peripheral tissues.
- Hyperglycemia and parallel changes in the osmolality of the extracellular space.
- Release of free fatty acids into the circulation from fat tissue leading to unrestrained hepatic fatty acid oxidation to ketone bodies with resulting ketonemia and metabolic acidosis.
- Loss of water, sodium, potassium and other electrolytes.

Precipitating Factors

- The precipitating factor is identifiable in 80% of the cases:
 - Infection: 30-40%
 - Cessation of insulin: 15-20%
 - Myocardial infarction, pancreatitis, stroke, alcohol abuse, drugs, trauma, other: 10-15%
 - No cause identified: 20-25%
- Special:
 - Drugs: corticosteroids, thiazides, sympathomimetic agents
 - Young patients: psychological problems, fear of weight gain

Presentation

- History: polyuria, polydipsia, polyphagia, weight loss, vomiting, abdominal pain, clouded sensorium.
- Physical examination: poor skin turgor, Kussmaul breathing, tachycardia, hypotension, altered mental status, shock, coma, normothermic or hypothermic because of peripheral vasodilation.

Laboratory

- **Initial lab**
 - Complete blood count, blood glucose, BUN, serum creatinine, serum ketones, electrolytes (calculate anion gap), osmolality, urinalysis, urine ketones, arterial blood gasses, magnesium, calcium, phosphorus and chest x-ray.
- **Additional lab**
 - EKG: if severely ill, has history of heart disease or over age 40.
 - Cultures (if indicated): urine, blood, throat, sputum, vagina, wound, spinal fluid or stool.
- **Comments**
 - Leukocytosis may be proportional to ketosis and not indicative of infection.
 - Hyponatremia can be due to flux of water from the intracellular space or falsely lowered by severe hypertriglyceridemia.
 - Serum potassium should be initially elevated due to extracellular shift caused by insulin deficiency, hypertonicity and acidemia; if initial serum potassium is not elevated, the patient may have severe total-body potassium deficiency and require cardiac monitoring and more vigorous potassium replacement.
 - If patient is stuporous or comatose and calculated effective or measured serum osmolality is not 320 or greater, then another cause for the mental status change needs to be looked for (calculated effective serum osmolality = $2 \times \text{serum sodium} + \text{serum glucose} / 18$).
 - “Corrected” serum sodium helps assess dehydration:
 - “Corrected” $[\text{Na}^+] = [\text{Na}^+] + 1.6 \times \text{blood glucose} - 100$ divided by 100.
 - An elevated corrected serum sodium indicates a greater free water deficit and intracellular dehydration.
 - As glucose is lowered with insulin, patients with a high corrected serum sodium will need larger quantities of normal saline to preserve intravascular volume before hypotonic fluids can be safely used.

Differential Diagnosis

- Starvation ketosis - bicarbonate usually not lower than 18 mEq/L
- Alcoholic ketoacidosis - glucose elevation mild (rarely >250 mg/dL)
- Lactic acidosis - elevated blood lactate
- Salicylate ingestion - elevated serum salicylate
- Ethylene glycol ingestion - calcium oxalate and hippurate crystals in the urine
- Methanol ingestion - elevated blood methanol
- Chronic renal failure - usually a hyperchloremic acidosis

Treatment

- **Successful treatment:**
 - Correction of dehydration, hyperglycemia and electrolyte imbalance.
 - Identification and treatment of comorbid conditions.
 - Frequent patient monitoring: electrolytes, blood glucose, BUN, creatinine, osmolality and venous pH should be measured every 2–4 hours.
 - Caution should be used in measuring ketones during therapy. Beta-hydroxybutyrate is the strongest and most prevalent ketoacid in DKA. During therapy it is converted back to acetoacetic acid and so measuring ketones by the nitroprusside method may be misleading.
 - Criteria for the resolution of DKA are: blood glucose <200 mg/dL; serum bicarbonate >18 mEq/L; and venous pH >7.30.

■ Fluid therapy

- In the absence of cardiac compromise, give normal saline at the rate of 15-20 mL per kg body weight per hour (1 to 1.5 L for the average adult).
- Subsequent hydration depends on state of hydration, electrolyte levels and urinary output.
- Half normal saline is indicated at 4-14 mL per kg per hour if corrected serum sodium is normal or high; give normal saline at the same rate if corrected serum sodium is low.
- Once urine output is established, the IV should include 20-30 mEq/L potassium until the patient is stable and can tolerate oral potassium.
- Fluid replacement should correct estimated deficits within the first 24 hours.

■ Insulin treatment

- Once hydration and, if needed, potassium replacement has started, a bolus of regular insulin at 0.15 units/kg (total 8-12 units for average adult) can be given and a continuous insulin infusion begun.
- The continuous insulin infusion should be at the rate of 0.1 units per kg per hour (5 to 9 units per hour in the average adult).
 - Usually add insulin in concentration of 10% or more (e.g., more than 100 units per 1,000 cc).
 - Mix well.
 - Discard the first 50 cc through the tubing before beginning the infusion.
- Plasma glucose should decline at a rate of 50-75 mg/dL per hour.
- If plasma glucose has not fallen by 50 mg/dL in the first hour, and hydration status is acceptable, insulin infusion rate may be doubled every hour until the above rate of decline is achieved.
- When plasma glucose of 250 mg/dL is reached, insulin infusion rate may be decreased to 0.05-0.1 u/kg/hr (3-6 u/hr in average adult) and dextrose added to the IV fluids to maintain the above plasma glucose until the acidosis is resolved.
- To prevent rebound acidosis and ketosis again, IV insulin can be continued for a full additional 24 hours before going back to subcutaneous insulin; there should always be at least 2 hours of overlap between initiation of subcutaneous insulin and cessation of IV insulin.

■ Potassium

- Insulin treatment, volume expansion, and correction of acidosis decrease what is usually an elevated serum potassium to start with.
- Potassium replacement is begun when serum potassium falls below 5.5 mEq/L, assuming there is an adequate urine output.

■ Bicarbonate

- At a pH of 7.0 or greater, fluid, insulin, and electrolytes resolve the ketoacidosis without the need for bicarbonate.
- Prospective randomized studies done when the arterial pH is between 6.9 and 7.1 have failed to show either benefit or harm from bicarbonate therapy.
- There are no prospective randomized studies of the use of bicarbonate in DKA when the pH is <6.9.
- Given that severe acidosis may lead to myriad adverse vascular events, the following guidelines may be followed:
 - If the arterial pH is <6.9, 100 mmol bicarbonate may be given in 400 mL IV fluid over a 2 hour period.
 - If the arterial pH is 6.9 - 7.0, 50 mmol bicarbonate may be given in 200 mL IV fluid over a 1 hour period.
- The arterial pH should be re-measured every 2 hours and the above therapy repeated until the arterial pH is 7.0.

■ Phosphate

- Despite whole body phosphate deficits in DKA, which are in the range of 1.0 mmol per kg body weight, serum phosphate levels are often normal or increased at presentation.
- Serum phosphate decreases with insulin treatment.
- Prospective randomized studies have failed to show any clinical benefit from phosphate therapy in DKA.

- Overzealous phosphate treatment can cause severe hypocalcemia. Nevertheless, careful phosphate replacement may be indicated in the presence of cardiac dysfunction, anemia, respiratory depression or the presence of a serum phosphate <1.0 . In that case, 10-30 mEq/L potassium phosphate may be added to IV fluids.

Complications of DKA

- Hypoglycemia - from over-corrected insulin therapy
- Hypokalemia - due to insulin and bicarbonate therapy and under-corrected potassium replacement
- Hyperglycemia - due to discontinuance of IV insulin treatment without adequate overlapping subcutaneous insulin treatment; subcutaneous regular insulin and IV insulin should overlap by at least 2 hr
- Cerebral edema
 - Seen in 0.7-1.0% of children with DKA and has been reported in young adults in their 20's
 - If present, is frequently fatal
 - Preventive measures that might decrease the risk are:
 - Gradual replacement of sodium and water in patients who are hyperosmolar (maximal reduction in osmolality 3 mosm/kg/hr)
 - The addition of dextrose to the IV once the plasma glucose reaches 250 mg/dL
- Non-cardiogenic pulmonary edema

Prevention of DKA

Educating the patient and family members on self-management training, recognition of potential DKA, and self-management of sick care may help prevent DKA. Self-management skills need to be combined with access to medical care and effective communication with health care provider.

G. Non-Ketotic Hyperosmolar Hyperglycemic State (HHS) in Adults

Definition

- Absolute or relative insulin deficiency with consequent severe hyperglycemia resulting in profound dehydration and electrolyte imbalance.
- Criteria: glucose >600 mg/dL; arterial pH >7.30 ; bicarbonate >15 ; trace or small serum ketones; effective serum osmolality >320 ; variable anion gap; stupor or coma.

Pathogenesis

- Reduction in the net effective action of circulating insulin.
- Elevation of counter-regulatory hormones: glucagon, catecholamines, cortisol and growth hormone.
- Increased hepatic and renal glucose production and impaired glucose utilization in peripheral tissues.
- Severe hyperglycemia and parallel changes in the osmolality of the extracellular space.
- Loss of water, sodium, potassium and other electrolytes.

Precipitating Factors

- Infection
- Cessation of insulin or oral medications
- Myocardial infarction, pancreatitis, stroke, alcohol abuse, drugs, trauma
- Drugs such as corticosteroids, thiazides, sympathomimetic agents

Presentation

- History: polyuria, polydipsia, polyphagia, weight loss, vomiting, clouded sensorium or coma
- Physical examination: poor skin turgor, tachycardia, hypotension, altered mental status, shock, coma, normothermic or hypothermic because of peripheral vasodilation in spite of infection

Laboratory

- Initial lab: Complete blood count, blood glucose, BUN, serum creatinine, serum ketones, electrolytes (calculate anion gap), osmolality, urinalysis, urine ketones, arterial blood gasses, magnesium, calcium, phosphorus and chest x-ray

- **Additional lab**
 - EKG: if severely ill, has history of heart disease or over age 40
 - Cultures (if indicated): urine, blood, throat, sputum, vagina, wound, spinal fluid or stool
- **Comments**
 - Leukocytosis may be proportional to ketosis and not indicative of infection.
 - Hyponatremia can be due to flux of water from the intracellular space or falsely lowered by severe hypertriglyceridemia.
 - Serum potassium should be initially elevated due to extracellular shift caused by insulin deficiency, hypertonicity and acidemia. If initial serum potassium is not elevated, the patient may have severe total-body potassium deficiency and require cardiac monitoring and more vigorous potassium replacement.
 - If patient is stuporous or comatose and calculated effective or measured serum osmolality is not 320 or greater, then another cause for the mental status change needs to be looked for (calculated effective serum osmolality = 2 x serum sodium plus serum glucose divided by 18).
 - “Corrected” serum sodium helps assess dehydration:
 - “Corrected” $[Na^+] = [Na^+] + 1.6 \times \text{blood glucose minus } 100 \text{ divided by } 100.$
 - An elevated corrected serum sodium indicates a greater free water deficit and intracellular dehydration.
 - As glucose is lowered with insulin, patients with a high corrected serum sodium will need larger quantities of normal saline to preserve intravascular volume before hypotonic fluids can be safely used.

Differential Diagnosis

- Starvation ketosis - bicarbonate usually not lower than 18 mEq/L
- Alcoholic ketoacidosis - glucose elevation mild (rarely >250 mg/dL)
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- Salicylate ingestion - elevated serum salicylate
- Ethylene glycol ingestion - calcium oxalate and hippurate crystals in the urine
- Methanol ingestion - elevated blood methanol
- Chronic renal failure - usually a hyperchloremic acidosis

Treatment

- **Successful treatment:**
 - Correction of dehydration, hyperglycemia and electrolyte imbalance.
 - Identification and treatment of comorbid conditions.
 - Frequent patient monitoring: electrolytes, blood glucose, BUN, creatinine, osmolality and venous pH should be measured every 2 - 4 hours.
- **Fluid therapy:**
 - In the absence of cardiac compromise, give normal saline at the rate of 15-20 mL per kg body weight per hour (1 to 1.5 L for the average adult).
 - Subsequent hydration depends on state of hydration, electrolyte levels and urinary output.
 - Half normal saline is indicated at 4-14 mL per kg per hour if corrected serum sodium is normal or high; give normal saline at the same rate if corrected serum sodium is low.
 - Once urine output is established, the IV should include 20-30 mEq/L potassium until the patient is stable and can tolerate oral potassium.
 - Fluid replacement should correct estimated deficits within the first 24 hours.
- **Insulin treatment:**
 - Once hydration and, if needed, potassium replacement has started, a bolus of regular insulin at 0.15 units/kg (total 8-12 units for average adult) can be given and a continuous insulin infusion begun.

- The continuous insulin infusion should be at the rate of 0.1 unit per kg per hour (5 to 9 units per hour in the average adult).
 - Usually add insulin in concentration of 10% or more (e.g., more than 100 units per 1,000 cc).
 - Mix well.
 - Discard the first 50 cc through the tubing before beginning the infusion.
- Plasma glucose should decline at a rate of 50–75 mg/dL per hour. If plasma glucose has not fallen by 50 mg/dL in the first hour, and hydration status is acceptable, then insulin infusion rate may be doubled every hour until the above rate of decline is achieved.
- When plasma glucose of 300 mg/dL is reached, insulin infusion rate may be decreased to 0.05–0.1 u/kg/hr (3–6 u/hr in average adult) and dextrose added to the IV fluids to maintain the above plasma glucose until the obtundation and hyperosmolarity is resolved.
- To prevent rebound hyperglycemia, IV insulin can be continued for a full, additional 24 hours before going back to subcutaneous insulin or oral agents.
- **Potassium**
 - Insulin treatment and volume expansion decrease what is usually an elevated serum potassium level.
 - Potassium replacement is begun when serum potassium falls below 5.5 mEq/L, assuming an adequate urine output.
 - Insulin treatment should be delayed until serum potassium is >3.3 mEq/L to avoid cardiac arrhythmias, cardiac arrest or respiratory muscle weakness.
- **Bicarbonate:** usually not necessary unless the HHS is accompanied by lactic acidosis.

Complications of HHS

- Hypoglycemia - due to over-corrected insulin therapy
- Hypokalemia - due to insulin therapy and under-corrected potassium replacement
- Hyperglycemia - due to discontinuance of IV insulin treatment without adequate overlapping subcutaneous insulin or oral agent treatment; to avoid hyperglycemia, subcutaneous regular insulin and IV insulin should overlap by at least 2 hrs
- Non-cardiogenic pulmonary edema

Prevention

Educating the patient and family members on self-management training, recognition of potential DKA, and self-management of sick care may help prevent DKA. Self-management skills need to be combined with access to medical care and effective communication with health care provider.

REFERENCE SECTION X

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