AMERICAN COLLEGE OF EMERGENCY PHYSICIANS
SCIENTIFIC ASSEMBLY
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Diabetic Emergencies: Update and Controversies

Management of the acutely ill diabetic patient is often complex. Prompt and accurate diagnosis and treatment are necessary to ensure a favorable outcome. This course will focus on controversies in the diabetic patient, as well as problems encountered with the newer oral agents.

- Discuss the controversies surrounding hypoglycemia, diabetic ketoacidosis, and hyperosmolar hyperglycemic states.
- Discuss the newer oral hypoglycemic agents and the problems associated with them.

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FACULTY

Rita K Cydulka, MD

Associate Professor, Case Western Reserve University School of Medicine; Residency Director, Emergency Medicine Residency Program, Case Western Reserve University, MetroHealth Medical Center; Consultant, Cleveland Clinic Foundation, Cleveland, Ohio

Glucose - Related Emergencies

Rita K. Cydulka, MD
MetroHealth Medical Center
Case Western Reserve University
The Cleveland Clinic Foundation
Cleveland, Ohio

Objectives:
1. Discuss the controversies surrounding hypoglycemia, diabetic ketoacidosis, and hyperosmolar hyperglycemic states.
2. Discuss the newer oral hypoglycemic agents and the problems associated with them.

Glucose Metabolism
- Glucose ingested
- Absorbed in intestine
- Metabolized intracelluarly (glycolysis)
- Stored in liver or muscle (glycogen)

In Liver:
- Breakdown of glycogenolysis
- Glycogen is broken down to glucose
- Synthesis of glycogenolysis
- A.A, TG, or Lactate Glucose

Glucose Homeostasis - Regulation
- Insulin
- Lowers blood glucose
- Facilitates glucose entry and utilization in cells
- Suppresses hepatic gluconeogenesis
- Suppresses glycogenolysis

Glucose Homeostasis - Counter Regulation
- Glucagon & Epinephrine
- Raise blood glucose
- Stimulate haptic gluconeogenesis and glycogenolysis

Glucagon
- Increases ketogenesis

Epinephrine
- Decreases glucose utilization
- Inhibits insulin secretion
- Stimulates glucagon secretion

Glucose Homeostasis
- Growth hormone & cortisol
- Inhibit entry of glucose into cells
- Cecrease glucose utilization

Diabetes
- Rate of hospital admissions for DM 4x greater than others
- Cost of ED use 3x greater
- Average hospital days/year=5

Hypoglycemia
- Definition: Fall in blood glucose that causes symptoms secondary to glucose deprivation in CNS
- Usually less than 40mg/100mi

Hypoglycemia
- Among diabetics-9% per year

Hypoglycemia
- Women tolerate lower glucose levels than men

Rate of fall affects clinical picture

Etiology of Hypoglycemia

Drug induced hypoglycemia: Most frequent cause
Example:
Sulfonylureas
Salicylates
Insulin
Alcohol
Haloperidol
Propoxyphene
Propanolol
Chlorpromazine
Pentamadine
Didanosine (DDI)

Drugs that potentiate sulfonylureas
Bishydroxycoumarin
Chloramphenicol
Clofibrate
Pnenylbutazone
Sulfonamides
Ranitidine
Tricyclic antidepressants
Reactive hypoglycemia

Newer Agents
Metformin (Glucophage)
Improves insulin sensitivity
No effect on pancreatic beta cells
No effect on insulin secretion
No hypoglycemia
Metformin

Lactic acidosis
0.03 cases/100 pt.yrs.
Caution with: Renal insufficiency pts.

Troglitazone (Rezulin)
"Glitazones"
Improves insulin sensitivity
May exacerbate CHF

Acarbose (Precose)
In combo with sulfonylurea: Causes hypoglycemia

Hypoglycemia Rx:
Oral glucose
Not sucrose

No hypoglycemia when used alone

Acarbose
Contradictions for use
DKA
Cirrhosis
Inflammatory Bowel Disease
Intestinal Obstruction
Treatment of hypoglycemia caused by acarbose + sulfonylurea
Oral glucose

Example:
- postgastric surgery
- early diabetes
- idiopathic
- posthyperalimentation
- hemodialysis
- pancreatic tumor

Glucose underproduction
Example:
- Hepatic dysfunction
- Adrenal failure
- Pituitary failure
- Extra pancreatic neoplasms

Glucose over utilization
Example:
- Insulinoma
- Inadequate growth hormone

Somogyi Phenomena
- Initiated by excess insulin dosage
- Unrecognized hypoglycemia during early am sleep
- Hypoglycemia because of couterregulatory response
- Rx: Decrease dose or change time of insulin

Symptoms of Hypoglycemia
Symptoms:
- Hypoglycemic effect on CNS
- Counter-regulatory hormones, i.e., epinephrine

Clinical Features of Hypoglycemia

Symptoms	Signs
Tachycardia/palpitations	Tachycardia
Paresthesias	Coma
Nervousness	Mental status changes
Headache	Diaphoresis
Irritability	Paralysis
Blurred vision	
Seizures	

Hypoglycemia Unawareness
- Decreased symptoms in elderly

Hypoglycemia without warning
- Rapid change mental status
- Previous exposure to low blood glucose
- Can be PPT by single hypoglycemic episode
- Laboratories
- Low blood glucose

Extracted glucose flux method of measurement
- Accurate between 50-400 ug/dl
- Polarized light

Initial treatment of hypoglycemia
Adults:

50ml of D50W IV; 1mg glucagon IM

Children:

2.5ml/kgDIOW IV, 10-20 ug/kg glucagon IM

Followed by:

D5W or D10W or D20W IV infusion
Meal
Determine etiology

Admit to hospital if:

Long acting insulin or oral hypoglycemic agent
Intentional OD
Unknown etiology
Prolonged or slowly resolving

Agent	**Onset Of Action (H)**	**Peak Effect (H)**	**Duration of Action (H)**
Insulin prep			
Regular	0.25-1	2-6	4-12
Semilente	0.5-1	3-6	8-16
NPH	1.5-4	6-16	12-24
Lente	1-4	6-16	12-28
PZI	3-8	14-24	24-48
Ultralente	3-8	14-24	24-48

Agent	**Onset Of Action (H)**	**Duration Of Action (H)**
Sulfonylureas		
Tolbutamide	0.5-1	6-12
Tolazamide	4.6	10-24
Gliprizide	1-3	12-24
Acetohexamide	0.5-1	12-24
Glyburide	0.5-1	24-60
Chlorpropamide	1-2	60-90

Diabetic Ketoacidosis

Definition: Insulin deficiency causing:

1. Muscle release of free fatty acid
2. Liver release of ketones through gluconeogenesis
3. Peripheral tissue unable to utilize glucose & ketones
4. Result: Hyperglycemia, ketonemia

DKA Etiologies

Absolute insulin deficiency
Stress
Infection
MI

DKA Signs and Symptoms

Thirst
Stupor
Nausea
Mental status change
Vomiting
Hypo/hyperthermia

- Abdominal pain
- Dehydration
- Polyuria
- Acetone breath
- Polydipsia
- Kussmaul's respirations
- Volume depletion
- Fever is not from DKA, r/o underlying disorder

DKA Laboratories
- Blood glucose over 300mg/dl
- Except euglycemic DKA

Increased serum ketones
- Acidosis
- venous vs. Arterial pH
- venous pH not significantly different from arterial pH

Low bicarbonate
- End tidal CO2 measurement
- infrared spectroscopy - sidestream aspirators on nasal cannula
- cheap
- painless
- reflectance meter
- rapid and specific enymatic test of betahydroxybuterate

Low sodium
- a decrease in 5 meq/1 for every increase of 180% glucose

Low chloride
- due to vomiting

Increased potassium early
- decreased potassium later...reflecting potassium depletion

Increased BUN/Cr

Low Mg, phos

Urine glucose, ketones

Increased Amylase
- salivary
- difficult to r/o pancreatitis

Search for precipitating cause

DKA Treatment: Takes 8-24 hours
- Rehydration - saline
- Average water deficit = 5-6liters
- First liter over 30 minutes
- Several liters in first few hours
- Change to 0.45 normal saline after initial replacement of intravascular volume
- No need for 20ml/kg volume replacement if no severe dehydration

Restoration of insulin - insulin
- Prime IV tubing with 10 units regular insulin
- Bolus 0.1 unit/kg regular insulin IV
- IV drip 0.1 unit/kg/hr regular insulin
- Continue insulin unit ketonemia and acidosis clears
- Add glucose when blood glucose drip below 250mg%
- Route : Can IM or SQ Insulin be used?
- Painful
- Theorectical Insulin accumulation

Slower decrement of acetoacetate and beta hyroxybuterate
Need to repeat loading doses

Correct electrolyte balance: Na, K, Phos, Mg
Sodium
Average sodium deficit - 500meq
Potassium
Average deficit = 400 - 1000meq (5-10 meq/kg)
Initial potassium secondary to hydration, renal function,
K+/H+ shifts during acidosis
Add 20-40 meq to each IV bottle after evaluating renal function
Phosphorus
Shifts intracellularly with treatment of DKA
Replacement is controversial
No clinical trials show replacement is beneficial
Replacement may ppt hypokalemia and hypomagnesemia

Correction of acid-base status- HCO3
Only if pH is < 7.0
44-100 meq

Side Effects
Paradoxical CSF acidosis
Hypokalemia
Shift oxyhemoglobin curve to left
Rebound alkalosis
Sodium overload
AND FINALLY
Treat precipitating cause
Consider Heparin
Frequent monitoring of blood glucose, ketone bodies, potassium bicarb/CO2
Flow sheets: Vital signs, level of consciousness, I&O, therapeutic measures, blood chemestries
Disposition:
Admit
D/C home
children with initial pH>7.35
HCO3>20 meq/L
resolution of clinical findings
tolerates P.O. fluid after 3-4 hours
reliable caretakers
no underlying etiology requiring admission
close followup

Morbidity and Mortality: 10%
Pulmonary edema secondary to fluid overload
Hypokalemia secondary to inadequate replacement
CSF acidosis secondary to excessive HCO3
Hypoglycemia secondary to excessinsulin
Cerebral edema (kids)
Venous thrombosis
ARDS

Morbidity and Mortality of DKA
Mortality increases with:

Serum osmolality
BUN
Glucose
Bicarb <10
Infection
MI
Renal disease
Cardiovascular disease
Old age
Cardiovascular collapse
Prolonged coma

Nonketotic Hyperosmolar Coma
Severe hyperglycemia
Severe dehydration
Hyperosmolity without ketosis
Usually in middle-aged or elderly patients

NHC Etiology
Serious illness: Infection, MI,CVA,GI bleed
Underlying chronic disease: cardiovascular or renal disease
Drugs -for example:
Diuretics
Thiazide
Dilantin
Diazoxide
NHC-Longer prodrome than DKA
Sings and symptoms
Thirst
1/3 fever
Neurological complaints
1/3 vascular collapse
Tachycardia

Neurological disturbances
VERY COMMONLY MISCIAGNOSED AS CVA
NHC
Osmolarity +2Na+2K+glucose/18 +bun/2.8
Normal =285 - 295 mOSm/l

NHC Laboratories
Blood glucose > 800mg/dl
Serum osmolality >350 mOSm/l
Negative serum ketones
Low sodium
Low potassium
Elevated BUN/CR
+/- metabolic acidosis
Leutococyksis with elevated PMN's common
12-15k
Stress response
Hg and HCT
Falsely elevated dehydration
MCV falsely elevated

relative hypotonically
Search for precipitating cause

NHC Treatment -takes about 36 hours
Rehydration_ Saline/REduce serum osmolality
Average fluid deficit = 8-12 liters
Replace ½ of estimated water deficit in first 12 hours, replace rest in 24 hours
Administer fluids until BP is stable, urine output 50ml/hour

Correction of Electrolyte Balance
Sodium
Average sodium deficit = 500meq
Potassium
Average deficit= 500 meq
Begin to add 10-20 meq potassium chloride per hour x 24-36 hours as soon as adequate renal function has been confirmed
Reduce Serum Glucose
Rehydration
Insulin - same dosage as for DKA
AND FINALLY
Consider low molecular weight heparin
Treat precipitating cause
Frequent monitoring: Blood glucose, Potassium, Bicarbonate/Carbon dioxide/Serum Osmolality
Flow sheet
Morbidity and Mortality of NHC “Best Results with Prompt Recognition”
Osmolality, hypernatremia are best predictors of mortality
Cerebral edema secondary to excess bicarbonate administration
Pulmonary edema secondary to fluid overload
Hypoglycemia secondary to excess insulin
Venous thrombosis
ARDS

Morbidity and Mortality of NHC
Mortality
1960's - 1970's: 10-60%
1980"s - 1995 :10-17%
Early vs late mortality
early - 1st 72 hrs
more common sepsis, shock, underlying disease

late- after 72 hrs
thrombolytic events
effects of treatment

Infection is a positive predictor of survival
Better antibiotic therapy and supportive care

Table 3 **CHARACTERISTICS OF ORAL SULFONYLUREAS**

Agent	Daily Dosage Range (mg)	Duration of Action (hrs)	Comments	
Tolbutamide* (Orinase)	500-3000	6-12	Metabolized by liver to an inactive product; taken 2-3 times per day	
Chlorpropamide (Diabines)	100-500	60	Metabolized by liver to less active metabolites (=70%) and excreted unchanged (=30%) by kidneys, can cause SIADH; taken once per day	
Acetohexamide (Dymelor)	250-1500	12-18	Metabolized by liver to an active metabolite; taken one to two	

			times per day	
Tolazamide* (Tolinase)	100-1000	12-24	Metabolized by liver to both active and inactive metabolites; taken one to two times per day	
Glipizide (Glucotrol)	5-20	12-24	Metabolized by liver to inert products; taken one to two times per day	
Glyburide* (DiaBeta, Micronase)	2.5-20	16-24	Metabolized by liver to mostly inert product; prolonged duration of action in renal failure; taken one to two times/day	
Glimepiride (Amaryl)	1-8	24	Metabolized by liver to both active and inactive metabolites; taken once per day	

*** MHMC Formulatory Agent**

Table 4. **COMPARISON OF MAJOR ACTIONS AND SIDE EFFECTS OF ORAL ANTIDIABETIC AGENTS**

Drug	Site and Actions	Primary Effects on Glycemia			Side Effects
		FPG (mg/dL)	PP-PG (mg/dL)	HhA(%)	
Acarbose	Small Intestine delays carbohydrate		50	0.5-1.0	Flatulence Diarrhea

	digestion and slows absorption				Abdominal discomfort
Metformin	Liver and Peripheral Tissues hepatic glucose prod. peripheral glucose uptake	50-60		1.0-2.0	Anorexia Diarrhea Lactic Acidosis in susceptible individuals
Sulfonylureas	Pancreas insulin secretion	50-60		1.0-2.0	Hypoglycemia Weight gain

FPG = Fasting Plasma Glucose Source Lebovitsz HE. Clinical Diabetes 1995;13:99-103
PP-PG = Postprandial Plasma Glucose
HbA = Hemoglobin A

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