Hyperosmolar hyperglycemic state

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Hyperosmolar hyperglycemic state (HHS) is a complication of diabetes mellitus (predominantly type 2) in which high blood sugars cause severe dehydration, increases in osmolarity (relative concentration of solute) and a high risk of complications, coma and death.

Rarer variety…..but a Life threatening emergency

Older names for HHS were ***hyperosmolar nonketotic coma (HONC), hyperosmolar hyperglycemic nonketotic coma, etc…***

Name changed to HHS in order to present the alterations in the mental status that occur without coma. ***Coma is found in fewer than 20% of patients with HHS***.

Diagnosis criteria

1) Plasma glucose level of 600 mg% or greater

2) Effective serum osmolality of 320 mOsm/kg or greater

3) Profound dehydration, up to an average of 9L

4) Serum pH greater than 7.30

5) Bicarbonate concentration greater than 15 mEq/L

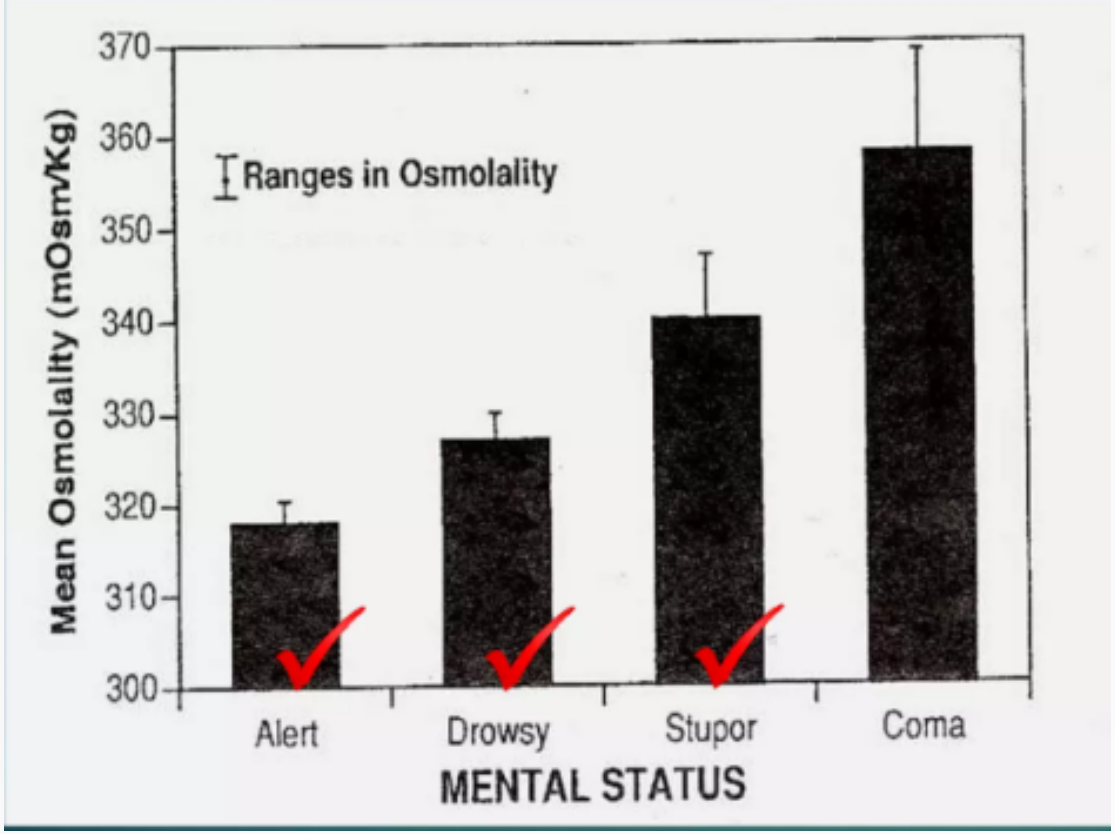
6) Small ketonuria and absent-to-low ketonemia

7) Some alteration in consciousness

serum osmolality

2(Na+ + K+) + (mg/dL of glucose/18) + (BUN/2.8)

Normal osmolality (285 – 295) mOsm/kg


370
360
350
340
330
320
310
300
Mean Osmolality (mOsm/Kg)
Ranges in Osmolality
Alert
Drowsy
Stupor
Coma
MENTAL STATUS

What may be the reason for occurrence of HHS in a Diabetic patient ?

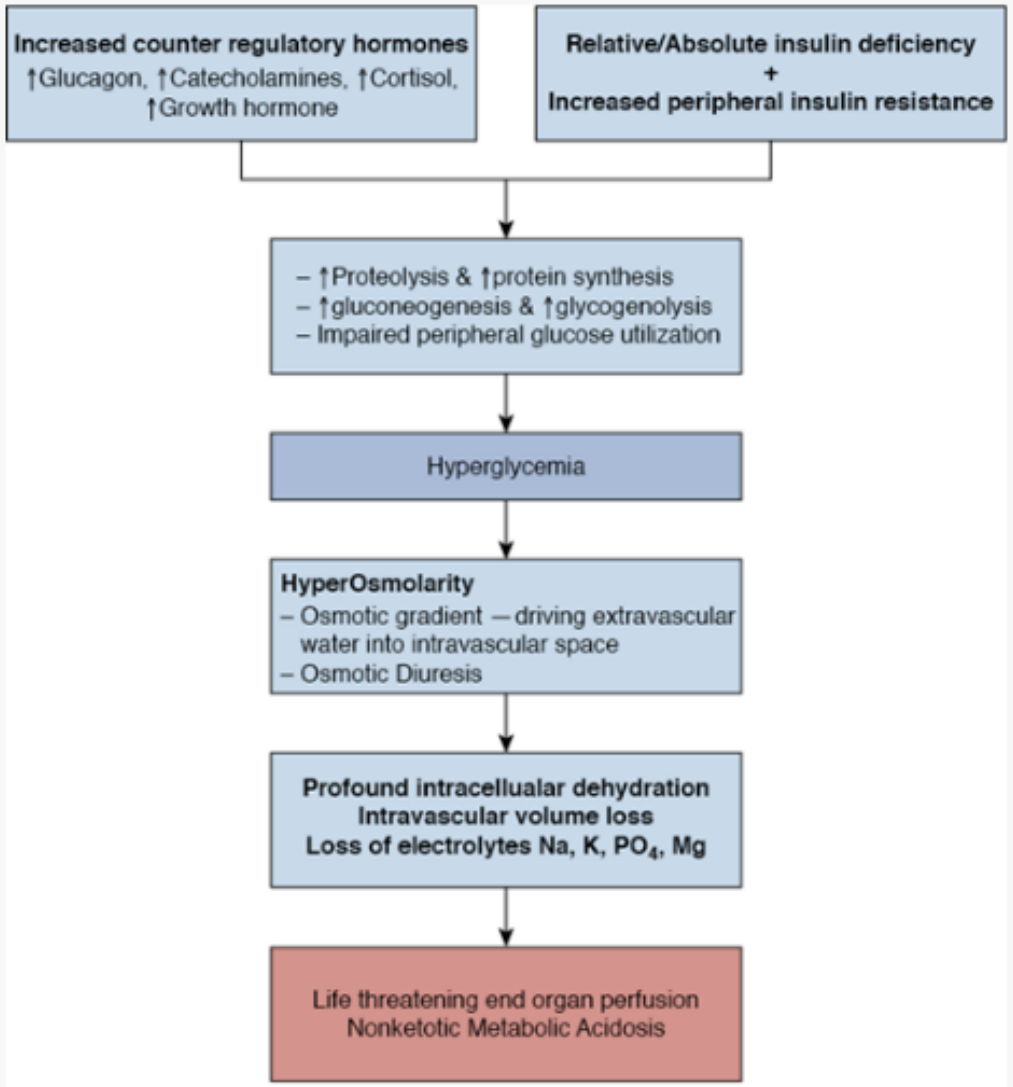
2 are notable……

- Irregular medication pattern
- Infection; causes the blood sugar to rise above baseline

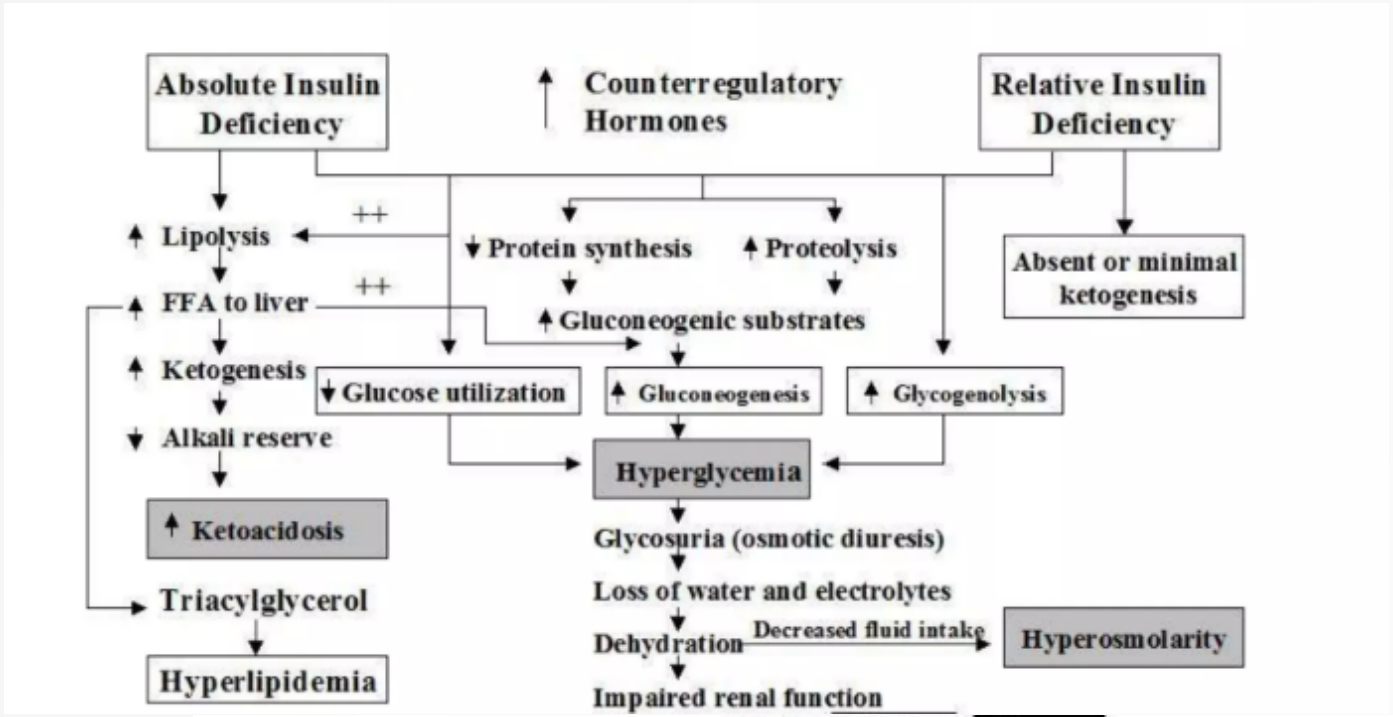
Others maybe: Alcoholism, Burns, Stroke, GI bleed, Surgery, etc…….

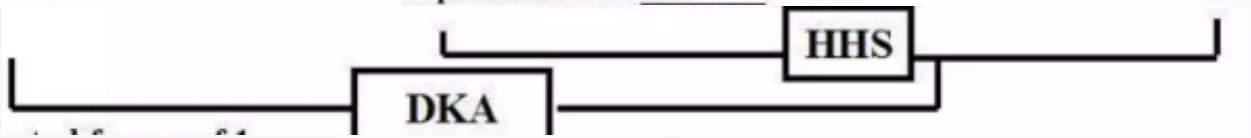
Precipitating factors

- Acute infection 30–40% (pneumonia, UTI, sepsis)
- CVA
- MI
- Acute pancreatitis
- Renal failure
- Thrombosis
- Severe burns
- Hypothermia
- Trauma
- Subdural hematoma


Increased counter regulatory hormones
↑Glucagon, ↑Catecholamines, ↑Cortisol, ↑Growth hormone
Relative/Absolute insulin deficiency
+
Increased peripheral insulin resistance
– ↑Proteolysis & ↑protein synthesis
– ↑gluconeogenesis & ↑glycogenolysis
– Impaired peripheral glucose utilization
Hyperglycemia
HyperOsmolarity
– Osmotic gradient — driving extravascular water into intravascular space
– Osmotic Diuresis
Profound intracellualar dehydration
Intravascular volume loss
Loss of electrolytes Na, K, PO_4, Mg
Life threatening end organ perfusion
Nonketotic Metabolic Acidosis

	Ketogenesis	Gluconeogenesis	Glycogenolysis	Glycolysis	Glycogen synthesis
Insulin	↓	↓	↓	↑	↑
Glucagon	↑	↑	↑	↓	↓
Cortisol	↑	↑	↑	↓	↓
Growth hormone	↑	↑	↑	↓	↓
Catecholamines	↑	↑	↑	↓	↓


Absolute Insulin Deficiency
Counterregulatory Hormones
Relative Insulin Deficiency
Lipolysis
++
Protein synthesis
Proteolysis
Absent or minimal ketogenesis
FFA to liver
++
Gluconeogenic substrates
Ketogenesis
Glucose utilization
Gluconeogenesis
Glycogenolysis
Alkali reserve
Hyperglycemia
Ketoacidosis
Glycosuria (osmotic diuresis)
Loss of water and electrolytes
Triacylglycerol
Dehydration
Decreased fluid intake
Hyperosmolarity
Hyperlipidemia
Impaired renal function


HHS
DKA

Diabetic Ketoacidosis Versus Hyperosmolar Hyperglycemic State*

Value	*Mild DKA*	*Moderate DKA*	*Severe DKA*	*HHS*
Plasma glucose				
mmol/L	>13.9	>13.9	>13.9	33.3
mg/dL	>250	>250	>250	>600
Arterial pH	7.25 to 7.30	7.00 to <7.24	<7.00	>7.30
Serum bicarbonate, mmol/L	15 to 18	10 to <15	<10	18
Urine ketones	Positive	Positive	Positive	Small
Serum ketones (β-hydroxybutyrate)	High	High	High	Normal
Effective serum osmolality, *mOsm/kg*†	Variable	Variable	Variable	>320
Anion gap†	>10	>12	>12	Variable
Alteration in sensoria or mental obtundation	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

CLINICAL FEATURES:

HISTORY AND PRESENTATION-

- Known history of diabetes mellitus (DM), which is usually type 2
- Patients may complain of increasing thirst, polydipsia, polyuria, weight loss, and weakness
- A wide variety of focal and global neurologic changes may be present, including drowsiness and delirium to hemiparesis and coma

PHYSICAL EXAMINATION-

- Examine the patient for evidence of HHS, focusing on hydration status, mentation(skin tugor), and signs of possible underlying causes, such as a source of infection.
- Tachycardia is an early indicator of dehydration; hypotension is a later sign suggestive of profound dehydration due to volume loss secondary to osmotic diuresis.
- Body weight is the single most important measurement in assessing the degree of hydration. For every 1 L of body fluids lost, 1 kg of body weight is lost.

LABORATORY FINDINGS:

Severe hyperglycemia is present, with blood glucose values ranging from 600 mg/dL to 2400 mg/dL.

In mild cases, where dehydration is less severe, dilutional hyponatremia as well as urinary sodium losses may reduce serum sodium to 120-125 mEq/L, which protects to some extent against extreme hyperosmolality. However, as dehydration progresses, serum sodium can exceed 140 mEq/L, producing serum osmolality readings of 330-440 mosm/kg.

Ketosis and acidosis are usually absent or very mild.

Prerenal azotemia is the rule, with serum urea nitrogen elevations over 100 mg/dL being typical.

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
ß-hydroxybutyrate (mmol/l)	1.0 ± 0.2	9.1 ± 0.85
Total osmolality (mosm/Kg)	380 ± 5.7	323 ± 2.5

Complications

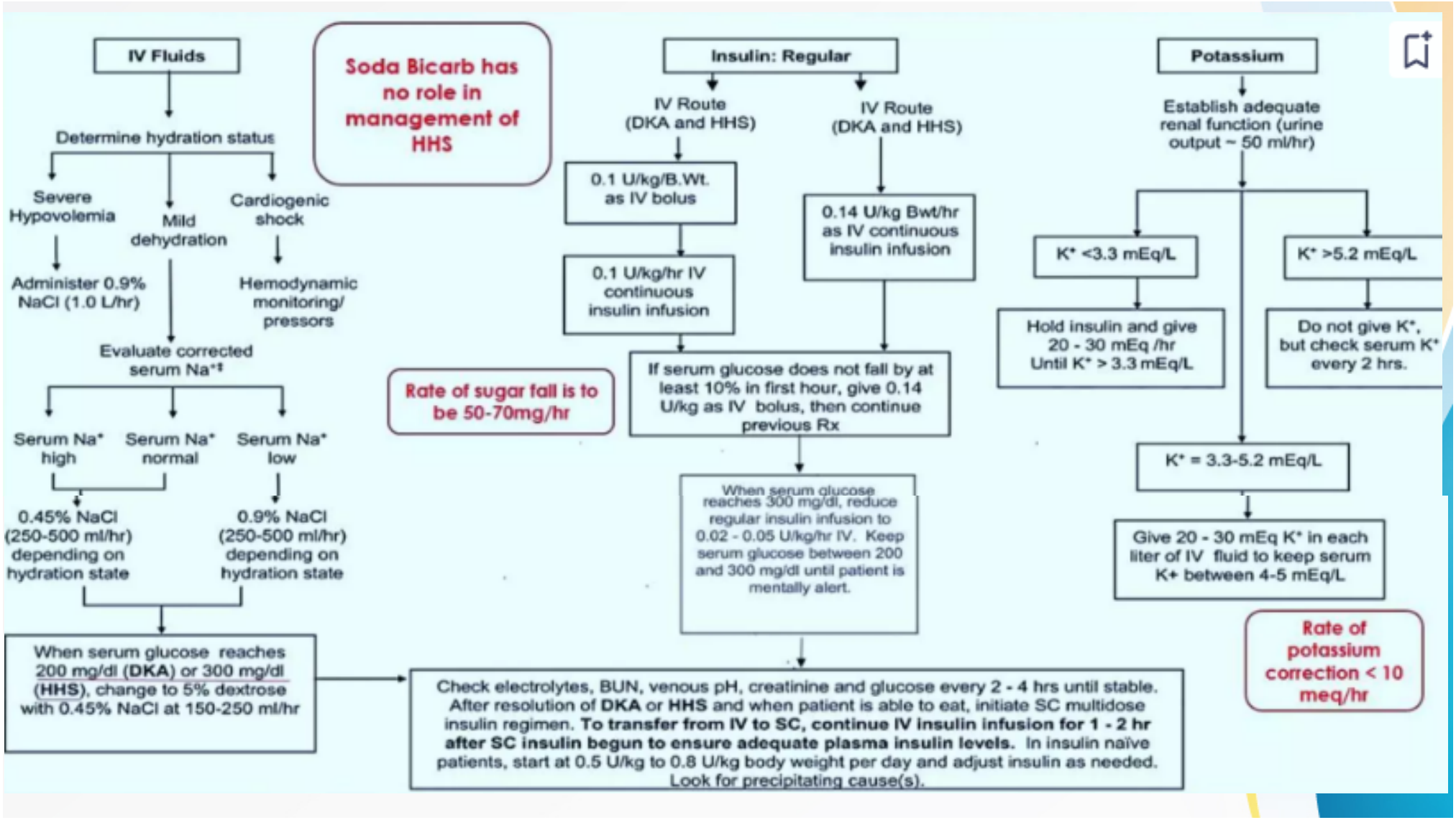
Cerebral edema may occur from rapid lowering of glucose levels and an ensuing rapid drop in plasma osmolarity

Acute respiratory distress syndrome, PE, MI, or pneumonitis *that has worsened with rehydration*-rapid correction of hyperglycemia and hyperosmolarity gives rise to pulmonary edema

Vascular complications like **hypotension** and **hyperviscosity** of the blood, both of which predispose patients to thromboembolic disease of the coronary, cerebral, pulmonary, and mesenteric beds

Management of Hyperosmolar Hyperglycemic State (HHS)

	Fluid replacement	Correction of hyperglycemia	Electrolyte management
Initial management	• **NS 15–20 mL/kg/h** initially, until BP and organ perfusion normalize • Then, subsequent fluid management should focus on free water replacement • **Total body water deficit ...**		


IV Fluids
Determine hydration status
Severe Hypovolemia
Mild dehydration
Cardiogenic shock
Administer 0.9% NaCl (1.0 L/hr)
Hemodynamic monitoring/ pressors
Evaluate corrected serum Na+‡
Serum Na+ high
Serum Na+ normal
Serum Na+ low
0.45% NaCl (250-500 ml/hr) depending on hydration state
0.9% NaCl (250-500 ml/hr) depending on hydration state
When serum glucose reaches 200 mg/dl (DKA) or 300 mg/dl (HHS), change to 5% dextrose with 0.45% NaCl at 150-250 ml/hr
Soda Bicarb has no role in management of HHS
Insulin: Regular
IV Route (DKA and HHS)
0.1 U/kg/B.Wt. as IV bolus
0.1 U/kg/hr IV continuous insulin infusion
IV Route (DKA and HHS)
0.14 U/kg Bwt/hr as IV continuous insulin infusion
Rate of sugar fall is to be 50-70mg/hr
If serum glucose does not fall by at least 10% in first hour, give 0.14 U/kg as IV bolus, then continue previous Rx
When serum glucose reaches 300 mg/dl, reduce regular insulin infusion to 0.02 - 0.05 U/kg/hr IV. Keep serum glucose between 200 and 300 mg/dl until patient is mentally alert.
Potassium
Establish adequate renal function (urine output ~ 50 ml/hr)
K+ <3.3 mEq/L
Hold insulin and give 20 - 30 mEq /hr Until K+ > 3.3 mEq/L
K+ >5.2 mEq/L
Do not give K+, but check serum K+ every 2 hrs.
K+ = 3.3-5.2 mEq/L
Give 20 - 30 mEq K+ in each liter of IV fluid to keep serum K+ between 4-5 mEq/L
Rate of potassium correction < 10 meq/hr
Check electrolytes, BUN, venous pH, creatinine and glucose every 2 - 4 hrs until stable. After resolution of DKA or HHS and when patient is able to eat, initiate SC multidose insulin regimen. To transfer from IV to SC, continue IV insulin infusion for 1 - 2 hr after SC insulin begun to ensure adequate plasma insulin levels. In insulin naïve patients, start at 0.5 U/kg to 0.8 U/kg body weight per day and adjust insulin as needed. Look for precipitating cause(s).

prognosis

The overall mortality rate of HHS is more than **ten times** that of diabetic ketoacidosis, chiefly because of its higher incidence in older patients, who may have compromised cardiovascular systems or associated major illnesses and whose dehydration is often excessive because of delays in recognition and treatment. When prompt therapy is instituted, the mortality rate can be reduced from nearly 50% to that related to the severity of coexistent disorders.