Case Conference

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Discussion

Beta-blocker intoxication

Clinical menifestation

- Bradycardia
- Hypotension
- Unconsciousness
- Respiratory arrest or insufficiency
- Hypoglycemia
- Seizure
- Symptomatic bronchospasm
- VT/VF
- Mild hyperkalemia
- Hepatotoxicity/mesenteric ischemia/renal failure

History

- Type of beta-blocker
- Quantity
- Timing
- Underlying medical condition

Differential diagnosis

- Bradycardia
  - Myocardial infarction
  - Electrolyte (eg hyperkalemia)
  - Drug
  - Toxins
- Hypotension

Differential diagnosis

- Shock
  - Cardiogenic shock
  - Hypovplemic shock
  - Septic shock
- Respiratory depression
- CNS symptoms
- Drug overdose
  - cholinergic agent
  - CCB
  - Clonidine

Clinical course

- Most patient develop symptoms within 2 hours following ingestion
- Nearly all become symptomatic whithin 6 hours
- Exceptions
  - Sustained release medications and sotalol
  - Delayed toxicity up to 24 hours after ingestion can occur

Toxicity

- Beta-adrenoreceptor blockage
- Membrane stabilizing agents (eg, propranolol, acebutolol)
  - inhibit myocardial fast sodium channels
  - widened QRS interval
  - potentiate dysrhythmias
- Beta blockers with high lipid solubility (eg, propranolol)
  - cross the blood brain barrier
  - predisposing to neurologic sequelae such as seizures and delirium
- Intrinsic sympathomimetic activity
- Class III antiarrhythmic property
  - Significant QTc prolongation can develop following sotalol overdose

Risk for severe toxicity

- Coingestion of other cardioactive agents
- Underlying cardiac disease (eg：heart failure)
- Ingestion of sotalol or another agent with membrane-stabilizing activity (eg：propranolol or acebutolol)

Further studies

- Electrocardiogram
- Fingerstick
  - If an insulin/glucose treatment regimen is used, glucose and potassium levels must be measured every 30 to 60 minutes
- Serum electrolytes including calcium, and blood urea nitrogen and creatinine levels
  - If calcium is administered repeatedly, levels should be measured every 4 to 6 hours

Therapeutic goal

- Improve EF (>=50%)
- Increase blood pressure(>=90mmHg)
- Adeqate heart rate(>=60bmp)
- Resolution of acidemia
- Euglyemia
- Adequate urine flow(1-2ml/kg/hr)
- Reverse cardiac conduction abnormalities (QRS<=120ms)
- Improve mentation

Management

- Resuscitation
  - Bolus of atropine, glucagon, fluid
- Stabilization
  - Infusion of Glucagon, insulin-glucose, Catecholamines, phosphodiesterase inhibitor
  - Early cardiac pacing if no response
  - Peripheral arterial and pulmonary artery catheter monitoring if refractory hypotension
  - Consider hemodialysis

Phamacological treatment

Table 1
Treatment options for BB and CCA toxicity

Indication	Treatment	Dose	Comments
↓ Contractility	Insulin-euglycemia (HIE)	1 IU/kg regular insulin + 0.5 gm/kg dextrose IV bolus, then 0.5–1 IU/kg/hr regular insulin + 0.5 gm/kg/hr dextrose continuous IV infusion	1) Initiate HIE simultaneously with either calcium, glucagon, or norepinephrine 2) If blood glucose is > 400 mg/dL (22 mmol/L), omit dextrose bolus 3) Titrate dextrose infusion to maintain blood glucose 100–250 mg/dL (5.5–14 mmol/L) 4) Monitor blood glucose q 20–30 min until stable, then q 1–2 hr 5) K+ replacement not needed unless < 2.5 mEq/L
	10% Calcium gluconate	0.6 mL/kg IV bolus, then 0.6–1.5 mL/kg/hr IV continuous infusion	1) Calcium chloride can be substituted but requires central IV access 2) Used primarily for CCA toxicity but can be considered for BB toxicity
	Glucagon	50–150 mcg/kg (3–10 mg) IV bolus, then 50–150 mcg/kg/hr continuous IV infusion	Used primarily for BB toxicity, but can also be used for CCA toxicity
	Norepinephrine	Titrate to age-appropriate systolic blood pressure	Administered via central IV access
↓ Peripheral resistance	Norepinephrine	Titrate to age-appropriate systolic blood pressure	Administered via central IV access
Heart rate < 50 bpm	Glucagon	50–150 mcg/kg (3–10 mg) IV bolus, then 50–150 mcg/kg/hr continuous IV infusion	Used primarily for BB toxicity, but can also be used for CCA toxicity
	Norepinephrine	Titrate to age-appropriate systolic blood pressure	Administered via central IV access
	Cardiac pacing		Target heart rate is 60 bpm
QRS > 120 ms	Sodium bicarbonate	1–2 mEq/kg IV bolus	Can repeat for recurrent QRS widening

Non-pharmacologic treatment

- Hemodialsis
  - Effective only with hydrophilic, minimally protein-bound beta blockers such as atenolol, Nadolol, sotalol, acebutolol, and atenolol
- Cardiac pacing
  - Optima pacing rate 50-60 bmp
  - Ventricular pacing (transthoracic ortransvenous) may be considered in refractory cases if bradycardia is assessed to significantly contribute to hypotension.
- Gastrointestinal (GI) decontamination
  - Ingestion within 1-2 hours

Non-pharmacologic treatment

- Gastrointestinal (GI) decontamination
  - Ingestion within 1-2 hours
- Intra-aortic balloon pump(IABP)
- Cardiopulmonary bypass

Table 1. Management issues before arrival in the intensive care unit

Resuscitation and stabilization	Assess airway Intubation and mechanical ventilation for airway protection, hypoventilation, or hypoxemia Assess hemodynamic status Isotonic fluids for hypotension Treat significant arrhythmias Interventions for altered mental status (1) 50% glucose (25–50 g intravenously) Thiamine (100 mg intravenously) Naloxone (0.4–2.0 mg intravenously, intramuscularly) Flumazenil (not routinely administered)
Initial clinical evaluation	History Type of drug and quantity Time of ingestion/exposure Available drugs in environment Physical examination Vital signs Neurologic findings Patterns of response (toxidromes)
Laboratory evaluation	As indicated by presentation Electrolytes, renal function Arterial blood gas Plasma osmolarity Electrocardiogram Qualitative toxicology screen (urine) Quantitative drug concentrations (serum)
Gastrointestinal decontamination	Gastric emptying (2–4) Ipecac not recommended Gastric lavage: consider only for life-threatening drug within 1 hr of ingestion Adsorption of poisons (5) Activated charcoal (1 g/kg) Decreased transit time in gastrointestinal tract (6, 7) Cathartics (no evidence to support routine use) Whole bowel irrigation (see text)

Conclusion

- The diagnosis of beta-blocker intoxication must be suspected in any case associating hypotension and bradycardia