Purpose: The purpose of these guidelines is to help you utilize high-dose insulin (HDI) Therapy, for the management of moderate to severe toxicity due to calcium channel antagonists (CCB) and beta-adrenergic antagonists (BB), in an up to date and evidence-based manner.

Indications for HDI:

- **Cardiogenic** shock resulting from CCB or BB-induced toxicity unresponsive to conventional measures including higher dose calcium therapy.
- HDI may be considered in other forms of toxin-induced cardiovascular shock, however, there is limited supporting data at this time.

Goals of HDI therapy:

- Maintain/improve cardiac output and tissue perfusion.
- Maintain MAP > 60 ideally. However, insulin is not a vasopressor and does not have direct effects on increasing systemic vascular resistance, in fact it acts to decrease systemic vascular resistance. In the case where the MAP < 60 but end-organ perfusion appears adequate according to the indicators discussed below, no dosing changes are necessary, nor are vasopressors indicated.
- Decrease or eliminate use of vasopressors, which have been shown to increase mortality in BB overdose.
- Maintain blood sugar 100-200 mg/dL
- Maintain potassium level greater than 2.5 mmol/L
- Maintain slightly elevated calcium levels (12-14 mg/dL)

Potential Adverse Effects:

- Hypoglycemia (easily monitored and treated)
- Fluid overload (prevented with higher concentration of insulin and dextrose)
- Hypokalemia (serious hypokalemia exceedingly rare with this treatment)

Recommended Procedure for BB/CCB overdose:

1. Evaluate initial and ongoing markers of organ perfusion:
    a. Mental status
    b. Urine output: place foley and maintain output at 0.5 mL/kg/hr
    c. Serum markers of tissue perfusion: basic metabolic panel, lactate, ABG or VBG
    d. MAP > 55 may be reasonable goal if UO adequate.
2. Evaluate initial and ongoing markers of cardiac function:
    a. Continuous cardiac output/index monitoring with pulse contour analysis (Flo Trac® or similar, arterial line necessary) is recommended strongly.
    b. If continuous cardiac output monitoring is not possible, you must obtain frequent cardiac ultrasounds.
3. Obtain central venous access and arterial access.
4. **Determine type of shock:**
    a. Hypotension with normal cardiac contractility:
        i. Calcium: goal is ionized Ca twice the upper limit of normal.
        ii. Norepinephrine and/or phenylephrine (there is no max dose as long as extremities are warm).
    b. For any evidence of cardiogenic shock (decreased contractility on ultrasound):
        i. Initiate epinephrine (no max dose). Continue to use ultrasound to determine which pressor should be titrated up: epi for hypotension with decreased contractility, norepi for hypotension with preserved contractility.
5. For refractory cardiogenic shock:
    a. Obtain baseline glucose at bedside by glucometer.
        i. If glucose < 250 mg/dL, give 0.5 g/kg of dextrose IV bolus.
    b. Insulin
        i. **Insulin is an inodilator! It will only help cardiogenic shock (diagnosed by ultrasound)!**
            1. Amlodipine overdoses may have inotropic effects or may be just vasodilatory shock. You must use your US skills to determine if insulin is indicated.
        ii. Bolus: 1 Unit/kg regular insulin IV push, then start infusion.
        iii. Infusion: start at 1 unit/kg/hr (concentration: 10 - 16 units/mL or 8,000 units in 500 mL of NS, tell pharmacy to just do it). **You must maximally concentrate the infusion to prevent volume overload.**
        iv. Insulin infusion may be increased by 2 unit/kg/hr every 30 minutes up to a maximum dose of 10 units/kg/hr if no response in cardiac output and tissue perfusion.
            1. Please note that an infusion rate as high as 20 unit/kg/hr, based on recent literature and clinical experience, MAY be indicated (expect considerable vasodilation at higher doses and need for high dose norepi).

c. Dextrose: Start an infusion of D50 – D70 at 0.5 g/kg/hr. Titrate to maintain blood glucose > 150 mg/dL.
    i. Additional boluses of D50 may be required.
    ii. Monitor bedside glucose every 10 minutes initially and while titrating infusion.
    iii. Once insulin infusion and blood glucose are stabilized monitor glucose every 30 minutes.
d. Monitor potassium every hour while titrating insulin infusion. Once the infusion is stabilized, monitor potassium every 4-6 hours.
    i. **Do not replete unless < 2.5 mmol/L.**
    ii. If repleting, use IV potassium only.

Recommendations for Decreasing Insulin Infusion:

1. Decrease vasopressors first. Wean off if possible before weaning insulin.
    a. Sometimes this is not possible, and patients will remain on low-dose vasopressors at the time insulin weaning started.
2. Decrease infusion by 1U/kg/hr while maintaining normal cardiac output and tissue perfusion.
3. Reassess hourly for further reduction.
4. Dextrose infusion may be required for an additional 12-24 hours after discontinuation of insulin infusion.
5. Monitor potassium every 6 hours while decreasing insulin infusion for potential potassium extracellular shift and for 24 hours following discontinuation of the insulin infusion. Can return to standard floor potassium repletion goals once dextrose infusion is discontinued.

Pitfalls:

1. Using high doses of vasopressors for cardiogenic shock.
2. Using insulin for vasoplegic shock with preserved cardiac contractility.
3. Administering excess IVF for BB/CCB overdoses.
    a. 1 L bolus ok initially however these patients are likely to receive very high volumes of fluid from the vasopressors, insulin, and dextrose infusions.
    b. These patients may have ATN with impaired ability to eliminate volume, and they won't tolerate HD due to hypotension.
    c. Whether vasoplegic or cardiogenic, a common result is pulmonary edema which will ultimately kill them.

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