

Hypocalcemia in Trauma Resuscitation

Introduction

1. Trauma is a leading cause of death in the US, and uncontrolled hemorrhage is often the primary cause of mortality.
2. The lethal triad of trauma includes coagulopathy, hypothermia, and acidosis with calcium being heavily involved in the coagulation cascade.
3. Calcium plays a vital role in coagulation and platelet, being required by clotting factors II, VII, IX, and X, proteins C and S, and plays a role in stabilizing fibrinogen and platelets in the developing thrombus.
4. Serum calcium is chelated due to the citrate used as a preservative in the Packed Red Blood Cells (PRBC's), Fresh Frozen Plasma (FFP), and other blood products.
5. While rapidly metabolized in healthy patients, citrate clearance is reduced in hemorrhagic shock and accumulated with rapidly infused blood products commonly used in massive transfusion protocol (MTP).
6. Previous work suggests that 2–15 units of blood are needed to produce a drop in calcium.

| Properties | | |
|---------------------------------------|--|---|
| | Calcium Chloride | Calcium Gluconate |
| Dose | 1-3 grams | 1-3 grams |
| Administration | Infusion of 200 mg/min <ul style="list-style-type: none"> • IV push in emergent situations • Central line administration preferred | Slow IV push administration over 5-10 minutes <ul style="list-style-type: none"> • May give through peripheral IV line • 200 mg/min |
| Formulation | 100 mg/mL (10%) contains 13.6 mEq /10mL | 100 mg/mL (10%) contain 4.65 mEq EC/10mL |
| Adverse Effects | Arrhythmias, bradycardia, cardiac arrest, syncope, tingling, necrosis of tissue (chloride > gluconate) | |
| Drug Interactions and warnings | Extravasation: Calcium is a vesicant, administration into tissue can cause necrosis Not to be used when patient is in ventricular fibrillation in cardiac resuscitation | |
| Compatibility | Epinephrine, norepinephrine, sodium bicarbonate, and blood products | |
| How supplied | 1 g/10 ml carpject syringe or vial only in code carts due to drug shortage | 1g vial (100 mg/mL) and 1-2 gram premix bags |
| Comments | Calcium Chloride has 3x higher elemental calcium than calcium gluconate | |

Hypothermia

- Cause decrease in liver metabolism of citrate
- Citrate not metabolized in the liver binds to Ca^{2+} leading to less Ca^{2+} available in the blood

Acidosis

- Low Ca^{2+} levels associated with low pH
- Lower pH prolongs clot formation

Coagulopathy

- Ca^{2+} in the plasma is necessary co-factor for clotting

Hypocalcemia

- Ca^{2+} levels drop due to blood loss
- Transfusion further exacerbates

Overview of Evidence

| Author, year | Design/ sample size | Interventions & Comparators | Outcome |
|--------------------------|---------------------------------------|-----------------------------|---|
| Vasudeva, 2020 | Retrospective review N=226 | | <ul style="list-style-type: none"> • 50% patients recording ionized hypocalcemia on presentation prior to any blood product transfusion • Ionized hypocalcemia was associated with coagulopathy in patients with shock index ≥ 1 • Admission ionized hypocalcemia was associated with death at hospital discharge 25% hypocalcemic patients vs 15% of normocalcaemic patients |
| Kyle, 2017 | Retrospective review N=297 | | <ul style="list-style-type: none"> • The incidence of hypocalcemia in the non-treatment group was 70.0% vs 28.3% in the treatment group. • In the non-treatment group, 26.6% had normal calcium levels vs 41.7% in those who received calcium. • After only 1 unit of blood, calcium levels drop below the lower limit of normal, suggesting • It was a dose response of calcium level to blood products with a significant decrease in calcium levels as the volume of blood products increased. |
| Giancarelli, 2016 | Retrospective review N=156 | | <ul style="list-style-type: none"> • 97% experienced hypocalcemia and 71% had severe hypocalcemia • Mortality was higher in the severe hypocalcemia group 49% vs 24%, • Patients in the $\text{iCa} < 0.90$ group received more blood products 34 vs 22 units |
| Webster, 2016 | Retrospective cohort analysis N=55 | | <ul style="list-style-type: none"> • 55% of patients were hypocalcemic on ED arrival • 89% patients were hypocalcemic after receiving any amount of blood product. |
| Magnotti, 2011 | Prospective cohort N=591 | | <ul style="list-style-type: none"> • Low iCa levels at admission were associated with increased mortality as well as an increased need for both multiple transfusions and massive transfusion • multivariable logistic regression analysis identified low iCa levels as an independent predictor of multiple transfusions |
| Vivien, 2005 | Prospective cohort N=212 | | <ul style="list-style-type: none"> • A normal iCa concentration was observed in 56 (26%) patients, a mild ionized hypocalcemia in 135 (64%) patients, and a severe iCa in 21 (10%) patients. • There was a significant correlation between iCa concentration with the amount of infused colloid |

iCa = Ionized Calcium

References

1. Calcium chloride. Micromedex [Electronic version]. Greenwood Village, CO: Truven Health Analytics. Retrieved June 17, 2020, from <http://www.micromedexsolutions.com/>
2. Vasudeva M, et al. Hypocalcaemia and traumatic coagulopathy: an observational analysis. Vox Sang. 2020;115(2):189-195. doi:10.1111/vox.12875
3. Kyle T, et al. Ionised calcium levels in major trauma patients who received blood en route to a military medical treatment facility. Emerg Med J. 2018;35(3):176-179. doi:10.1136/emmermed-2017-206717
4. Giancarelli A, et al. Hypocalcemia in trauma patients receiving massive transfusion. J Surg Res. 2016;202(1):182-187. doi:10.1016/j.jss.2015.12.036
5. Webster S, et al. Ionised calcium levels in major trauma patients who received blood in the Emergency Department. Emerg Med J. 2016;33(8):569-572. doi:10.1136/emmermed-2015-205096
6. Magnotti LJ, et al. Admission ionized calcium levels predict the need for multiple transfusions: a prospective study of 591 critically ill trauma patients. J Trauma. 2011;70(2):391-397.
7. Vivien B, et al. Early hypocalcemia in severe trauma. Crit Care Med. 2005;33(9):1946-1952. doi:10.1097/01.ccm.0000171840.01892.36
8. Ditzel RM, et al. A review of transfusion- and trauma-induced hypocalcemia: Is it time to change the lethal triad to the lethal diamond?. J Trauma Acute Care Surg. 2020;88(3):434-439.