PHARMACY FRIDAY PEARLS
A PHARMACY EDUCATIONAL SERIES
PHARMACYFRIDAY.COM

Hypocalcemia Resulting from Trauma & Blood Product Transfusion

Introduction

- Trauma is a leading cause of death in the US, and uncontrolled hemorrhage is often the primary cause of mortality.
- The lethal triad of trauma includes coagulopathy, hypothermia, and acidosis with calcium being heavily involved in the coagulation cascade.
- Calcium plays a vital role in coagulation and platelet aggregation 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.
- Citrate in large quantities and rapidly infused like in massive transfusion protocol (MTP), a chelating agent, is used in the Packed Red Blood Cells (PRBC's), Fresh Frozen Plasma (FFP), and other blood products to prevent calcium from interacting with the clotting factors
- While rapidly metabolized in healthy patients, citrate clearance is reduced in hemorrhagic shock and accumulated with rapidly infused blood products commonly used in MTP.
- Previous literature 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	Slow IV push in emergent situations over 2-5 minutes. • Central line administration recommended • If no central line available, can use large bore IV (avoid use of hand and foot IV's)	Slow IV push administration over 2 -5 minutes • May give through peripheral IV line
Formulation	100 mg/mL (10%) contains 13.6 mEq /10mL	100 mg/mL (10%) contain 4.65 mEq EC/10mL
Adverse Effects	Arrythmias, 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 carpuject syringe or vial	1g vial (100 mg/mL) and 1-2 g premix bags
Comments	Calcium Chloride has 3x higher elemental calcium than calcium gluconate	

Jlpruitt@gmh.edu; jipruitt@augusta.edu;
EC= elemental Calcium; iCa= ionized calcium

Mechanisms of Hypocalcemia During Trauma Resuscitation

Hypothermia
- Cause decrease in liver metabolism of citrate
- Citrate not metablolized 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 necesarry co-factor for clotting

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

Overview of Evidence

Author, year	Design/ sample size	Outcome
Vasudeva, 2020	Retrospective review of trauma patients N=226	• **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 of trauma patients N=297	• 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**
Giancarelli, 2016	Retrospective review of trauma patients N=156	• 97% experienced hypocalcemia and 71% had severe hypocalcemia • **Mortality was higher in the severe hypocalcemia group 49% vs 24%,** • **Patients in the iCa < 0.90 group received more blood products 34 vs 22 units**
Webster, 2016	Retrospective cohort analysis of trauma patients N=55	• 55% of patients were hypocalcemic on ED arrival • 89% patients were hypocalcemic after receiving any amount of blood product.
Magnotti, 2011	Prospective cohort of trauma patients N=591	• 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 of trauma patients N=212	• 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 blood products**

Conclusion: Consider giving calcium salts after 2 units of blood products and routinely monitor ionized calcium levels during resuscitation

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.12875Giancarelli A, et al. Hypocalcemia in trauma patients receiving massive transfusion. J Surg Res. 2016 May; 202(1):182-187.
3. Kyle T, et al. Emerg Med J. 2018;35(3):176-179. doi:10.1136/emermed-2017-206717
4. Giancarelli A, et al. J Surg Res. 2016;202(1):182-187. doi:10.1016/j.jss.2015.12.036
5. Webster S, et al. Emerg Med J. 2016;33(8):569-572. doi:10.1136/emermed-2015-205096
6. Magnotti LJ, et al. J Trauma. 2011;70(2):391–397.
7. Vivien B, et al. Crit Care Med. 2005;33(9):1946-1952. doi:10.1097/01.ccm.0000171840.01892.36
8. Ditzel RM, et al. J Trauma Acute Care Surg. 2020;88(3):434-43

Jlpruitt@gmh.edu; jipruitt@augusta.edu;

EC= elemental Calcium; iCa= ionized calcium

For educational purposes only