Hypocoagulation Caused by Metabolic / Respiratory-Induced Acidosis is not Reversed by pH Correction.

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Introduction

Approximately 25% of trauma patients with severe injuries are coagulopathic (INR≥1.5). These patients have a mortality rate four times higher than trauma patients without coagulopathy. This coagulopathy is manifest as an inability to form haemostatic clots resulting in diffuse persistent bleeding (1).

Coagulopathy that is associated with hemorrhage/trauma has been reported to be caused by a number of factors, one of which is acidosis. Metabolic acidosis occurs in severe hemorrhagic shock and trauma. Experimental acidosis that is induced by HCl infusion decreases thrombin generation and fibrinogen concentration, increases bleeding time and alters platelet function. Acidosis decreases clot strength and rFVIIa activity *in vitro*.

Although severe hemorrhage is associated with both hypo-coagulation and acidosis, it is not know if correction of the acidosis in severe hemorrhage will correct or attenuate the coagulopathy.

1) Brohi, Cohen and Davenport. Acute Coagulopathy of Trauma: mechanism, identification and effect. Curr Opin Crit Care 13:680, 2007.

Objective:

To determine if correction of the acidosis with bicarbonate will correct or attenuate the hypo-coagulation seen after severe hemorrhagic shock.

Methods

We used 40kg swine that had been instrumented with cannulas in the femoral artery and vein, and in the right jugular and carotid vessels. The pig was intubated with an endotracheal tube and a surgical plane of anesthesia established and maintained using isoflurane inhalant anesthetic (1 – 3%), and ketamine 100-400µg/kg*min.

Baseline pH was 7.41±0.01and ET pCO_2 was 45.3±1.9 mmHg (range from 36 to 52).

The swine (n=8) were made acidotic by controlled hemorrhage to bring down and maintain MAP at 35mmHg by bleeding or reinfusion of shed blood. In addition, ventilation (tital volume and/or rate) was also reduced until an arterial pH=7.1 was reached (Figure 1).

The acidosis was then corrected (pH7.1 to 7.4) by iv infusion of 100ml/40kg of 8.4% Sodium Bicarbonate inj., and adjusting ventilation back to pre-hemorrhage levels.

Arterial blood samples (30ml) were taken at baseline (pH 7.4), T1 (pH7.1) and T2 (pH corrected back to 7.4) as shown in Figures 1 and 2 for determination of coagulation. Cardiovascular parameters were monitored via the carotid cannula. A representative pig is illustrated (Figure 2).

Figure 1

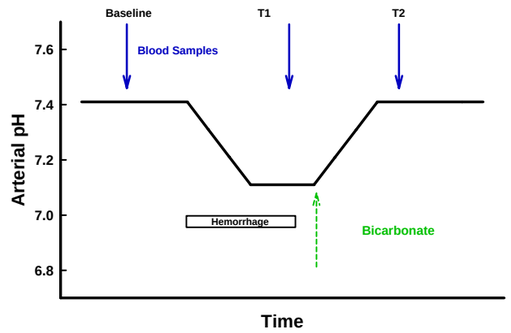


Figure 2

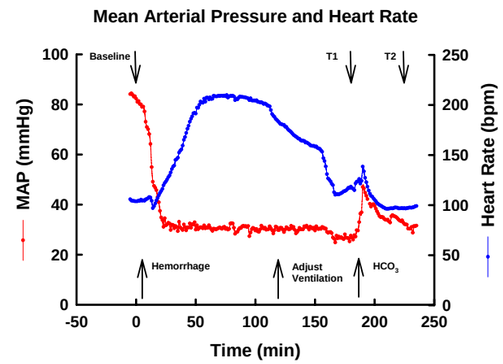


Figure 3

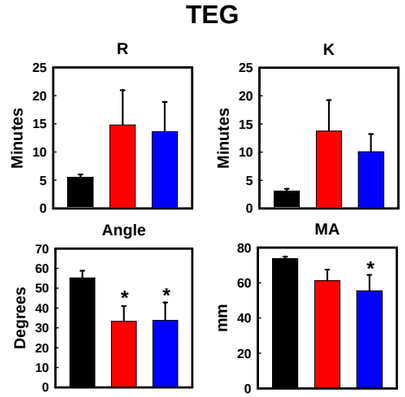


Figure 4

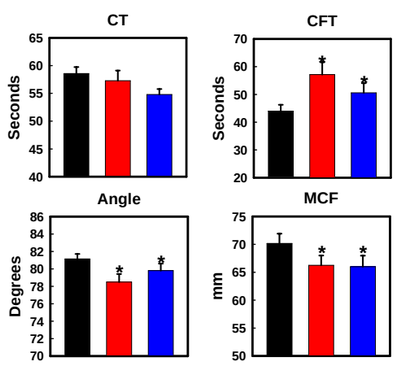


Figure 5

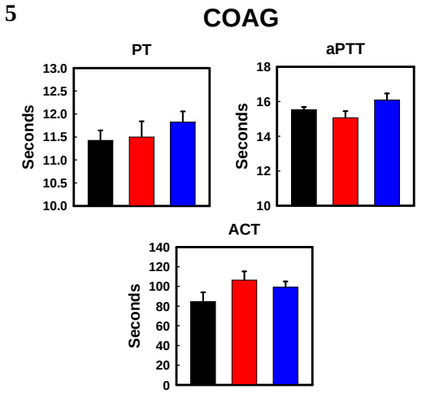
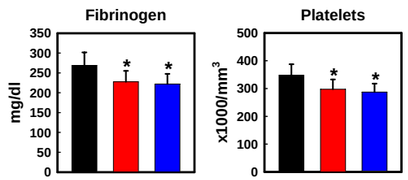


Figure 6



*** P<0.05 as compared to baseline by 1-way ANOVA CRM followed by pairwise comparisons (Holm-Sidak method). ata expressed as Mean±SE.**

Results

1) **Severe arterial acidosis (pH7.1) was induce by a combination of a decrease in a) blood volume and b) respiration in anesthetized swine (Figures 1 and 2).**
2) **Hemorrhagic/respiratory acidosis led to a hypo-coagulatory state as shown by Thromboelastograph (TEG, Figure 3) and by Rotation Thromboelastometry (Rotem, Figure 4). However, classic coagulation tests PT, aPTT and ACT did not show significant changes (Figure 5).**
3) **Correction of pH from 7.1 to 7.4 with bicarbonate infusion did not restore TEG or Rotem coagulation parameters to baseline (Figures 3 and 4).**
4) **Fibrinogen concentration and platelet number showed a slight but significant decreased after hemorrhage. This is presumably due to movement of extra-vascular fluid into the vascular space leading to a dilution of fibrinogen and platelets (Figure 6). Also, some loss could be due to consumption.**

Conclusions

1) **This metabolic/respiratory acidosis model is associated with hypo-coagulation.**
2) **The hypo-coagulation produced by this model was not corrected or attenuated after returning pH to 7.4 with Na Bicarbonate.**
3) **This suggests that hypo-coagulation is either a) not caused by the acidosis per se, or b) cannot be reversed simply by correcting the arterial pH.**
4) **Clinically, this type of coagulopathy is likely not corrected simply by normalizing arterial pH alone.**

Legend for Figures 3-6

- **pH 7.4 (baseline)**
- **pH 7.1**
- **pH 7.1 corrected to 7.4**