Alterations In Tissue Oxygenation And Metabolic Variables During Acute Cyanide Toxicity

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Introduction:

The term cyanide (CN) refers to any chemical compound that contains the cyano group (C≡N), and consists of a carbon atom triple-bonded to a nitrogen atom [1]. Organic compounds that have a –C≡N functional group are called nitriles. Of the many CN compounds, some are gases, others are solids or liquids. Those that can release the cyanide ion CN− are highly toxic to animals and humans [2]. Cyanide (CN) toxicity has been reported following smoke inhalation, industrial accidents, sodium nitroprusside overdose and could potentially occur as an act of bioterrorism. In this study, we describe the changes in tissue oxygenation and metabolic variables during acutely induced CN toxicity in a young pig model. For the first time we report on brain and skeletal muscle regional saturation of oxygen by using a non-invasive externally applied regional oximetry system – this measures the balance of oxygenated and deoxygenated hemoglobin in the cerebral cortex and skeletal muscle[4].

Methods:

Twenty six piglets (19-29 kg) were anesthetized, allowed to spontaneously breathe via an endotracheal tube and were percutaneously canulated (arterial and pulmonary artery catheters). We monitored blood CN and lactate levels, continuous SvO_2, continuous cardiac output (CCO), regional brain O_2 (cerebral cortex) and skeletal muscle O_2 (deltoid) saturation, arterial and mixed venous PO_2, arterial and mixed venous pH, central venous pressure (CVP), heart rate (HR), systemic pressure and pulmonary artery pressure. After obtaining baseline control data, all animals were started on an infusion of NaCN (0.55 mg/kg/hr). The infusion continued until the occurrence of sustained apnea (≥3 minutes). Scatter plots were made of all the data points and the cubic spline trend lines were provided. Significance was determined using the generalized estimating equation with a compound symmetric correlation structure within each pig[5]. Where relevant, Pearson correlations between two variables were calculated.

Results:

CN infusion resulted in toxic levels of blood CN accompanied by lactic acidosis (p<0.0001, figures 1, 2). In addition, there was a progressive increase in CO, SvO_2, heart-rate, elevation of CVP and and pulmonary artery blood pressure (see figures 3-6; all p<0.0001). Mean blood pressure did not change significantly (figure 7). Skeletal muscle rSO2 progressively and significantly decreased with increasing lactate and CN levels (see figures 8, 9). However, there was no significant change in brain rSO2 (figure 9). Figure 10 displays the changes observed in arterial and mixed venous oxygen tensions.

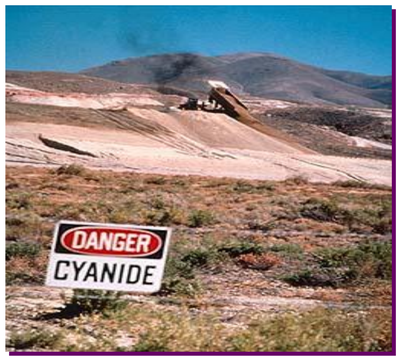


Figure 1

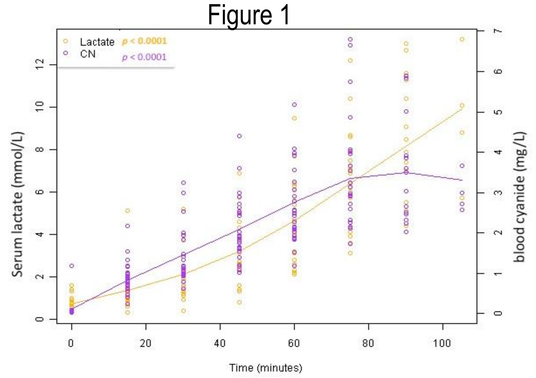


Figure 2

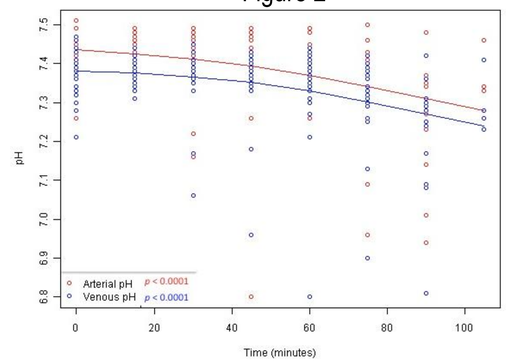


Figure 3

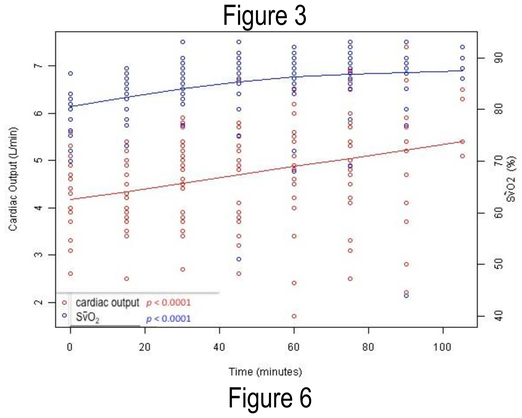


Figure 4

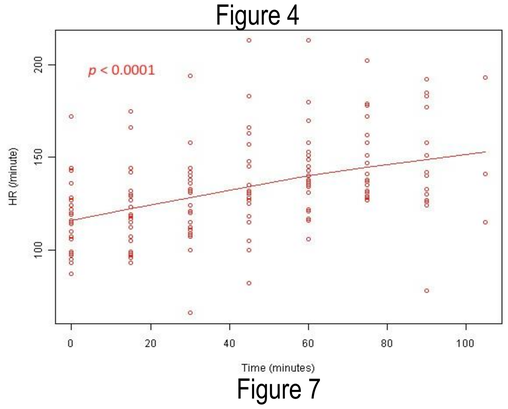


Figure 5

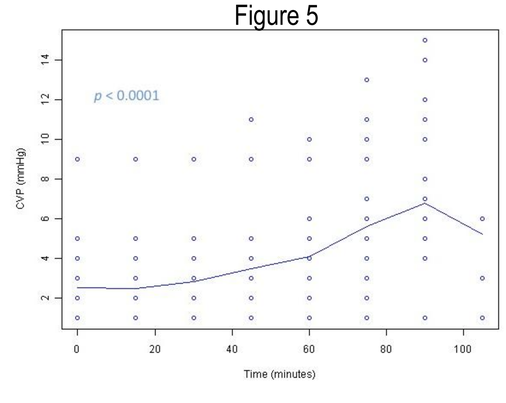


Figure 6

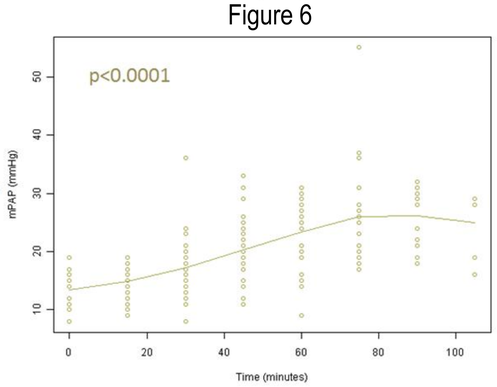


Figure 7

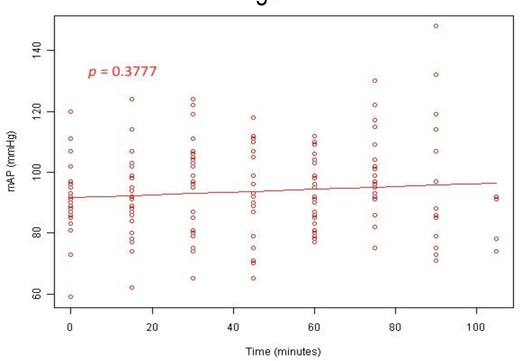


Figure 8

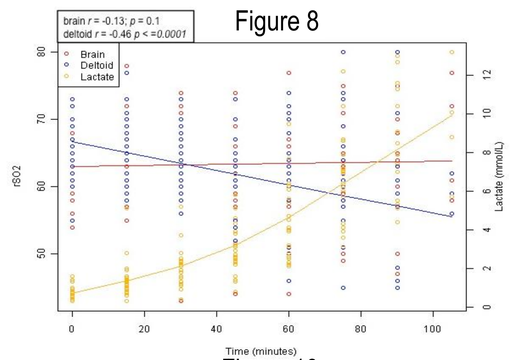


Figure 9

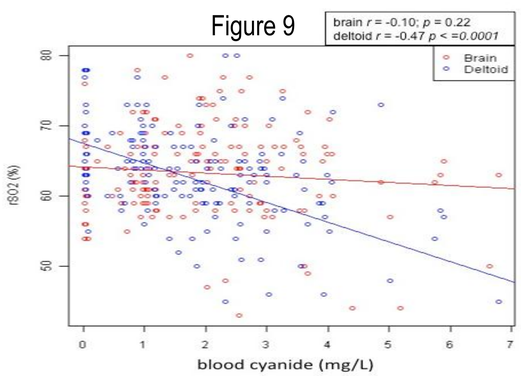
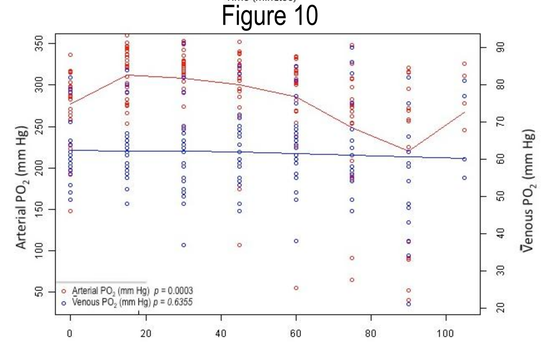


Figure 10



References: [1]Greenwood, N. N.; & Earnshaw, A. (1997). Chemistry of the Elements, Oxford:Butterworth-Heinemann.
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[5] Reinsch, C.H. (1967), "Smoothing by Spline Functions," Numerische Mathematik, 10, 177-183

Discussion :

The gradual infusion of cyanide to induce cyanide toxicity results in a progressive increase in serum lactates resulting in significant metabolic acidosis, accompanied by an increase in SvO_2, CO, CVP, heart rate and pulmonary artery blood pressure. These signs are reflective of cellular hypoxia despite adequate oxygen delivery. For the first time, we have shown that during CN toxicity there are peripheral regional (skeletal muscle) oxygenation changes detectable by a non-invasive regional oximetry system as demonstrated by the significant decline in skeletal muscle rSO_2. The decrease in rSO2 correlated significantly with increase in serum lactate levels (figure 8). Surprisingly, brain rSO_2 did not follow the same pattern as did skeletal muscle. This may be due to protective mechanisms aimed at delaying toxic manifestations in the brain and deserves further elucidation.

Conclusions:

Acute CN toxicity results in significant lactic acidosis, pulmonary hypertension accompanied by tachycardia, increase in CO and SvO_2. Skeletal muscle rSO_2 decreases significantly. However, brain rSO_2 does not change significantly.

Acknowledgements:

1. Sensors for regional SO_2 were provided by Nonin Medical Inc, Plymouth, MN
2. Aaron Lobbestael provided bio-statistical assistance

(supported by : Grant 1U01NS058087-01, National Institutes of Health, NINDH)