Title: ACTIVATED COAGULATION TIME DURING ACUTE RESPIRATORY ACIDOSIS AND ALKALOSIS

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Introduction. It has been noted that the activated coagulation time (ACT) is affected by several factors such as hypothermia and hemodilution during open heart surgery. The purpose of the present study is to investigate in dogs the effect of acute respiratory alkalosis and acidosis on ACT.

Methods. Sixteen mongrel dogs weighing 18 to 26 kg were anesthetized with thioental, intubated, and mechanically ventilated with 100% oxygen. Anesthesia was maintained with ketamine and pancuronium. A femoral artery was cannulated to monitor arterial blood pressure and for blood sampling. The arterial line was flushed with heparin-free saline intermittently. Body temperature was kept normothermic by external measures. The pH of arterial blood was measured with a BMS Micro System (Radiometer, Copenhagen). The ACT was measured by one person in the usual manner with a Hemochron 400 (International Technidyne Co.) on 3 ml blood. After the control measurements of the pH and ACT, dogs were divided into two groups of eight each. In group 1, dogs were hyperventilated for one hour (Vt=5-7 ml/kg, f=40/min) in order to produce acute respiratory acidosis.

During this period ACT was measured for both non-heparinized and heparinized (13.3 U/ml) blood samples at certain intervals. The pH of each sample was also measured. In group 2, dogs were hyperventilated (Vt=25-30 ml/kg, f=30-40/min) and the same measurements were performed. The pH values were rounded off to the nearest 0.025 pH unit and ACT was plotted with respect to the pH values.

Results. The results are shown in figure 1. When heparin was added, the ACT was prolonged by increasing the degree of both acidosis and alkalosis. The correlation was statistically significant in both instances. When the blood was not heparinized, the ACT was shortened by increasing the degree of acidosis, however, it was not altered when the degree of respiratory alkalosis was increased.

Discussion. It has been shown that acidosis can affect blood clotting by several mechanisms. It can activate the intrinsic system of coagulation, and it may increase the viscosity of blood, thus shortening the clotting time. Increased endogenous catecholamine release secondary to acidosis can also shorten the clotting time. This might explain why the ACT decreases as acidosis increases when the blood is not heparinized. It is difficult to explain why the ACT was prolonged by acidosis when heparin was added. Low pH itself may increase the effectiveness of heparin and potentiate the interaction between heparin and antithrombin III, resulting in the prolongation of the ACT. A parallelism has been noted between activation of blood coagulation and fibrinolysis during disseminated intravascular coagulation (DIC). These phenomena may appear with acidosis, since it is one of the factors inducing DIC. Heparin may interact with the fibrinolytic process and prolong the ACT as acidosis increases. It has been shown that the bicarbonate itself and the resultant alkalosis interfere with the clotting process, resulting in the prolongation of clotting time. In this study, the ACT was prolonged with an increasing degree of alkalosis only when heparin was added. The reason for this is not clear. Alteration of the interaction between heparin and coagulation factors, or the decreased level of ionized calcium due to the alkalosis could account for the prolongation of the ACT by alkalosis. Heparin is negatively charged, so the ionized fraction of heparin may increase with alkalosis, which may augment the anticoagulant effect of heparin. In summary, the ACT was prolonged by increasing the degree of both respiratory acidosis and alkalosis when the blood was heparinized. Alkalosis shortened the ACT when the blood was not heparinized. The reasons must be multifactorial. The changes in ACT due to the alterations of acid base balance should be considered in the clinical situation.

Fig. 1: a) acidosis study, b) alkalosis study. Both solid and open circles above the pH line are for samples that were heparinized.

References.