Title: EFFECTS OF TRANSIENT ACID-BASE CHANGES ON AFTERDEPOLARIZATIONS AND TRIGGERED ARRHYTHMIAS IN THE DOG HEART

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Introduction. Changes in acid-base balance can induce cardiac arrhythmias but their mechanisms are not well understood. The purpose of this study was to investigate effects of transient acidosis and alkalosis on delayed afterdepolarizations (DADs) and triggered arrhythmias (TA) in dog coronary sinus cells and to compare these effects with those in Purkinje fibers from the same heart.

Methods. Dog coronary sinus (CS) was isolated and cut open along its length[1]. Small strips were dissected and placed in a fast flow system side-by-side with Purkinje fibers (PF). They were superfused with 5% CO_2/95% O_2 (12 mM HCO_3, pH_e 7.15-7.2) and 0.05-0.2 mg/l norepinephrine. Respiratory acidosis (RACID) or alkalosis (RALK) was induced by saturation with 20% CO_2/80% O_2 or 100% O_2 respectively. Metabolic changes were induced by changing bicarbonate concentration. Preparations were also exposed to salts of weak acids (20 mM sodium propionate or lactate), to 20 mM NH_4Cl and to chloride-free solutions (NaCl replaced by Na isethionate). Exposure time varied between 30 sec and 20 min. Membrane potentials were recorded with intracellular glass microelectrodes. Twitch tension developed by stimulated CS strips was also recorded. PF were not stimulated.

Results. RACID decreased or suppressed and RALK increased DADs, twitch tension (T) and aftercontractions in CS. During acidosis it was impossible to induce TA whereas during alkalosis TA started promptly and continued as long as alkalosis lasted. Accordingly, in PF physiological automaticity (slow diastolic depolarization) and also oscillations at the lower level of membrane potential (-30 to -50 mV) or early afterdepolarizations were suppressed by RACID and enhanced by RALK. The membrane potentials of depolarized PF were switched to well polarized levels by RACID. Effects exerted by metabolic acidosis and alkalosis were the same but slow to occur. Effects of RACID were potentiated by salts of weak acids. When extracellular pH was stabilized by increasing HCO_3 concentration (Fig.1 and 2) effects of RACID were equally pronouced which demonstrates that they are due to intracellular acidosis. Wash out of CO_2 led to a dramatic potentiation of DADs and initiation of TA in CS (Fig.1 and 2) and oscillatory activity in PF (Fig.2). Force of contraction which was dramatically decreased by intracellular acidosis (Fig.1 and 2) increased well above the control level on washing out CO_2. Chloride-free solutions prolonged the wash out phase (Fig.2).

Discussion. This study shows that alkalosis is arrhythmogenic while acidosis exerts transient antiarrhythmic effects. However, recovery from acute intracellular acidosis is strongly arrhythmogenic. The "wash out" arrhythmias are probably due to transient intracellular alkalosis induced by HCO_3 accumulated by the cells in compensation for acid load. During wash out, CO_2 leaves cells quickly, leading to an excess of intracellular HCO_3. As HCO_3 is pumped out in exchange for Cl, removal of extracellular chloride prolongs the wash out phase. It follows from this study that care should be taken to protect artificially ventilated patients from drastic changes in acid-base balance such as those caused e.g. by an abrupt correction of hypercapnia. Moreover, the "wash out" effect described above may be responsible for reperfusion arrhythmias following transient coronary occlusion when ischemic cells can become become transiently acidotic.

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References.

1. Wit AL, Cranefield PF: Triggered and automatic activity in the coronary sinus. Circulation Res. 41: 435-445, 1977

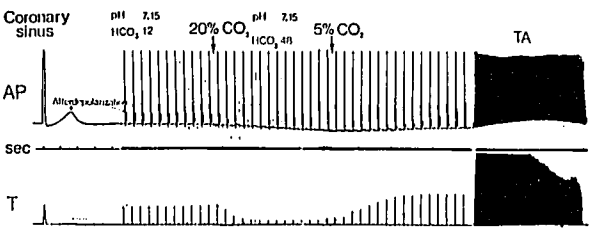

Fig.1 Effects of short (140 sec) hypercapnia on CS action potential (AP), DADs and twitch tension (T). Middle trace (sec) shows time marks (1/sec). Extracellular pH (pH_e) was stabilized by increasing HCO_3. Wash out of CO_2 was followed by an increase in amplitude of DADs reaching the threshold and initiation of a triggered arrhythmia (TA).

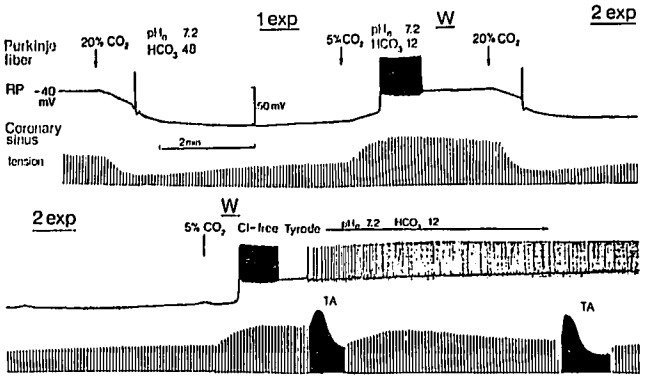

Fig.2 Effects of hypercapnia on membrane potential of a quiescent PF and on tension developed by CS strip. Lower panel is a continuation of the recordings in the upper one. Note the absence of TA in CS during wash out phase (W) after first exposure (1 exp) and the occurrence of two bursts of TA after the second exposure (2 exp) when preparations are superfused with chloride-free Tyrode. Spontaneous activity in PF markedly increased by Cl-free Tyrode.

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