Posthypercapnic Myocardial Potassium Movements[1] (37271)

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Severe cardiac arrhythmias can be consistently produced in the dog by suddenly switching to room air after a period of ventilation with 30–40% carbon dioxide (1–4). These arrhythmias have been attributed to hyperkalemia (5), serum Ca^{2+}/K^{+} (6), and "altered myocardial ionic balance" (4). More recently, Goott *et al.* (7) proposed that these arrhythmias resulted from "a very rapid loss of K^{+} from the myocardium incident to a drop in plasma catecholamine level."

Respiratory acidosis without hypoxemia is associated with an uptake of potassium by the myocardium (8, 9). We have shown by beta-adrenergic blockade with propranolol that this uptake is secondary to the increased catecholamine level which accompanies hypercapnia (10). Nahas and Poyart (11) have shown that hydrogen ions (H^{+}) may have a beta-adrenergic blocking effect. If this is true, then some of the beta-adrenergic effect of the increased level of catecholamines which accompanies hypercapnia might be blocked by the increased $[H^{+}]$. During the posthypercapnic period, if the $[H^{+}]$ falls faster than the catecholamine level, there would be an increase in the effective beta-adrenergic activity. Later, as the catecholamines were metabolized there would be a decrease in this activity. If these assumptions are true then one would expect a diphasic movement of myocardial potassium in the posthypercapnic period; *i.e.*, an increased uptake followed by a loss. The series of experiments reported here was designed to evaluate the validity of this proposal.

Methods. Mongrel dogs (18–30 kg) were anesthetized with sodium pentobarbital (30 mg/kg, iv). The dogs were intubated and hyperventilated with a positive pressure respirator at a minute volume of approximately 500 ml/kg. During the control period they breathed the control gas mixture (CGM) consisting of 75% O_2 and approximately 22% N_2 with 3% CO_2. The inspired CO_2 was adjusted as necessary to bring the arterial pCO_2 during the control period to approximately 40–45 mm Hg. After the control period the dogs were ventilated with the hypercapnic gas mixture (HGM) consisting of 75% O_2 and 25% CO_2; following this they were ventilated with the posthypercapnic gas mixture (PHGM) of 100% O_2. Cannulas were placed in the right and left femoral arteries to obtain arterial blood samples and pressure and in the right femoral vein for administration of drugs. The dogs were given 20,000 units of sodium heparin to prevent blood clotting. The pH and pCO_2 of anaerobically drawn arterial blood were intermittently measured at 37.5° with a thermostatically controlled pH and pCO_2 meter (Radiometer, Copenhagen).

Two separate sets of experiments were carried out under identical conditions. The first set of experiments measured the arterial plasma $[K^{+}]$ minus the coronary sinus plasma $[K^{+}]$, $(K^{+}_{A\text{-}V})$. In seven dogs the heart was exposed by a right lateral approach. A cannula passing through the right external jugular vein was placed in the coronary sinus. The placement of this cannula was periodically checked by palpation during the experiment and by examination at autopsy. A cannula for measurement of LVP was passed through an incision in the left auricle into the left ventricle in five of the seven experiments. Simultaneously drawn arterial and coronary sinus blood samples were taken at 10 min intervals during the control and hy-

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percapnic periods. During the posthypercapnic period they were collected at 30 sec intervals for 3 min and then at 5 and 8 min into the posthypercapnic period. All blood samples for K^+ determination were immediately centrifuged, the plasma was decanted and the $[K^+]$ was determined on an Instrumentation Laboratory flamephotometer.

The second set of experiments measured coronary artery blood flow instead of K^+_{A-V} and LVP. In four dogs a velocity sensitive catheter tip flowmeter (12) was inserted through the right common carotid artery and placed in the left coronary artery or one of its branches. As in the first series of experiments the heart was exposed via a right lateral approach. The position of the flowmeter tip was validated by observing the hyperemic response following coronary artery occlusion and by examination at autopsy. Flow was measured continuously throughout the experiment and the results were tabulated at the same points in time as K^+_{A-V} was measured in the first set of experiments.

In both sets of experiments, after the instruments were appropriately placed, the dogs were ventilated with the CGM for a 20 min control period. The dogs were then switched to the HGM for 1 hr and then to the PHGM.

Results. The results from the first set of experiments are shown in Fig. 1. During the control period when the dogs were breathing CGM, the arterial blood pH averaged 7.35,

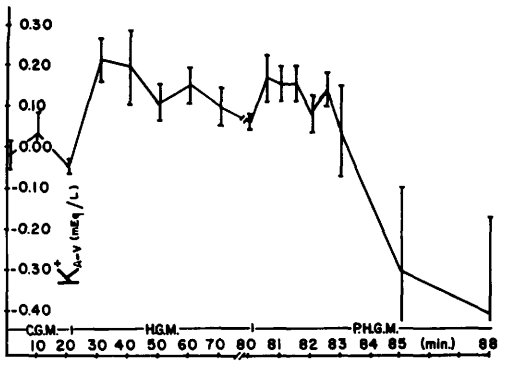

FIG. 1. Posthypercapnia K^+_{A-V}. The effect of switching from control gas mixture (CGM) to hypercapnic gas mixture (HGM) to posthypercapnic gas mixture (PHGM) on mean arterial–coronary sinus K^+ difference (K^+_{A-V}) measured in seven dogs; vertical bars indicate ± SEM.

the pCO_2 ranged from 40–45 mm Hg, and the K^+_{A-V} was slightly negative. After 20 min of CGM, the dogs were switched to the HGM. The pH fell to 6.85 and K^+_{A-V} became positive and remained positive for the duration of ventilation with HGM. After 1 hr of ventilation with HGM the dogs were switched to the PHGM. Sixty seconds after switching from HGM to PHGM the arterial pCO_2 had returned to 40–45 mm Hg and the pH had risen to 7.15–7.25. The first K^+_{A-V} during the PHGM period was increased over the last K^+_{A-V} value during the HGM period by almost 200%. The K^+_{A-V} remained positive for at least 3 min posthypercapnia while the samples taken at 5 and 8 min were negative. Thus during this period there was a diphasic K^+ movement; *i.e.*, an increased positive K^+_{A-V} followed by a negative K^+_{A-V}. In some of the experiments premature ventricular contractions occasionally occurred during the immediate posthypercapnic period.

The results from the second set of experiments are shown in Fig. 2. During the control period the arterial blood pCO_2 and pH were essentially the same as in the first set of experiments. Peak diastolic coronary blood flow was stable at approximately 30–40 ml/min. After 20 min of CGM the dogs were switched to the HGM and the pH fell to the same level as in the first set of experiments. The peak diastolic coronary blood flow gradually increased during the first 10 min of hypercapnia and continued to rise throughout the hypercapnic period to approximately 10 times that of the control period while heart rate remained below control levels. After 1 hr of ventilation with HGM the dogs were switched to the PHGM. The pH and pCO_2 values were again similar to the first set of experiments. Thirty seconds after switching to the PHGM the flow as slightly greater than the last measurement during the HGM period and the heart rate had increased approximately 10%. The flow then gradually declined from this peak while heart rate continued to increase toward control values. In only one of the four experiments did the flow return to control levels during our 8 min period of observation during the PHGM period.

A record of left intraventricular pressure

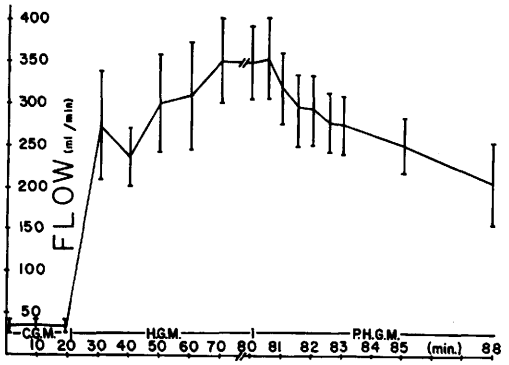

FIG. 2. Coronary blood flow. The effect of switching from control gas mixture (CGM) to hypercapnic gas mixture (HGM) to posthypercapnic gas mixture (PHGM) on mean peak diastolic coronary blood flow measured in four dogs; vertical bars indicate ± SEM.

during the switch from HGM to PHGM is shown in Fig. 3. The most prominent feature is the decrease in peak LVP of approximately 50%. This was a consistent finding in all of the experiments in which we measured this parameter. Aortic pressure, stable during the control period, initially fell during the hypercapnic period and then returned to normal values. During the posthypercapnic period there was a moderate fall in aortic blood pressure. The degree of this decrease is reflected in the change in peak LVP in Fig. 3. This fall was occasionally preceded by a slight transient increase in systolic blood pressure.

Discussion. Our data demonstrate a diphasic K^+ movement in the immediate posthypercapnic period, *i.e.*, an increased uptake followed by a loss of K^+ from the heart. This is consistent with our hypothesis of an increased myocardial sensitivity to catecholamines secondary to a decrease in $[H^+]$ during this period.

Other possible causes of the increase in $K^+_{A\text{-}V}$ at 30 sec after switching from HGM to PHGM must also be considered. Sarnoff *et al.* (13) have shown that an increase in heart rate or an increase in aortic pressure is associated with a loss of K^+ from the myocardium. In our experiments the heart rate increased slightly in the posthypercapnic period. This cannot explain the increase in $K^+_{A\text{-}V}$. If an increase in aortic pressure is associated with a loss of K^+ from the myocardium, then a decrease might be associated with an uptake. During the posthypercapnic period there was a decrease in aortic pressure. This probably does not explain the increase in $K^+_{A\text{-}V}$ since the decrease in aortic pressure continues but the $K^+_{A\text{-}V}$ decreases and eventually becomes negative.

In other experiments Gilmore and Gerlings (14) show that an increase in peak LVP in an isovolumic heart, and thus presumably an increase in wall tension, is associated with a loss of K^+ from the myocardium. Then a decrease in peak LVP might be associated with an uptake of K^+. Peak LVP did decrease as shown in Fig. 3. We can estimate left ventricular volume on the basis of Wildenthal and co-workers' data (15, 16) which showed that left ventricular end diastolic pressure (LVEDP) gives a reasonable estimate of left ventricular volume. Although it is not shown in Fig. 3, we did measure LVEDP and it was essentially unchanged during the posthypercapnic period, relative to the hypercapnic period. The decrease in peak LVP (Fig. 3) does not explain the increase in $K^+_{A\text{-}V}$ because the decreased peak LVP continues but the increased $K^+_{A\text{-}V}$ does not.

Simultaneous measurement of $K^+_{A\text{-}V}$, LVP, and coronary blood flow would have required placement of three separate catheters in the heart. Therefore, we ran two sets of experiments under as identical conditions as possible measuring $K^+_{A\text{-}V}$ and LVP in one set and coronary blood flow in the other. In one experiment in which we did not measure LVP we were able to simultaneously measure

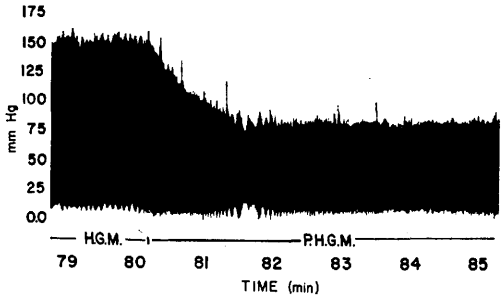

FIG. 3. Left ventricular pressure (posthypercapnia). The effect of switching from hypercapnic gas mixture (HGM) to posthypercapnic gas mixture (PHGM) on left ventricular pressure.

K^+_{A-V} and coronary blood flow. There was no substantial difference among these experiments.

Summary. Our experiments demonstrate a diphasic K^+ movement in the myocardium in the immediate posthypercapnic period. Changes in heart rate, aortic pressure, peak LVP or coronary blood flow do not appear to explain the increased uptake of K^+ following the switch from hypercapnic gas mixture to posthypercapnic gas mixture.

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