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Effect of Respiratory and Metabolic Acidosis on Coronary Vascular Resistance[1] (38528)

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An increase in coronary flow has been observed during acute hypercapnia (1–4). On the other hand, metabolic acidosis has been shown to produce an increase (5), or a decrease (2, 6) in coronary vascular resistance. Similarly inconsistent results have been observed when either respiratory or metabolic alkalosis was produced (2, 4–6). The apparent contradiction between different studies may be due to one or more of the following. In the first place, changes in the coronary circulation were observed in the presence of changes in the systemic circulation, notably arterial blood pressure and heart rate, making it difficult to determine to what extent coronary changes are a reflection of systemic circulatory changes (1, 5, 6). Secondly, acid-base changes are capable of altering the O_2 requirements of the heart which in turn strongly affect the coronary circulation. This variable has not always been taken into account in the interpretation of the results (2, 4, 6). Finally, in some cases simultaneous changes in pH, P_{CO_2} and HCO_3^- concentration have thwarted attempts to ascertain which of these parameters is responsible for the changes observed (5, 6).

The present experiments were undertaken to study the effect of metabolic and respiratory acidosis on coronary vascular resistance. A preparation where hemodynamic variables and O_2 requirements could either be controlled or their influence accounted for was employed.

Methods. The experiments were performed using isolated perfused rabbit hearts. Rabbits were anesthetized with a mixture of chloralose and urethane. The thorax was opened under artificial ventilation and a metal cannula was introduced into the aorta, with its tip oriented towards the ventricle and close to the valve. Perfusion of the coronary circulation with Ringer's solution, equilibrated at 37° with 95% O_2, 5% CO_2 was started immediately with a roller pump. Coronary venous effluent was collected through a cannula in the pulmonary artery. Perfusion pressure was measured with a transducer connected to the aortic cannula. A wide bore needle was introduced into the left ventricle through the apex and connected to another transducer to record left ventricular pressure. The left ventricle was maintained empty by a catheter introduced in the cavity and connected to a small pump. Adequate Thebesian drainage was checked by the level of left ventricular pressure that was always equal to or lower than atmospheric. Heart rate was maintained constant by atrial pacing. Coronary venous flow from the pulmonary artery was measured by timed collection. P_{O_2} of the coronary venous effluent was continuously measured with a flow-through electrode. Perfusion pressure, left ventricular pressure and venous P_{O_2} were continuously recorded on a polygraph. Samples of arterial and venous perfusate were analyzed in triplicate for pH, P_{O_2} and P_{CO_2} with appropriate electrodes. Pressure-flow curves of the coronary circulation were obtained by changing the flow of the perfusion pump. Each curve consisted of at least four different flows. Arterial and venous perfusate samples for the determination of pH, P_{CO_2} and P_{O_2} were obtained at every flow level when a steady state was reached.

Three series of experiments were performed. In the first series, pressure flow curves were obtained during perfusion of the coronary circulation with control Ringer's solution (pH_a = 7.47 ± 0.01, P_aCO_2 = 34.6 ± 0.5 mmHg) and during perfusion with hypercapnic Ringer's solution (pH_a = 6.87 ± 0.004, P_aCO_2 = 141.8 ± 1.7 mmHg). In the second series of experiments, the

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effect of metabolic acidosis was studied. Pressure flow curves obtained during perfusion with control solution (pH_a = 7.43 ± 0.02, P_aCO_2 = 30.6 ± 0.9 mmHg) were compared with those obtained during perfusion with low HCO_3^- solution (pH_a = 6.98 ± 0.03, P_aCO_2 = 30.7 ± 1.0 mmHg). In order to avoid the influence of time, the hearts were perfused with different flows and different solutions in a random sequence. In a third group of five experiments, coronary flow was set at approximately 2.5 ml × min^{-1} × g^{-1}, and maintained unchanged throughout the experiment. The coronary circulation was perfused in a random sequence with control solution, hypercapnic solution and low HCO_3^- solution. The same variables as in the previous two groups were measured. In preparing the solution, special care was taken to attain the same pH with respiratory and metabolic acidosis.

Results. The results of the first series of experiments are shown in Fig. 1. In panel A, perfusion pressure values are plotted as a function of coronary flow for the control and hypercapnic solutions. No significant changes were observed during respiratory acidosis as compared to control; that is, for any given flow perfusion pressure was essentially the same in both conditions. Panel B shows the values of venous P_{O_2} for the same groups of experiments, plotted as a function of flow. A difference between control and acidosis is now evident. For any given flow, venous P_{O_2} was lower in control than in acidosis. Panel C shows a plot of perfusion pressure as a function of Pv_{O_2}. For any given Pv_{O_2}, perfusion pressure was substantially higher for the control experiments.

Essentially the same results were obtained when metabolic acidosis was produced (Fig. 2). A plot of perfusion pressure as a function of flow fails to show any difference between perfusion with control or low HCO_3^- solutions (panel A). On the other hand, when Pv_{O_2} is plotted as a function of flow, it can be seen that Pv_{O_2} was higher in acidosis for any given flow (panel B) and that for any given Pv_{O_2} perfusion pressure was lower during acidosis than control (panel C).

Table I shows the results obtained in the third series of experiments when both respiratory and metabolic acidosis were produced in the same preparation. Essentially the same venous pH was attained when P_{CO_2} was increased as when HCO_3^- was lowered. While flow was maintained unchanged induction of either type of acidosis did not significantly alter perfusion pressure. However, for a similar coronary resistance Pv_{O_2} was higher during acidosis than during control. No difference in Pv_{O_2} was seen between metabolic and respiratory acidosis.

Discussion. The preparation used in the present experiments had several features that made it specially suited for the study of the effect of acid-base alterations on the coronary circulation. By isolating the heart, neurohumoral and systemic circulatory influences were eliminated. Changes in extravascular compression were also avoided by keeping the left ventricle empty. Heart rate changes were eliminated by pacing the heart. pH could be changed by independently altering either HCO_3^- or P_{CO_2}. In addition, since arterial and venous P_{O_2} were measured at every point in the pressure flow curves, changes in myocardial O_2 consumption secondary to acidosis could be detected and their influence upon coronary vascular resistance taken into account.

No significant difference was observed between the pressure-flow curves of either respiratory or metabolic acidosis and their respective controls. In other words, for any given flow, perfusion pressure was essentially the same during perfusion with acid or control solution. These results indicate that, under this particular set of experimental conditions, acidosis did not alter the resistance to flow across the coronary vascular bed. Thus, it would be concluded that acidosis does not have a direct effect on the coronary vasculature. However, another explanation can be offered if the venous O_2 values are taken into consideration. It is well known that coronary vascular resistance is profoundly affected by changes in O_2 requirements (7, 8) and a relationship between $M\dot{V}O_2$, and coronary resistance has been amply demonstrated (9). When the coronary flow was increased in the present experiment, Pv_{O_2} increased both in control and acidosis, as it would be expected if $M\dot{V}O_2$ was not flow-limited. However, for any given flow, Pv_{O_2} was higher for acidosis

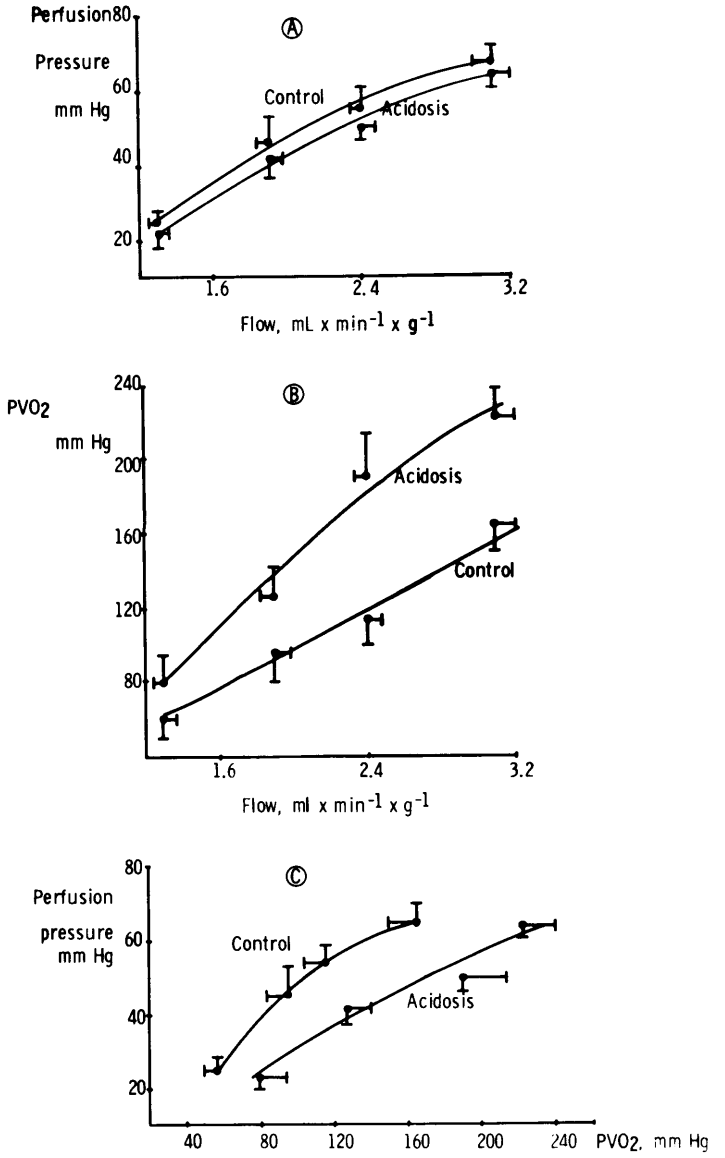

FIG. 1. Effect of respiratory acidosis on the coronary circulation. Panel A. Perfusion pressure is plotted as a function of coronary flow. In panel B, the P_{O_2} of the coronary effluent (P_{vO_2}) is plotted as a function of the corresponding coronary flow. Panel C shows the values of perfusion pressure of the same experiments plotted as a function of P_{vO_2}.

than for control (Figs. 1 and 2, panel B). The increase in Pv_{O_2} with acidosis for any given flow rate reflects a decrease in $M\dot{V}O_2$ probably secondary to the decrease in contractility that is known to accompany acidosis (2, 5, 10, 11). Also, for any given Pv_{O_2}, perfusion pressure is lower for acidosis than for control (Figs. 1 and 2, panel C). This indicates that, for any given level of Pv_{O_2}, the coronary resistance is lower during acidosis. If acidosis would have no effect whatsoever on coronary resistance it would be expected that, following a decrease in $M\dot{V}O_2$ associated with lowering pH, an increase in coronary resistance would occur. This was not the case, and the fact that acidosis was associated with a lower resistance to flow for any given Pv_{O_2} suggests that

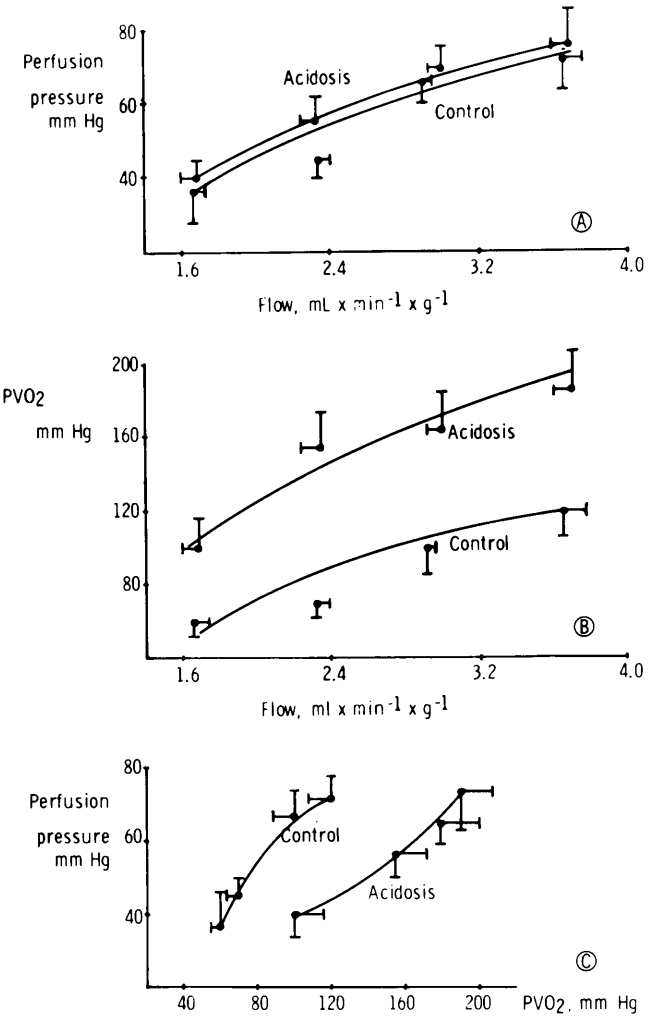

FIG. 2. Effect of metabolic acidosis on the coronary circulation. The results have been plotted in the same way as in Fig. 1.

TABLE I. RESULTS OF THE EXPERIMENTS OF GROUP III.[a]

	pH_v	P_{vCO_2} mm Hg	P_{VO_2} mm Hg	Flow ml/min/g	Arterial pressure mm Hg
Control	7.29 ± 0.02	47 ± 3	66 ± 7	2.5 ± 0.1	38 ± 4
Respiratory acidosis	6.86[b] ± 0.02	138 ± 3	109[b] ± 9	2.6 ± 0.1	47 ± 7
Metabolic acidosis	6.81[b] ± 0.03	42[c] ± 1	111[b] ± 17	2.5 ± 0.1	40 ± 5

[a] While coronary flow was maintained constant, perfusate was switched in random sequence to control solution, low HCO_3^- solution, or hypercapnic solution. pH_v, P_{vCO_2}, and P_{vO_2} refer to the coronary effluent.

[b] Significantly different from control.

[c] Significantly different from respiratory acidosis.

acidosis does indeed have a vasodilating effect upon the coronary vasculature. This vasodilating influence was masked in the present experiments, by an opposing influence exerted by the decrease in $M\dot{V}O_2$ secondary to acidosis. These results suggest that acidosis not only affects the coronary vessels directly, but also indirectly by changing the myocardial O_2 requirements. Accordingly, the net effect of a change of pH will depend on the relative influence of each of these two parameters. It is possible that failure to take into consideration the influence of changes in $M\dot{V}O_2$ during acidosis can account for the discrepant results obtained in the past.

The present results indicate that both respiratory and metabolic acidosis have a vasodilating effect on the coronary circulation. Moreover, when the same degree of acidosis was produced by either changing P_{CO_2} or HCO_3^- concentration similar quantitative changes in coronary vascular resistance were observed suggesting that one of the primary determinants of the changes observed is the pH of the perfusate.

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