Significance of Correction of Metabolic Acidosis on the Cardiovascular Dynamics

— Experimental Study and Clinical Observation Following Cardiopulmonary Bypass —

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The importance of correction of acid-base derangement for the care of surgical patient has been stressed recently. Despite of intensive study of the hemodynamic aspects of its derangement, these results were not entirely consistent. Accordingly, evaluations were made concerning the influence of metabolic acidosis and its correction on myocardial performance and vascular resistance in dogs and clinically the effectiveness of correction of metabolic acidosis on myocardial contractility after an open-heart surgery. The result indicated that metabolic acidosis had a considerably adverse effect on the myocardium and the peripheral circulation, and that correction of metabolic acidosis was quite beneficial to restore cardiovascular dynamics.

UPON the advent of open-heart surgery, more complicated intracardiac operations are now performed resulting sometimes in severe metabolic acidosis. In such instances, metabolic acidosis is primarily caused by low cardiac output and prolonged cardiopulmonary bypass. Metabolic acidosis, per se, is commonly assumed to have an adverse effect on circulatory dynamics. Accordingly, a vicious cycle of circulatory disturbance and metabolic acidosis may occur.

In the present investigation, evaluations were made concerning the influence of metabolic acidosis and its correction on myocardial performance and vascular resistance in dogs and clinically the effectiveness of correction of metabolic acidosis on myocardial contractility after an open-heart surgery.

I) Experimental Study

1) Effect of metabolic acidosis, its correction and alkalosis on myocardial contractility

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Received for publication April 24, 1967.

METHODS

Experiments were conducted in healthy mongrel dogs weighing 10 to 14 Kg. Anesthesia was induced with 30 mg./Kg. pentobarbital administered intravenously. After insertion of an endotracheal tube, intermittent positive pressure ventilation was maintaining adjusting rate and tidal volume to maintain an arterial P_{CO_2} in normal range. The experiments which showed P_{CO_2} below 20 and above 60 mm.Hg were excluded from this study.

Aortic pressure was obtained via catheter inserted into a femoral artery. The contralateral artery was used for withdrawal of blood for intermittent blood samples. Measurement of arterial pH was done with Astrup microelectrode, and P_{CO_2} and base excess were estimated by means of Astrup's microequilibration method and Siggaard-Andersen nomogram. Changes in ventricular contractile force (VCF) or isometric systolic tension were measured with the Walton-Brodie strain gauge arch.¹¹ Right thoracotomy was performed and a strain gauge arch was sutured directly to the myocardium of the right ventricle with stretch of the muscle segment of approximately 30 per cent between the 2 legs of the arch.

Group A: Acidosis was induced by repeated injections of HCl in dosage of 40 ml. of 0.1 N solution in saline. Thereafter, several intravenous injections of 40 ml. of $NaHCO_3$ (7%) or tromethamine (THAM) (pH 10) were carried out. Arterial acid-base balance was measured just before each injection, and VCF, arterial pressure and pulse rate were recorded 0.5, 1, 2 and 3 min. after each injection.

Group B: Sodium bicarbonate was injected first to reveal the effect of metabolic alkalosis on the cardiovascular system.

Group C: Normal saline was injected repeatedly throughout the experiment serving as a control to reveal the influence of hypervolemia.

RESULTS

Group A: The reduction of arterial pH and base excess by the infusion HCl was associated with a progressive depression in VCF in all experiments (Fig. 1, 2). The depression was most marked immediately after the injection of HCl and tended to recover gradually. Arterial pH was reduced to average 7.01 (6.94–7.09) and base deficit increased to average 19.5 (15–23) mEq./L. at the end of the fourth injection of HCl. At that stage, VCF was markedly depressed by average 24 (20–30) per cent.

The acidosis was corrected by injecting $NaHCO_3$ in 12 experiments and by THAM in 8. In both groups, the correction of acidosis was associated with a progressive improvement in VCF. However, the rapid injection of both $NaHCO_3$ and THAM transiently depressed VCF.

During the infusion of HCl, arterial pressure varied but little. The arterial pressures at the end of experiments were average 158/84 mm.Hg in the $NaHCO_3$ group and average 124/76 mm.Hg in the THAM group. The

Fig. 1. VCF, pulse rate and arterial pressure in metabolic acidosis and its correction. Correction by NaHCO_3 (12 dogs).

Fig. 2. VCF, pulse rate and arterial pressure in metabolic acidosis and its correction. Correction by THAM (8 dogs).

Fig. 3. Metabolic alkalosis and its correction (3 dogs).

control arterial pressures before injections were average 144/102 and 138/100 mm.Hg respectively.

Group B: The increase of arterial pH to average 7.52 (7.42–7.61) and base excess to 17 (14–21) mEq./L. by the infusion of NaHCO_3 was associated

Fig. 4. Control studies with NaCl (5 dogs).

Fig. 5. Relation between VCF and metabolic acidosis.

rather with increase in VCF, although transient decrease in VCF and arterial pressure was noted following the initial injection (Fig. 3).

Group C: The gradual increase in VCF and arterial pressure was noted by the injection of normal saline (Fig. 4). This alteration seems to be mainly due to the effect of hypervolemia, although the influence of slight but progressive decrease in arterial pH and base excess can not entirely be disregarded. Accordingly, the results obtained in Group A and B should be estimated deducting the influence of hypervolemia.

The degree of metabolic acidosis represented by pH and base deficit was compared with the degree of depression in VCF in Group A and B (Fig. 5). A significant fall of VCF was observed when arterial blood pH fell below 7.2 and base deficit below 10 mEq./L.

(II) Effects of metabolic acidosis, its correction and alkalosis on left ventricular function curve

METHODS

Mongrel dogs weighing 11 to 14 Kg. were anesthetized with intravenous pentobarbital (30 mg./Kg.). Following endotracheal intubation, the right chest was opened and heparin was injected 3 mg./Kg. The both cavae and the azygos vein were cannulated and connected to the controlled venous inflow circuit which was primed with fresh heparinized blood and low molecular weight dextran (Fig. 6). Body temperature was maintained with a heat exchanger at 36°C. At increasing flow rates from 600 to 3,000 ml. per min., the pulse rates and the mean left atrial and aortic pressures were recorded. The construction and evaluation of left ventricular function curve were done by a method previously described.²⁾

Fig. 6. Controlled venous inflow circuit.

After the control function curve was obtained, the function curve in metabolic acidosis by the infusion of 0.3 N HCl into the venous reservoir, the curve after correction of acidosis and that in metabolic alkalosis by the infusion of NaHCO_3 or THAM were obtained successively in this order.

RESULTS

Three technically successful experiments were obtained (Fig. 7). Maximum stroke work and percentage of ventricular function to compare experimental curves with the control curve are tabulated in Table I.

Fig. 7. Left ventricular function curves in metabolic acidosis and alkalosis.

Reduction of arterial pH to 7.0–6.9 with concomitant base deficit to 19–23 mEq./L. was associated with slight or moderate depression in left ventricular function. When metabolic acidosis was corrected by the infusion of NaHCO_3 or THAM, the ventricular function curve recovered to the control or little more than that. Additional infusion of these materials producing metabolic alkalosis again depressed the ventricular function curve. However, the degree of depression was less marked compared with that seen in acidosis.

Table I. Ventricular Function in Acidosis and Alkalosis

No.	Maximum stroke work (Gm.-M.)				% function			
	Control	Acidosis	After correction	Alkalosis	Control	Acidosis	After correction	Alkalosis
I	26	19	27		100	77	117	
II	40	28	38	32	100	58	92	89
III	20	14	19	16	100	74	104	86
Average	29	20	28	24	100	70	104	88

Maximum stroke work was depressed most in metabolic acidosis and recovered to the control level when it was corrected. In metabolic alkalosis, it was again depressed.

(III) Effects of metabolic acidosis and alkalosis on total systemic and pulmonary vascular resistance

METHODS

Mongrel dogs which weighed 12 to 16 Kg. were utilized in these experiments. The controlled venous inflow circuit was established, and perfusion with a constant flow of 100 ml. per Kg. per min. was instituted (Fig. 6). The mean aortic, pulmonary, left atrial and femoral venous pressures were recorded.

Acidosis was induced by injections of 0.3 N HCl into the venous reservoir. Then, NaHCO_3 or THAM was infused in 3 experiments respectively for correction of acidosis and for alkalosis. Arterial pH, Pco_2 and base excess were measured frequently with simultaneous pressure measurement. As the cardiac output is constant, the alteration of total systemic vascular resistance is expressed simply by the arterial pressure minus venous pressure and pulmonary vascular resistance by the pulmonary arterial pressure minus left atrial pressure.

RESULTS

Representative experiments are shown in Fig. 8. The gradual reduction of arterial pH was associated with a progressive reduction of total systemic vascular resistance and a gradual increase of pulmonary vascular resistance. The increase of arterial pH was associated also with a reduction of systemic resistance, but no change in pulmonary vascular resistance. These alterations were quite reversible by correction of pH.

Change in total systemic and pulmonary vascular resistance in each experiment was compared with the degree of acidosis and alkalosis (Fig. 9). Total systemic resistance was highest in pH range of 7.25 to 7.30. It progres-

Fig. 8. Changes of systemic and pulmonary vascular resistance in metabolic acidosis and alkalosis.

- Mean aortic pressure minus venous pressure
- Mean pulmonary arterial pressure minus left atrial pressure

Fig. 9. Relation between pH and systemic and pulmonary vascular resistance.

sively declined below pH value of 7.20. It again declined at pH levels above 7.35.

Although pulmonary vascular resistance remained essentially unchanged in metabolic alkalosis, it increased gradually and progressively after a pH of less than 7.20 was reached.

(II) Clinical Study

CLINICAL MATERIALS AND METHODS

Thirty-four patients undergoing open-heart surgery for congenital or acquired heart disease were included in this study. When circulatory

Fig. 10. Response in VCF and arterial pressure by correction of metabolic acidosis after cardiopulmonary bypass.

Fig. 11. Increase in VCF by correction of metabolic acidosis (NaHCO₃)

state became stable after cardiopulmonary bypass, a Walton-Brodie strain gauge arch was sutured to the right ventricle to record myocardial contractile force. Arterial pressure was monitored continuously with an electric manometer. Arterial pH, P_{CO_2} and base excess were measured with Astrup's method before and 5 min. after correction of metabolic acidosis. Correction of metabolic acidosis was performed with the intravenous slow infusion of either $NaHCO_3$ or THAM. No inotropic drugs were employed before or during the study period. The cases which showed moderate or severe respiratory acid-base derangements were excluded from the data.

RESULT

The improvement in cardiovascular function was generally observed following correction of metabolic acidosis. Fig. 10 is a typical illustration of the response in VCF and arterial pressure by correction of metabolic acidosis.

Change in metabolic acidosis represented by pH and base excess was compared with the degree of improvement in VCF (Fig. 11, 12). VCF increased in general along correction of metabolic acidosis. In some cases

Fig. 12. Increase in VCF by correction of metabolic acidosis (THAM).

slight decrease in VCF was observed. VCF increased by 9.2 per cent in the NaHCO_3 group when pH was improved from 7.19 to 7.3 and base deficit from 9.3 to 1.6 mEq./L. In the THAM group, VCF increased by 5.2 along

Fig. 13. Changes in arterial pressure by correction of metabolic acidosis.

Fig. 14. Comparison of the type of disease with the degree of increase in VCF by correction of metabolic acidosis.

Fig. 15. Comparison of the length of cardiopulmonary bypass and myocardial anoxia with the degree of increase in VCF by correction of metabolic acidosis.

improvement in pH from 7.17 to 7.31 and base deficit from 9.1 to 2.0 mEq./L.

Arterial pressure seemed to increase slightly after correction of acidosis in the NaHCO₃ group, but no alteration was found in the THAM group (Fig. 13).

The degree of improvement in VCF following correction varied significantly according to the type of disease and operation (Fig. 14). VCF was increased average 3% in ASD and 6% in VSD, however, 16 to 18% in radical operations of Fallot's tetralogy and aortic valve replacements.

Total length of repeated myocardial anoxia or cardiopulmonary bypass was compared with the degree of improvement in VCF after correction of acidosis (Fig. 15). Longer periods of aortic occlusion or cardiopulmonary bypass usually resulted in more response in VCF after correction of acidosis.

These evidences indicate that correction of metabolic acidosis is quite beneficial to restore cardiac function in serious cases.

DISCUSSION

Recently the importance of correction of acid-base derangement for the care of surgical patients has been stressed. Despite of intensive study of the hemodynamic aspects of its derangement, these findings of each report were

not entirely consistent. The present investigation indicated that metabolic acidosis had a considerably adverse effect on the myocardium and the peripheral circulation, although the effect of alkalosis seemed to be minimal.

The myocardial contractile force was depressed significantly below a pH of 7.2 and base excess -10 mEq./L. The depression of VCF was reversible by correction of metabolic acidosis infusing NaHCO_3 or THAM. The ventricular function curve was also slightly or moderately depressed by induction of metabolic acidosis, and it was recovered to the control level by correction of acidosis. These results agree with generally accepted concepts of the effect of metabolic acidosis on the myocardium.³⁾⁻⁷⁾

However, there are considerable confusions against this conclusion.⁸⁾⁻¹⁰⁾ Smith et al.¹¹⁾ described that the discrepancy between these reports was partly explained by the influence of heart rate, indicating that a decrease in heart rate accompanied a decrease in force of contraction. In the present study, the pulse rate during experiments changed but little, and moreover it is reported that changes in pulse rate in the range between 80 and 160 beats per min. had only minimal effect.¹²⁾

Clowes et al.¹³⁾ found that a significant decrease in cardiac output occurred after the blood pH fell below 7.1 in animals rendered acidotic by administration of HCl.

Kittle et al.¹⁴⁾ found that cardiac output declined when pH values of less than 7.2 were reached, although it remained fairly normal for the initial period of acidosis by the infusion of HCl. They also demonstrated that the output returned to normal with the restoration of a higher pH by NaHCO_3 .

Smith et al.¹¹⁾ reported that cardiac output and left ventricular work decreased to about half their original value at a pH of 6.9 by lactic acid infusion.

These results agree with that in the present investigation, since the strain gauge arch closely reflects stroke work measurements.¹⁵⁾ However, Anderson et al.⁸⁾ and Richardson et al.¹⁶⁾ reported that metabolic acidosis induced by the lactic acid injection resulted in no change or an increase in cardiac output. Although measurement of cardiac output as an index of cardiovascular performance has yielded conflicting results in various experimental studies, the discrepancy may be related to employment of lactic acid rather than HCl to induce acidosis, severity of acidosis or increased production of catecholamine.

Correction of metabolic acidosis with either NaHCO_3 or THAM was associated with the recovery in VCF and ventricular function curve in this acute experiment. This result agrees with that of Kittle et al.¹⁴⁾ In the clinical study, correction of metabolic acidosis improved VCF in the majority of cases after cardiopulmonary bypass.

On the other hand, there are negative opinions regarding the effect of artificial correction of metabolic acidosis for cardiac benefits.^{8), 18), 19)} However, in these studies the severity of acidosis to be corrected was not so marked.

The effect of control of metabolic acidosis on the course of hemorrhagic shock seems to be minimal. Although correction of metabolic acidosis by THAM improved survival rate in shocked dogs,^{20), 21)} the effect is considered to be nonspecific and due to increase in intravascular volume and diuresis.^{22)–25)} However, Malm et al.¹⁷⁾ indicated that metabolic acidosis accompanying hemorrhagic shock markedly increased plasma catecholamine levels which increased peripheral resistance, reducing microcirculation and resulting in increased metabolic acidosis.

There exists confliction also about the influence of metabolic acidosis on total systemic vascular resistance. In the present study where cardiac output was controlled, total systemic vascular resistance was highest in a pH of 7.25 to 7.30, and it declined progressively below a pH of 7.20. Downing et al.⁹⁾ found a large reduction of total systemic resistance in metabolic acidosis manifested by the pressure-flow curve. Carrier et al.²⁶⁾ found the same trend studying on isolated artery segments.

However, Clowes et al.,¹³⁾ Kittle et al.,¹⁴⁾ and Smith et al.¹¹⁾ noted a steady increase in total systemic vascular resistance with a simultaneous decrease in cardiac output during infusion of either HCl or lactic acid in dogs. When cardiac output changes considerably, it seems to be inadequate to conclude the direct effect of acid-base derangements on systemic vascular resistance, because of the presence of hormonal and neurogenic blood pressure regulating mechanism.

Since metabolic acidosis, per se, is a significant stimulus to catecholamine production,¹⁷⁾ this might explain the evidence that total systemic vascular resistance was highest in the pH range of moderate metabolic acidosis in this study. Peripheral vascular collapse seems to occur in severe metabolic acidosis.

Pulmonary vascular resistance was markedly increased in metabolic acidosis and entirely reversible by correcting acidosis in this study. This observation is consonant with the findings of Downing et al.⁹⁾ and Liljestrand.²⁷⁾

In conclusion, a primary cause of metabolic acidosis must be recognized and treated first whatever the primary abnormality might be low cardiac output or hypovolemia etc. The secondary depression of cardiovascular performance by the resultant metabolic acidosis due to a primary cause is considered to be preventable and correctable by artificial correction of metabolic acidosis.

SUMMARY

The cardiovascular effects of metabolic acidosis and alkalosis and its correction were studied experimentally and clinically.

Metabolic acidosis induced by HCl resulted in a depression in VCF and ventricular function curve. When cardiac output was controlled to be constant, metabolic acidosis resulted in a reduction of systemic vascular resistance and a concurrent increase of pulmonary vascular resistance. These cardiovascular derangements were manifested below a pH of 7.2 and reversible by correction of metabolic acidosis. Correction of metabolic acidosis after open-heart surgery usually improved myocardial performance.

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