Effects of Metabolic Acidosis — a review with case reports

by A.A. Khawaja
MBBS (Pb), DTM & H (Eng), DA (Eng), FFA, RCS
Department of Anaesthesiology,
University of Malaya,
Kuala Lumpur.

METABOLIC ACIDOSIS occurring during anaesthesia has been shown to produce respiratory, circulatory and central nervous system depression. Brooks and Feldman (1962) described the clinical picture in such a situation: at the end of the operation, the patient remains unconscious or very confused. Respiration is absent or inadequate and is frequently gasping in nature, associated with tracheal and jaw tug. Cardio-vascular impairment is manifested by a progressive hypotension and cardiac arrythmias may occur. Peripheral cyanosis is usually present. Death results from circulatory failure despite adequate artificial ventilation and the use of vasopressor drugs. These workers showed that this picture of "neostigmine – resistant curarisation" was, in fact, due to metabolic acidosis and could be successfully treated by the infusion of sodium bicarbonate.

There is also much other evidence that metabolic acidosis causes impairment of the cardiovascular and other systems. Price and Helrich (1955) found that a decrease in pH of 0.4 – 0.5 units is associated approximately with a 50% decrease in the mechanical ability of the heart. Wildenthal et al (1968) found that after an initial positive inotropic effect, acute lactic acidosis exerted a direct negative inotropic effect on the dog left ventricle and reduced the ventricular responsiveness to exogenous catecholamines. Significant depression in ventricular contractility was apparent at pH 7.10. Their data provide further evidence for the rationale behind the clinical use of alkalinising agents in acidosis.

Kittle and his co-workers (1965) reported that the mean arterial blood pressure declined slightly and gradually during metabolic acidosis. When pH values of less than 7.20 were reached, cardiac output declined and peripheral resistance increased. Clowes et al (1961), studying the effects of acidosis on cardiovascular function in surgical patients, were of the opinion that metabolic acidosis, with pH values above 7.2, may well cause serious circulatory disturbance. They noted that when arterial pH was reduced to a level between 7.25 and 7.20, it was usually associated with a serious reduction in the cardiac output and an increase of the total peripheral resistance. Stewart et. al. (1965) observed that, clinically and in animals, extreme acidosis resulted in a sequence of arrythmias which progressed through sinus tachycardia, electrical alternans, two – to – one heart block, and asystole. The sequence was reversed and cardiac function restored after administration of bicarbonate. In cardiac arrest, too, the heart is easier to restart and the rhythm is better when the metabolic acidosis present has been corrected (Ledingham and Norman, 1962; Brooks and Feldman, 1962; Lancet 1962; Stewart, Stewart and Gillies, 1962; Brooks, 1967).

Metabolic acidosis affects other body systems as

well. Lowering the blood pH raises the pulmonary arterial pressure (Silove et. al., 1968), and pulmonary non-elastic resistance and work increase in metabolic acidosis (Peters and Hedgpeth, 1966). Bersentes and Simmons (1967) found that while moderate acidosis resulted in renal vasodilation, more severe acidosis caused vasoconstriction. The vasodilation appeared to be a local effect of CO2 and in metabolic acidosis, there was a greater preponderance of constrictor effects over vasodilation. Nahas and Poyart (1967) reported that a decrease in arterial pH to 7.0 exerted an inhibiting effect on norepinephrine induced lipolysis and calorigenesis. They concluded that the ability of the body to mobilise fuel stores and to increase metabolism above basal levels is inhibited by an acid pH. Metabolic acidosis also produces conditions least favourable to synthesis of liver glycogen (Geddes, 1967). Dintenfass (1965) postulated that metabolic acidosis, by increasing the internal rigidity of the red cell and hence increasing the local blood viscosity, may be a factor in the pathogenesis of thrombosis.

Recently, however, some evidence has been put forward to show that metabolic acidosis may not be responsible for the cardiovascular depression and other derangements that it has traditionally been thought to cause. Andersen et al (1967) found that metabolic acidosis produced no depression of cardiac output until the pH fell below 6.9, and that there was no significant change in arterial blood pressure or peripheral vascular resistance, though there was a progressive increase in pulmonary arterial pressure and resistance. The responsiveness to adrenaline was retained down to a pH of 6.8.

In an earlier paper, these workers (Andersen and Mouritzen, 1966) showed that when metabolic acidosis was produced by the injection of lactic acid in dogs, as the pH fell, the cardiac output increased and at pH 6.8, the output was 185% of control, and peripheral resistance was decreased. They suggested a re-evaluation of the practice of artificial correction of a moderately depressed pH for presumed cardiac benefits.

Anderson (1968), investigating the relation between metabolic acidosis and cardiac arrythmias in acute myocardial infarction, concluded that the apparent predisposition of patients with metabolic acidosis to develop arrythmias was probably related to the greater severity of their illness rather than a direct result of the acidosis, particularly since correction of the acidosis, although improving the general condition, did not correct the arrythmia. Metabolic acidosis, hypotension and arrythmias were closely associated. He was of the opinion that the metabolic acidosis was a result of the hypotension caused by circulatory insufficiency resulting from the arrythmia rather than the cause of the arrythmia.

And Rand et al (1968), investigating the effect of pH on blood viscosity, stressed that viscosity changes that accompany acidosis and alkalosis were negligible when compared with those found in other conditions.

It is difficult to reconcile these conflicting reports. Some of the variations may be due to the particular animal studied and whether the organism was intact or a heart-lung preparation. It may be that the metabolic acidosis produced in animals by the infusion of hydrochloric or lactic acid is in some way different from the clinical metabolic acidosis of hypoxia and anaerobic metabolism. Or a possible basis for reconcilation of the conflicting results may lie in the observations of Wildenthal et al (1968), who demonstrated that inortropic effects of acidosis on the heart may be interpreted as positive, negative or no change, depending on sympatho-adrenal function and on the time of observation. Clinically, however, it is apparent that when a metabolic acidosis of greater than mild degree is present, not only is there no benefit in withholding alkalinising agents but that improvement usually follows correction of the acid-base balance. The following cases, where post-operative cardio-respiratory impairment was corrected by infusion of sodium bicarbonate, are reported as illustrating the point.

CASE REPORTS

Case 1.

A 31-year-old woman, who had had a previous Caesarean section and had a history of pre-eclamptic toxaemia during the present pregnancy, presented for a repeat section because she had made little progress during a 12-hour trial of labour. At this stage, she was having strong contractions and was rather distressed. Her pulse rate was 106 beats/minute and the arterial blood pressure, which previously was in the region of 130/90 mm of Hg, had risen 160/100 mm Hg. She had pitting ankle and sacral oedema, and her urine contained a trace of acetone.

Anaesthesia was induced with thiopentone and suxamethonium, preceded by 0.6 mg of atropine, and, after endotracheal intubation, was maintained with N_2O_2,O and curare. The baby was delivered about 12 minutes after induction. At this stage, he placenta was found to be adherent and, during the separation, she lost about a litre of blood in a period of five minutes. Her systolic BP fell to 65 mm Hg.

She was given a rapid infusion of 500 ml of lactated Ringer's solution and 500 ml of whole blood. With this therapy, her colour improved and the systolic BP rose to 100 mm Hg. A further unit of blood was given somewhat more slowly. At the end of the operation, the systolic blood pressure was 120 mm Hg. The curare reversed satisfactorily with atropine and neostigmine and the patient was conscious within a few minutes.

About one quarter of an hour later, in the recovery ward, she was drowsy, blood pressure had fallen, pulse was weak and colour poor, she was sweating and obviously hyperventilating. Although the estimated blood loss had been replaced, she was given 500 ml of haemacel, a plasma expander. When this did not have an appreciable effect, she was suspected to be acidotic. An arterial blood sample was, therefore, taken anaerolically into a heparinised syringe for blood gas analysis and she was given 90 m Eq of sodium bicarbonate. Also, since she was hyperventilating, to cut down the work of respiration, she was re-intubated and respiration assisted using a Bird ventilator. This resulted in marked improvement of her blood pressure and pulse. Blood gas analysis showed: ph: 7.26; pCO_2: 23 mmHg; B.E.: – 15.5 mEq/L; standard bicarbonate: 13.4 mEq/L, i.e. a severe metabolic acidosis partially compensated for by a respiratory alkalosis. She was given a further 135 mEq of sodium bicarbonate.

When seen about three-and-one-half hours later, her condition was much improved, with a good colour and pulse, an arterial blood pressure of 130–140/80 mm of Hg, and a good urine output. Respiratory assistance was, however, continued overnight to allow her to be well-sedated and to get a good night's rest. Her further post-operative course was uneventful except for a mild chest infection.

Case 2.

This 55-year-old man presented initially with colicky pain in the right loin. Intravenous pyelography revealed bilateral renal calculi. Apart from a mild hypertension (BP 170/130), other systems were essentially normal and his blood urea varied between 37 mg and 47 mg%.

A right-sided nephrolithotomy and nephrostomy was done. Initially, there was good urine output from the nephrostomy and per urethra but then the nephrostomy started leaking into the tissues. To further complicate matters, a few days later he started bleeding from a duodenal ulcer, for which a Bilroth II partial gastrectomy was done. When seen on the present occasion, he presented for closure of a duodenal fistula. His general condition was rather poor.

On the day before the operation, his serum electrolyte and blood urea results were: Na+: 119 mEq/L; K+: 6.2 mEq/L; Cl–: 93 mEq/L; blood urea: 78 mg%. The next day, however, the urea and serum potassium had come down to 65 mg% and 5.5 mEq/L and serum sodium and chloride had gone up and it was decided to proceed with the operation. Anaesthesia was induced with methohexitone and continued with nitrous oxide, oxygen, intermittent halothane, curare and moderate hyperventilation. His systolic blood pressure was 110 mm of Hg before induction of anaesthesia and throughout the operation, which lasted a little less than two hours, remained between 110 and 130 mm of Hg. Operative blood loss was estimated to be about 400 ml and he was given 500 ml of lactated Ringer's solution and 450 ml of whole blood. Curare reversal at the end of the operation was satisfactory. About 45 minutes later, however, he was drowsy, blood pressure was 190/90 mm and pulse rate 120 beats per minute. Respiration was rather laboured and colour poor. Residual curarisation was suspected to be present, but a dose of neostigmine of 0.5 mg had no effect. At this stage, the presence of acidosis was suspected. Blood was taken for analysis and he was given 90 mEq of sodium bicarbonate. Blood gas results showed: Po_2: 123 mmHg (breathing O_2 enriched air); pH: 7.13; pCO_2: 43 mmHg; BE: – 15.5 mEq/L; standard bicarbonate: 13.2 mEq/L, i.e. a severe uncompensated metabolic acidosis. Calculation, according to the formula of Mellemgaard and Astrup (1960), showed the deficit of base in the extracellular compartment of body water to be 270 mEq. He was accordingly given a further 180 mEq of Na HCO . Since respiration was rather laboured, he was re-intubated and respiration assisted with a Bird ventilator. About two hours later, his condition was satisfactory and he was extubated and returned to the ward.

Case 3

A 44-year-old man presented with chronic gout, a right renal calculus and chronic renal failure. A radioisotope renogram showed complete right ureteric obstruction, and a non-functioning left kidney. While awaiting surgery, his blood urea climbed from 90 mg to 500 mg per 100 ml of blood. This was treated by peritoneal dialysis. It was noted that he tended to develop metabolic acidosis which required oral supplements of sodium bicarbonate. He underwent several operations. On the present occasion, he was ope-

rated upon because of a ureteric stricture for which a Davies' intubated ureterotomy was done. His preoperative condition was fair, with essentially normal serum electrolytes and a blood urea of 68 mg%. Anaesthesia was induced with thiopentone and maintained with curare, nitrous oxide, oxygen and moderate hyper-ventilation.

During the operation, which lasted a little over six hours, he lost an estimated three litres of blood and received 2000 ml of lactated Ringer's solution, 2225 ml of whole blood, and, towards the end of the operation, 200 ml of 20% mannitol. A further two units of blood was transfused in the post-operative period.

Because of his tendency to develop metabolic acidosis and because of the long duration of the operation, he was expected to have similar post-operative problems as the first two cases. A few minutes before the end of the operation an arterial blood sample was, therefore, taken for blood gas analysis. This showed a marked metabolic acidosis with a B.E. of −13.5 mEq/L, which was being compensated for by the intermittent-positive-pressure-hyperventilation. He was given 180 mEq of sodium bicarbonate i.e. the calculated deficit of base in the extracellular fluid. When the operation ended a few minutes later, the curare was reversed satisfactorily and there were no problems in the immediate post-operative period.

Discussion

In the first case described, the severe metabolic acidosis was probably a result of the summation of the acidosis of labour (Derom, 1968), and that due to the period of hypotension and oligaemia with a contribution from the acidotic stored blood that was transfused (Lancet, 1962) and a minor contribution from the acidosis of anaesthesia and hyperventilation (Papadopoulos and Keats, 1959). In the second case, there was little blood loss and the acidosis was probably due to the chronic renal failure and loss of base through the duodenal fistula. Both these cases illustrate how severe metabolic acidosis may go unsuspected. And in both cases, correction of acidosis resulted in prompt clinical improvement.

The third patient, who was anaesthetised a few days after the second case, was expected, on the basis of his history of chronic renal failure and in the light of previous experience, to develop a metabolic acidosis. This, indeed, proved to be the case. Intraoperative correction of the acidosis prevented problems that might have been expected in the post-operative period.

These cases show that, notwithstanding experimental evidence to the contrary, metabolic acidosis may be expected to give rise to cardiorespiratory and central nervous depression in he post-operative period, though sometimes there may be a compensatory hyperventilation instead of the more usual respiratory depression described by Brooks and Feldman (1962). In either case, sodium bicarbonate infusion can be expected to improve the patient's general condition and cardiovascular respiratory function. If the presence of metabolic acidosis is suspected and diagnosed during the operation, as in the case of the third patient, treatment can be expected to prevent the post-operative upsets seen in the first two patients.

While disturbances of acid-base balance should always be diagnosed and treated on the basis of results of blood gas analysis, where facilities for such analysis are not available, a good case can be made out for a therapeutic trial of sodium bicarbonate infusion in patients suspected to have acidosis of metabolic origin. An infusion of $NaHCO_3$ of 1 – 1.5 mEq/kg body weight may be expected to produce some improvement in the patient's condition in the presence of a metabolic acidosis and is not likely to do any harm even if such acidosis is not present.

Summary

Some of the recent literature on the effects of metabolic acidosis on the cardiovascular and other body systems is reviewed. Two cases are reported where metabolic acidosis produced cardio-respiratory and central nervous depression in the immediate post-operative period and sodium bicarbonate infusion reversed this depression. A third case is reported where the post-operative depression could have been expected but was prevented by the intra-operative correction of the acidosis.

References

Andersen, M.N., Border, J.R., Mouritzen, C.V. (1967). Acidosis, Catecholamines and Cardiovascular Dynamics: When does Acidosis Require Correction? *Ann. Surg.*, **166**, 344.

Andersen, M.N., and Mouritzen, C. (1966). Effects of Acute Respiratory and Metabolic Acidosis on Cardiac Output and Peripheral Resistance. *Ann. Surg.*, **163**, 161.

Anderson, R. (1968). The Relation Between Metabolic Acidosis and Cardiac Arrythmias in Acute Myocardial Infarction. *Amer. Heart J.*, **76**, 1.

Annotation (1962). Acidosis in Cardiac Arrest. *Lancet*, **2**, 976.

Annotation (1962). Stored Blood. *Lancet*, **1**, 965.

Bersentes, T.J. and Simmons, D.H. (1967). Effects of Acute Acidosis on Renal Haemodynamics. *Amer. J. Phsiol.*, **212**, D.K. (1967). Resuscitation., 190. London: Edward Arnold.

Brooks, D.K. and Feldman, S.A. (1962). Metabolic Acidosis, A New Approach to 'Neostigmine Resistant Curarisation'. *Anaesthesia*, **17**, 161.

Clowes, G.H.A., Sabga, G.A., Konitaxis, A., Tomin, R., Hughes, M., and Simeone, F.A. (1961). Effects of Acidosis on Cardiovascular Function in Surgical Patients. *Ann. Surg.*, **154**, 524.

Derom, R.M. (1968). Maternal Acid-base Changes During Labor. *Clin. Obstet. Gynaec.*, **11**, 110.

Dintenfass, L. (1965). Some Rheological Factors in the Pathogenesis of Thrombosis. *Lancet*, **2**, 370.

Geddes, I.C. (1967). Modern Trends in Anaesthesia, 3, p. 14. London: Butterworth.

Kittle, C.F., Aoki, H., and Brown, E.B. (1965). The Role of pH and CO_2 in the Distribution of Blood Flow. *Surgery*, **57**, 139.

Ledingham, I. McA., Norman, J.N. (1962). Acid-base Studies in Experimental Circulatory Arrest. *Lancet*, **2**, 967.

Mellemgaard, K. and Astrup, P. (1960). The quantitative Determination of Surplus Amounts of Acid or Base in the Human Body. *Scandinav. J. Clin. Lab. invest.*, **12**, 187.

Nahas, G.G., and Poyart, C. (1967). Effect of Arterial pH alterations on Metabolic Activity of Norepinephrine. *Amer. J. Physiol.*, **212**, 765.

Papadopoulos, C.N., and Keats, A.S. (1959). The Metabolic Acidosis of Hyperventilation Produced by Controlled Ventilation. *Anaesthesiology*, **20**, 156.

Peters, R.M., and Hedgpeth, E. McG. (1966). Acid-base Balance and Respiratory Work. *J. Thor. Cardiovasc. Surgery*, **52**, 649.

Price, H.L. and Helrich, M. (1955). The Effect of Cyclopropane, Nitrous Oxide, Thiopental and Hydrogen ion Concentration on Myocardial Function of the Dog Heart-lung Preparation. *J. Pharm. Exp. Ther.*, **115**, 206.

Rand, P.W., Austin, W.H., Lacombe, E. and Barker, N. (1968). pH and Blood Viscosity. *J. Appl. Physiol.* **25**, 550.

Silove, E.D., Inone, T. and Grover, R.F. (1968). Comparison of Hypoxia, pH and Sympathomimetic Drugs on Bovine Pulmonary Vasculature. *J. appl. Physiol.*, **24**, 355.

Stewart, J.S.S., Stewart, W.K., and Gillies, H.G. (1962), Cardiac Arrest and Acidosis. *Lancet*, **2**, 964.

Stewart, J.S.S., Stewart, W.K., Morgan, H.G. and McGowan, S.W. (1965). A Clinical and Experimental Study of the Electrocardiographic Changes in Extreme Acidosis and Cardiac Arrest. *Brit. Heart J.*, **27**, 490.

Wildenthal, K., Mierzwiak, D.S., Ywers, R.W. and Mitchell, J.H. (1968). Effects of Acute Lactic Acidosis on Left Ventricular Performance. *Amer. J. Physiol*, **214**, 1352.