Acid–Base Status in Dogs during Long Term Anaesthesia

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ABSTRACT

The acid–base status in dogs anaesthetized with chloralose or combinations of chloralose and barbiturates was studied. No surgical procedures were used to elucidate whether the anaesthesia *per se* caused changes in the acid–base status. Irrespective of the anaesthetic used, a progressive metabolic acidosis developed after 2–3 hours. This progressed for several hours despite normal arterial blood pressure and pulse rate. A theoretical model, based on the results, is presented. Even the induction of anaesthesia caused an impairment of the peripheral circulation. This impairment, in combination with rising body temperature, might be strong enough to cause a detectable metabolic acidosis. It is concluded that, as compared with blood pressure and pulse rate, the acid–base status of the blood is a reliable and early sign of the impairment of circulation during anaesthesia.

INTRODUCTION

During conventional anaesthesia, a more or less profound reduction of central and peripheral circulation is observed which has been documented extensively (for a review, see Price and Cohen (7). For this reason, traditionally circulatory parameters are routinely checked during most forms of anaesthesia. An impaired central circulation, however, is not by necessity detected with ordinary pulse rate and arterial pressure measurements. First of all, the anaesthetic agent *per se* might increase the tone in compensatory mechanisms (6), and secondly the reduced central circulation initiates a negative feed-back control, probably via an increased sympathetic tone.

We believe that an impaired central circulation, via the peripheral circulation, increases the anaerobic metabolism and thus creates a metabolic acidotic state. We also believe that this metabolic acidosis during an impaired circulation is an early phenomenon, and thus a valuable parameter to check during anaesthesia. However, remarkably few papers report the acid–base status of the experimental animals when using barbiturates and chloralose, the most common agents for inducing long term anaesthesia in laboratory animals.

The aim of the present study was to check the acid–base balance and common circulatory and respiratory parameters during long term anaesthesia with barbiturates, chloralose and combinations of them. Special interest was given to the possibility that prolonged anaesthesia might keep ordinary circulatory parameters normal, in spite of an increasing metabolic acidosis.

MATERIALS AND METHODS

The Astrup equilibration technique was used in this study to check the acid–base blood status of the dogs. This technique, with its nomograms was developed to fit patients in a clinical routine, however. Thus the normal acid–base status in conscious dogs was primarily checked and expressed in terms designed for man.

Conscious dogs

Three beagle dogs weighing 10–15 kg were anaesthetized intravenously using sodium pentobarbital (Nembutal®, Abbott) in a dosage of 15–20 mg/kg b.wt. A sterilized nylon catheter (o.d. 1 mm) was inserted through a small arterial branch into the main femoral artery. This vessel was not obliterated with the technique used. Arterial blood samples for analysis were easily drawn through the catheter during the operation and the following four days, when the dogs were awake. During the four days, the animals had free access to water and food.

Anaesthetized dogs

Eighteen dogs weighing 8–16 kg were anaesthetized without premedication for acute experiments. All dogs were breathing spontaneously through endotracheal tubes. Catheters were introduced into the saphenous vein and the femoral artery. Infusions of anaesthetics were conducted intravenously. The dogs were divided into three groups according to the type of anaesthetic:

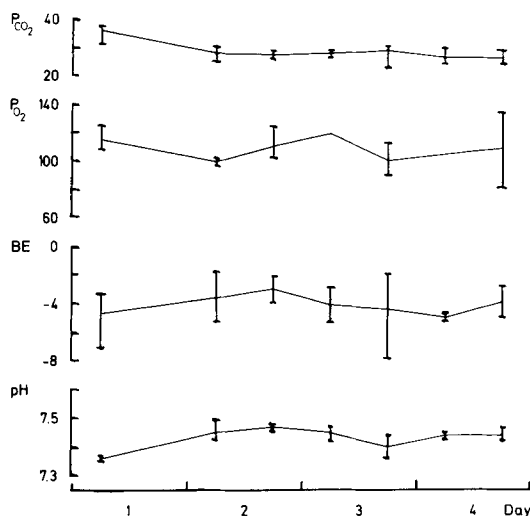1. *Chloralose* (alfa-chloralose Merck, Darmstadt, West

Fig. 1. The acid–base parameters and arterial oxygen tension during the first four days following the arterial catheter insertion. The figure shows the means and ranges from conscious dogs.

Germany) was given intravenously to six dogs for the induction and maintenance of anaesthesia. Each chloralose solution was prepared freshly as an 0.8% solution in saline, heated to a maximum of 65°C. For the induction of anaesthesia, 56–64 mg/kg b.wt. was given to the animals and this produced surgical anaesthesia within 10–20 min. This depth of anaesthesia was maintained by intermittent dosages of 6–9 mg/kg b.wt. · hour of freshly prepared chloralose solutions.

2. *Sodium thiopental and chloralose.* For the rapid induction of anaesthesia, sodium thiopental (Pentothal®, Abbott, England) was given intravenously to 8 dogs as a 5% freshly prepared solution, in a dosage of 10–20 mg/kg b.wt. Full anaesthesia was then obtained by a single injection of a chloralose solution in a dosage ranging from 40–60 mg/kg b.wt. The maintenance dose of chloralose was then given as described in the preceding paragraph.

3. *Thiopental, chloralose and sodium pentobarbital.* The induction and full anaesthesia was obtained as described in the preceding paragraph. The maintenance dosage of chloralose then given was less than that previously described, because the anaesthesia was supplemented with small, intermittent doses of pentobarbital (2–4 mg/kg b.wt. · hour) given when the shivering pattern appeared, a characteristic phenomenon for chloralose anaesthesia.

Measurements

Arterial blood pressure, pulse rate, breathing frequency as well as the rectal temperature was regularly checked. Arterial blood samples (1 ml) were unaerobically taken in a syringe with a luer cone prefilled with 0.1 ml of a Heparin solution (1%). Analysis of Po_2 as well as of the acid–base status were performed as described by Siggaard-Andersen (9) using the nomograms for man. All gas mixtures for the equilibration were analyzed in a Haldane apparatus (4).
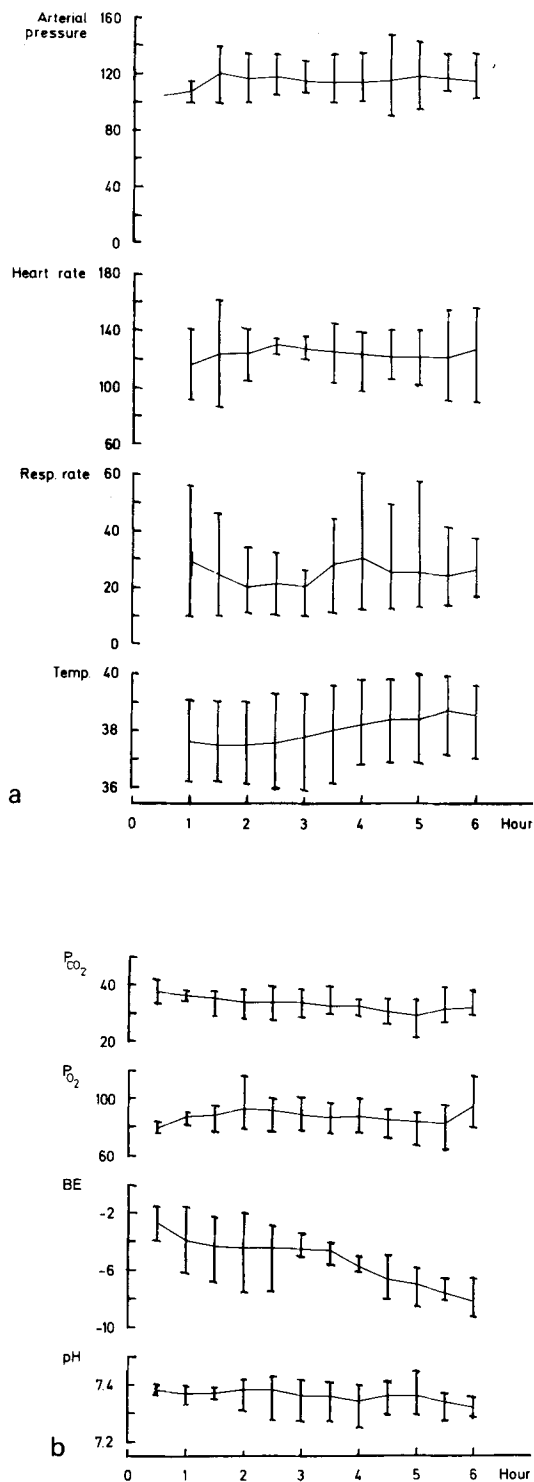

Fig. 2. Some general parameters and acid–base status during unsupplemented chloralose anaesthesia. The graphs show the means and ranges from 6 dogs.

RESULTS

Conscious dogs

The results from the conscious dogs are shown in Fig. 1. The abscissa in the graphs refers to the day after the short operation. It is obvious that as compared with man, the conscious dogs normally have a lower base excess. During the short period of pentobarbital anaesthesia, when the arterial catheter was inserted, the arterial blood pH decreased about 0.05 units. This seems to have been mainly due to a metabolic acidosis, which is compensated by a respiratory alkalosis during the first two days. The persistent low Pco_2 on days three and four, are as yet unexplained, but might be hyperventilation as a result of a slight fever reaction.

Anaesthetized dogs

1. *Chloralose*. The initial acid–base values of dogs anaesthetized with unsupplemented chloralose were only slightly lower than those for the conscious dogs (see Figs. 1 and 2). After a few hours of anaesthesia, however, the base excess decreased gradually without any change in blood pH, indicating a respiratory compensation of a growing metabolic acidosis. This acidosis is indicated in the decreasing values of the arterial values of the arterial Pco_2 (Fig. 2). After 5 hours the compensatory mechanism seemed to be insufficient and the pH dropped. It is remarkable that despite the progressive metabolic acidosis the blood pressure and pulse rate remained rather constant (Fig. 2).

The depths of anaesthesia was even, there were no response to painful stimuli and no spontaneous movements by the dogs. They were, however, more than normally sensitive to auditive stimuli and often showed a marked tendency to shiver, which is a typical chloralose effect. Finally, it is shown that after 3–4 hours, the chloralose anaesthesia caused an increase in body temperature.

2. *Sodium thiopental and chloralose*. The dogs in these experiments (Fig. 3) had an arterial pH on the same level as the dogs anaesthetized with only chloralose. The base excess value also fell gradually in the same manner as the dogs anaesthetized
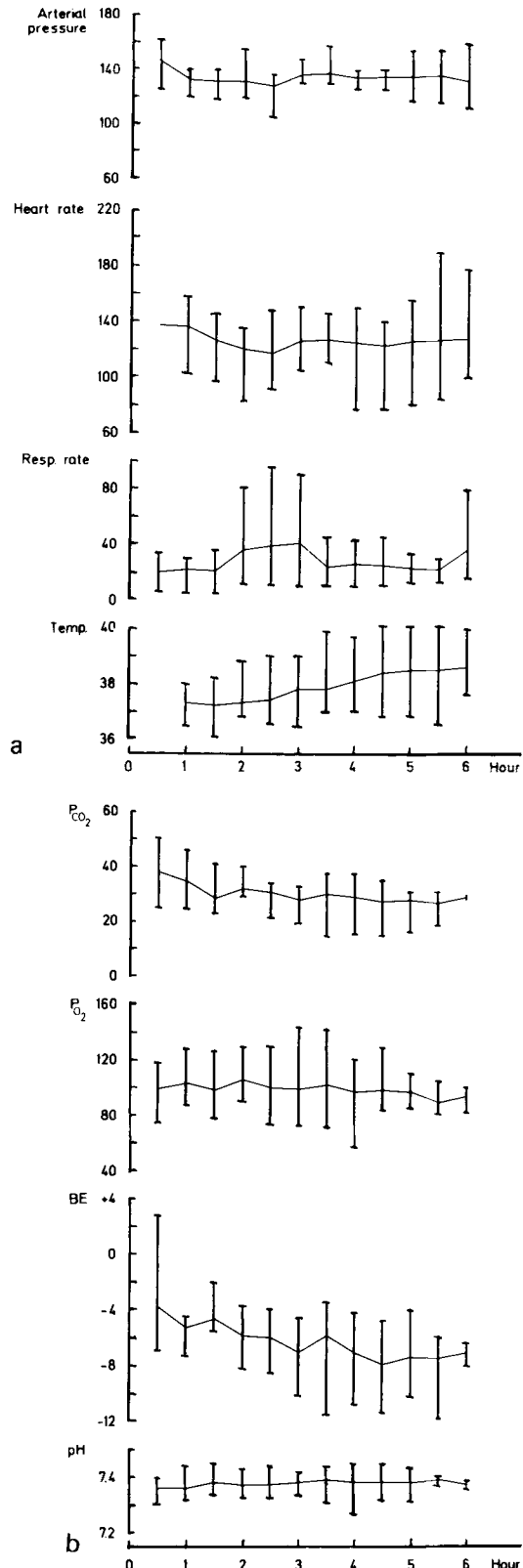

Fig. 3. Some general parameters and acid–base status during chloralose anaesthesia following the induction with thiopental. Values are means and ranges from 8 dogs.

with unsupplemented chloralose. Other circulatory parameters were similar to group I, as well as the rise in body temperature.

3. *Thiopental, chloralose and sodium pentobarbital.* The results from 4 dogs anaesthetized according to the third method (above) are shown in Fig. 4. In this group, rapid acidosis is developed during the first hour, but is gradually respiratory compensated. The falling base excess during the anaesthesia is notable here too, but is somewhat less accentuated as compared with other anaesthetic methods. A somewhat increasing pulse rate is here interpreted as an increasing sympathetic tone, which in turn is supposed to be a response to an impairment of central circulation. As in the preceding groups, the body temperature rose during the 6-hour period.

DISCUSSION

In the present investigation the metabolic component of the acid–base status, the base excess, was regarded as reflecting the reduction of the peripheral blood flow and the oxygen supply to the tissues. A metabolic acidosis might thus indicate a shift from aerobic to unaerobic metabolism in the cells.

The acid–base status found for conscious dogs in this study (Fig. 1) is quite similar to that found by Arfors et al. (1). Under similar conditions they found that the mean pH was 7.41, Pco_2 33.7 mmHg and base excess −2.8 mEq/l. The results obtained from the conscious dogs in our study are somewhat different from the corresponding values from human beings (9). Thus, compared with man, the dogs have a lower Pco_2 and a lower excess. This is an important consideration in acid–base studies on dogs, when using terminology and nomograms pertaining to man.

Neither the unsupplemented chloralose anaesthesia, nor the barbiturate/chloralose anaesthesia in this study was found to influence the arterial blood pressure to any great extent. During barbiturate anaesthesia, the cardiac output is known to be significantly decreased; but the blood pressure is usually well maintained, largely due to increased peripheral resistance (10). As regards blood pressure, heart frequency and respiratory rate, there was no essential difference between the different forms of the anaesthesia. During the ex-
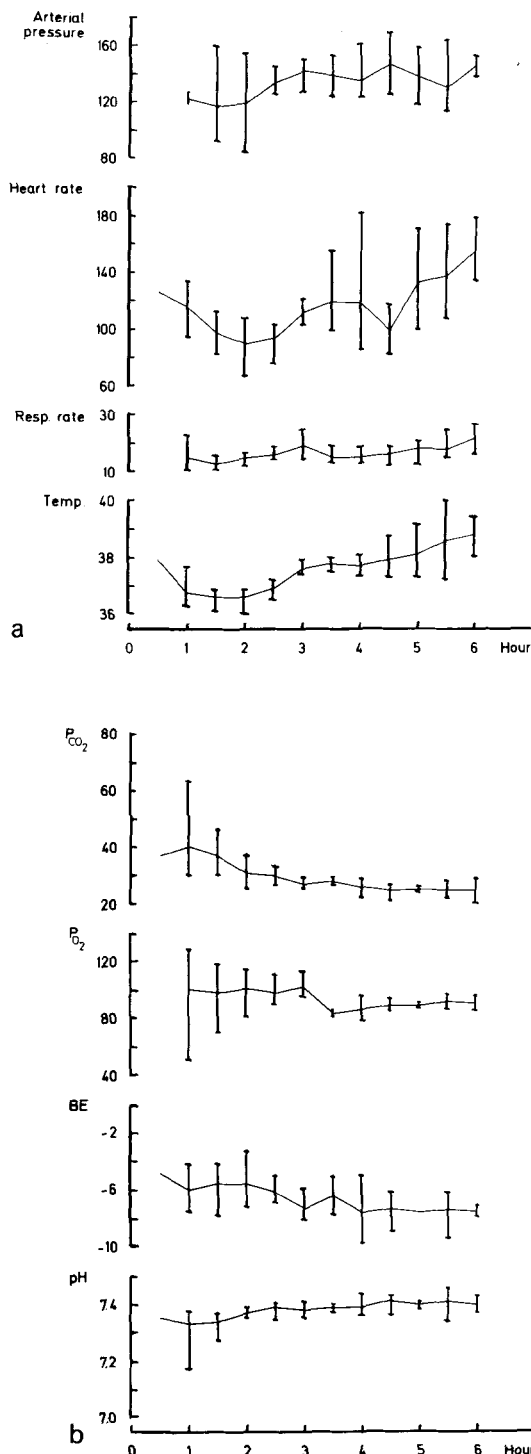

Fig. 4. Some general parameters and acid–base status during chloralose pentobarbital anaesthesia following induction with thiopental. Values are means and ranges from 4 dogs.

periments, the body temperature of the dogs constantly rose during the 6-hour period. The reasons for this temperature increase may be several, but we propose that it is a reaction on the anaesthetic agent or the anaesthetic condition itself, similar to a hyperthermic reaction sometimes seen in man and in some strains of pigs. The increased body temperature can initiate an increased ventilation and this in turn may cause a respiratory alkalosis. The raised body temperature can also increase the oxygen demand which may be one factor in the generation of the metabolic acidosis. The temperature of the animals should therefore be kept constant, e.g. by controlling the temperature of the operating table.

No significant difference was found between the different forms of anaesthesia in terms of acid–base balance. During the first two or three hours, the arterial pH was kept constant in spite of increasing metabolic acidosis. Subsequently, the acidosis grew enough to decrease the arterial pH gradually. It seems difficult, with the forms of anaesthesia used, to keep an animal anaesthetized over long periods (i.e. more than a few hours) without a progressing metabolic acidosis. As mentioned above, the metabolic acidosis is here regarded as a result of a reduced peripheral blood flow as compared with the metabolic rate; but other reasons could be for example a hyperchloremic acidosis (5, 8), or an impaired kidney function—this, however, seems to be less likely, according to Danielson et al. (3).

One disadvantage with unsupplemented chloralose anaesthesia is that it produces a hyperexcited state. This means that the slightest noice or body contact may induce a lot of rapid reflex movements in the experimental animal. (In this study, however, this state could be circumvented by small doses of pentobarbital.) Skeletal neuromuscular reflexes in these dogs are exaggerated as compared with those in the unanaesthetized dogs as proposed by Chenoweth & van Dyke (2). They also reported that chloralose has an atropine-like effect on the vagus, which may account in part for the high blood pressure often observed during this type of anaesthesia. This, however, may be a matter of dosage since in our results the blood pressure was found to be 100–135 mmHg (during pure chloralose anaesthesia), while Ledsome et al. (5) using pure chloralose in a two or three times higher dosage found an arterial blood pressure of 180–200 mmHg and a more pronounced metabolic acidosis, which probably was an effect of
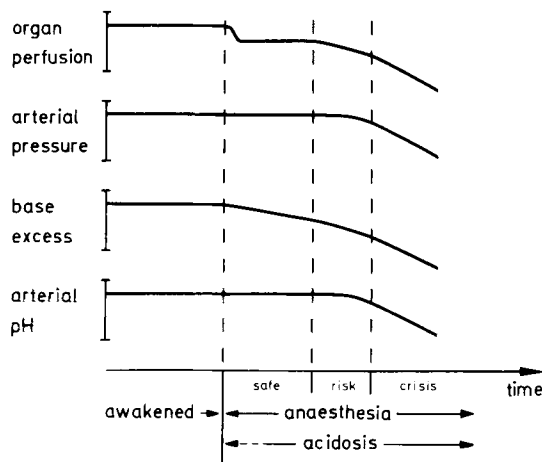

Fig. 5. The circulation and acid–base parameters theoretically represented during the awakened state as well as during prolonged anaesthesia. It is shown that an impaired peripheral circulation can be detected as a decreasing base excess even before entering the risk zone. The arterial pH as well as the blood pressure might be quite normal in the risk zone.

the anaesthesia. The low solubility of chloralose necessitates large volumes for achieving anaesthesia. The administration of high dosages of chloralose, thus creates expansion of extracellular volume, which might also be responsible for the higher blood pressure found in that study.

Fig. 5 shows a theoretical model for the circulation and acid–base status during prolonged anaesthesia. The impaired circulation during general anaesthesia, though virtually adequately carried out, leads to an accumulation of non-volatile acids, which is not reflected in blood pH, due to the buffer capacity of blood and a very effective respiratory compensation. The metabolic acidosis could, however, be revealed by measurement of the base excess, which is a very sensitive test of the circulatory impairment during anaesthesia. Reduction of base excess signalled circulatory impairment much earlier than changes in pulse rate and arterial blood pressure could be recorded. Thus, control of blood acid–base status might be another usable way of detecting progressive circulatory failure during general anaesthesia.

ACKNOWLEDGEMENTS

REFERENCES

1. Arfors, K. E., Arturson, G. & Malmberg, P.: Effect of prolonged chloralose anaesthesia on acid–base balance and cardiovascular functions in dogs. Acta Physiol Scand *81:* 47–53, 1971.
2. Chenoweth, M. B. & van Dyke, R. A.: Anaesthesia in biomedical research. Fed Proc *28:* 1383, 1969.
3. Danielson, B. G., Grängsjö, G., Persson, E., Ulfendahl, H. R. & Wolgast, M.: Renal function in the dog in acute disturbances of the acid–base balance. Acta Anaesth Scand *17:* 88–102, 1973.
4. Enghoff, H.: Apparat zur Gasanalyse. Acta Med Scand, Suppl. *170:* 307–323, 1946.
5. Ledsome, J. R., Linden, R. J. & Norman, J.: The effect of light chloralose and pentobarbitone anaesthesia on the acid–base state and oxygenation of arterial blood in dogs. J Physiol (Lond.) *212:* 611–627, 1971.
6. Page, I. H., del Greco, F. & Corcoran, A. C.: Effects of pentobarbital anaesthesia, high spinal cord section and large doses of ganglioplegic agents on hemodynamic functions measured by dye dilation. Am J Physiol *179:* 601–606, 1954.
7. Price-Cohen, L.: Effects of Anaesthetics on the Circulation. Thomas, Springfield, Ill., 1964.
8. Shires, T. & Holman, J.: Dilution acidosis. Ann intern Med *28:* 557, 1948.
9. Siggaard-Andersen, O.: The Acid-Base Status of the Blood. 4th ed. Munksgaard, Copenhagen, 1974.
10. Strobel, G. E. & Wollman, H.: Pharmacology of anaesthetic agents. Fed Proc *28:* 1386, 1969.

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