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Acid-base status and cardiovascular function in pigs anaesthetized with α-chloralose

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INTRODUCTION

Blood gas tensions, acid-base status and cardiovascular function have previously been examined in Göttingen mini-pigs anaesthetized with halothane and methoxyflurane or intravenous metomidate hydrochloride (*Svendsen & Carter* 1989). Neither of the methods was fully acceptable for experiments that required stable blood pressure and acid-base balance within a narrow normal range.

α-chloralose has been used extensively as an anaesthetic in physiological experiments since it was first reported by *Vincent & Thompson* 1928 that the arterial blood pressure remained stable during anaesthesia in cats. Examinations in dogs have confirmed that arterial blood pressure and heart rate are higher and reflexes more active than under other anaesthetics (*Brown & Hilton* 1955 & 1956 and *Bass & Buckley* 1966).

In a study of the effects of different anaesthetics on the balance between central and chemoreceptor control of respiration in dogs, it was demonstrated that the central response to CO_2 was considerably diminished and the sensitivity of the chemoreceptors increased during α-chloralose anaesthesia. α-chloralose thus seems to cause a shift in the balance between two factors involved in respiratory control, so that the part played by direct chemical stimulation of the respiratory centre is diminished and the part played by the chemoreceptor reflexes is augmented (*Dripps & Dunke* 1943).

The side effects of α-chloralose on respiratory and circulatory parameters in pigs have never been thoroughly investigated, although the drug has been used as an anaesthetic in studies on chemoreceptor and baroreceptor reflexes in this species (*Booth et al.* 1960, *Bredeck et al.* 1961 and *Adams et al.* 1987). In a comparison between halothane, α-chloralose, pentobarbitone and etomidate anaesthesia on gastric function, α-chloralose was found to increase gastric acid secretion following stimulation with pentagastrin (*Stødkilde-Jørgensen et al* 1985).

The aim of the present study was to examine the effects of α-chloralose anaesthesia on the cardiovascular and respiratory systems in pigs during in an experimental study of acid neutralization in the duodenum.

MATERIALS AND METHODS

The study involved 47 female Danish Landrace pigs weighing between 23 and 34 kg. The animals originated from an SPF breeding unit, and were kept in the laboratory for at least 48 hours prior to anaesthesia. The animals were treated initially with azaperone (Sedaperone vet. 4 %) at 2 mg/kg (i.m.), and were after 30 min anaesthetized with metomidate hydrochloride (Hypnodil vet. 5 %) at 4 mg/kg (i.v.), intubated and maintained at a surgical level with 1 % halothane in 100 % oxygen (group 1) or 60 % oxygen and 40 % air (group 2) for approximately 90 min. During this period the surgical interventions were completed and the animals prepared for the experiment. The halothane was removed and anaesthesia was maintained by intravenous infusion of α-chloralose 0.25 % (100 mg/kg). Two thirds of the dose was given as a bolus, and one third as continuous infusion throughout the remaining experimental period. The animals were

divided into two groups, one maintained on spontaneous respiration using 100 % O_2 (Komesaroff Small Animal Anaesthetic Machine) (n = 22), and the other (n = 25) in which respiration was supported by an artificial ventilator (Servo ventilator 900. Elema Schönander, Sweden). The respiratory frequency was 20 breaths per min with an inspiratory time of 25 %, a pause time of 10 % and a deep sigh function. The O_2 level was 60 %. The minute volume was adjusted according to the arterial blood gas measurements.

The femoral artery was exposed and catheterized. Arterial blood pressure was measured with a pressure transducer and amplifier (Simonsen & Weel, Denmark) at 15 min intervals, beginning 60 min after withdrawal of halothane. Heart rate was measured with a pulse monitor placed on a front leg, or from the electrocardiogram. Two ml of heparinized blood was drawn from the femoral artery at 45 min intervals, beginning 45 min before halothane was removed, and analyzed at 37°C for pH and pCO_2 (BMS 2 MK Blood Micro System, Radiometer, Denmark).

The experiments lasted for 5–6 hours from initial preanaesthetic medication until the animal was euthanized. Homeostasis was affected by removal of pancreatic and hepatic secretions and by perfusion of the isolated duodenum with solutions of varying pH. During the entire experiment isotonic saline was given by intravenous infusion.

The following commercial preparations were used: azaperone (Sedaperone vet. 4 %, Janssen Pharmaceutica, Beerse, Belgium); metomidate hydrochloride (Hypnodil vet. 5 %, Janssen Pharmaceutica, Beerse, Belgium); α-chloralose with 10 % β-isomer (Sigma, St. Louis, NO., U.S.A.) in which the solution was prepared immediately before use by dissolving 2.5 gram of α-chloralose in 1 l isotonic NaCl at 60°C; and halothane (Halocarbon Laboratories Inc., Hackensach, N.J., U.S.A.).

RESULTS

Azaperone produced sedation sufficient to perform intravenous injection within 10–30 min. However, intravenous injection into an ear vein of metomidate hydrochloride frequently caused a reaction involving violent head shaking. This could be prevented by giving part of the metomidate hydrochloride intraperitoneally at the same time as azaperone.

Tracheal intubation was easily performed after induction with metomidate hydrochloride. Respiratory arrest was never observed.

Values for arterial blood gas tension, acid-base status, blood pressure and heart rate in unanaesthetized Göttingen mini-pigs (*Svendsen & Carter* 1989) are used as reference values in this study.

Fig. 1 shows the mean arterial blood pressure from 60 to 180 min after withdrawal of halothane inhalation. A stable pressure of about 85 mm Hg was obtained in pigs breathing spontaneously. These values were significantly below reference values, whereas in pigs ventilated artificially, mean blood pressure was significantly higher and within the reference range.

Heart rates during the same period are shown i Fig. 2. Spontaneously breathing pigs showed heart rates similar to reference values, whereas the artificially ventilated animals had a higher heart rate, but not significantly above the reference values.

The product of systolic arterial blood pressure and heart rate, the rate pressure product (*Kitamura et al.* 1972), is shown in Fig. 3. Values were higher in artificially ventilated pigs than during spontaneous respiration.

Figs. 4 and 5 show arterial pCO_2 and arterial pH. Spontaneously breathing animals had significantly elevated pCO_2 and consequently developed acidosis. Using the ventilator, it was possible to adjust respiration and normalize arterial pCO_2 and pH. The respiratory minute volume necessary to nor-

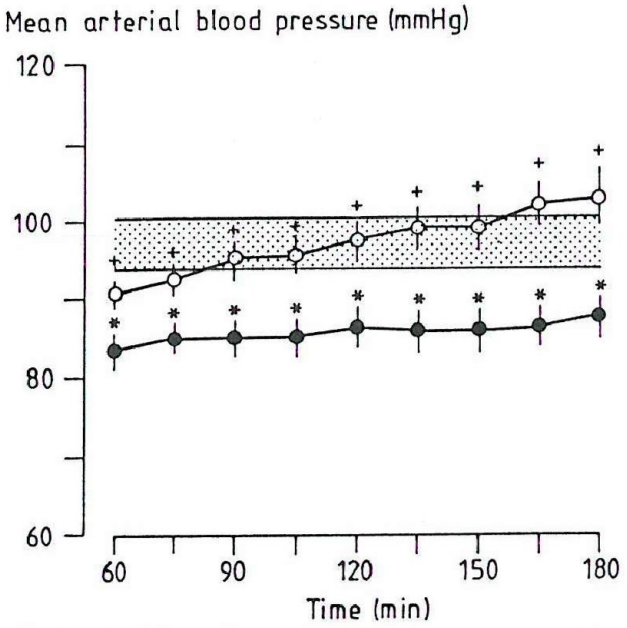

Figure 1. Effect of α-chloralose on mean arterial blood pressure in pigs. Horizontal lines delineate reference values for conscious animals. Spontaneous respiration (○), artificial respiration (●). (*) indicates significant difference from reference values, (+) indicates significant difference between the two groups. Values are means ± S.E.M.

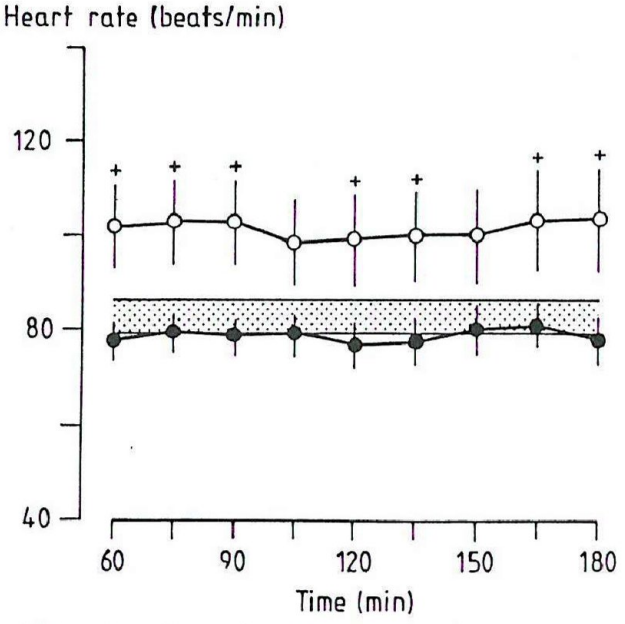

Figure 2. Effect of α-chloralose on heart rate in pigs. Horizontal lines delineate reference values for conscious animals. Spontaneous respiration (○), artificial respiration (●). (+) indicates significant difference between the two groups. Values are means ± S.E.M.

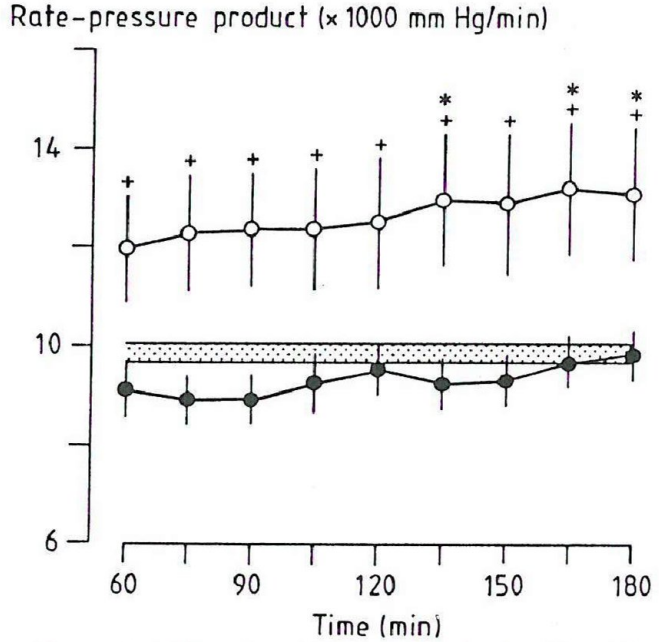

Figure 3. Effect of α-chloralose on the product of systolic arterial blood pressure and heart rate. Horizontal lines delineate reference values for conscious animals. Spontaneous respiration (○), artificial respiration (●). (*) indicates significant difference from reference values, (+) indicates significant difference between the two groups. Values are means ± S.E.M.

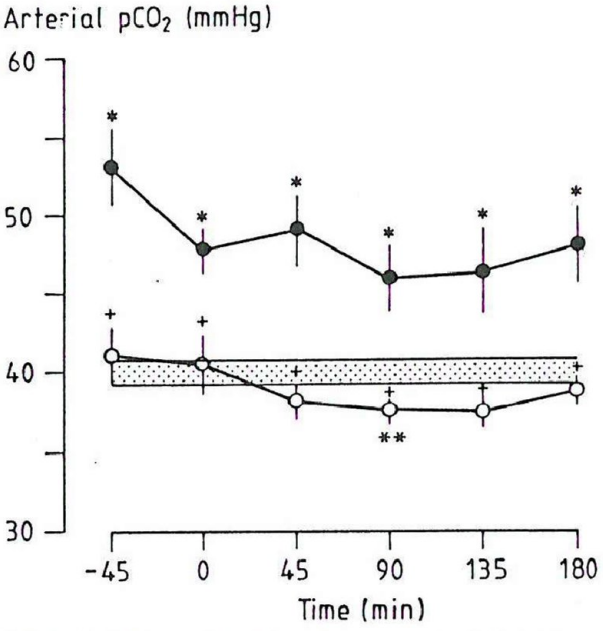

Figure 4. Effect of α-chloralose on arterial pCO_2. Horizontal lines delineate reference values for conscious animals. Spontaneous respiration (○), artificial respiration (●). (*) indicates values significantly above reference values, (**) indicates values significantly below reference values, (+) indicates significant difference between the two groups. Values are means ± S.E.M.

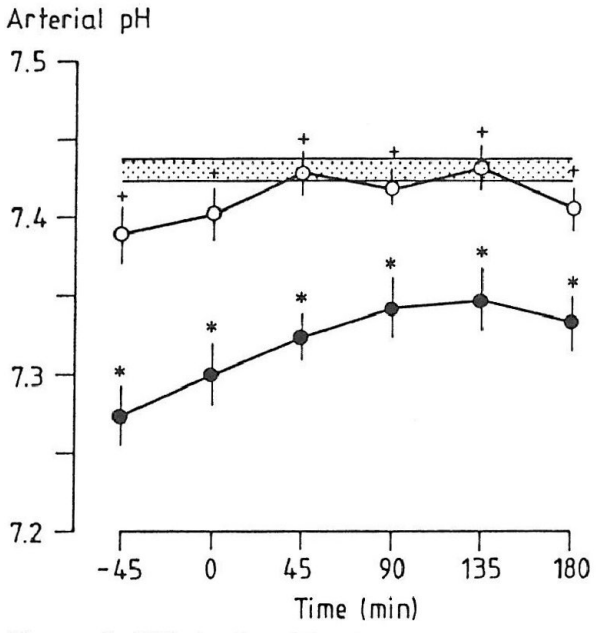

Figure 5. Effect of α-chloralose on arterial pH. Horizontal lines delineate reference values for conscious animals. Spontaneous respiration (○), artificial respiration (●). (*) indicates values significantly below reference values, (+) indicates significant difference between the two groups. Values are means ± S.E.M.

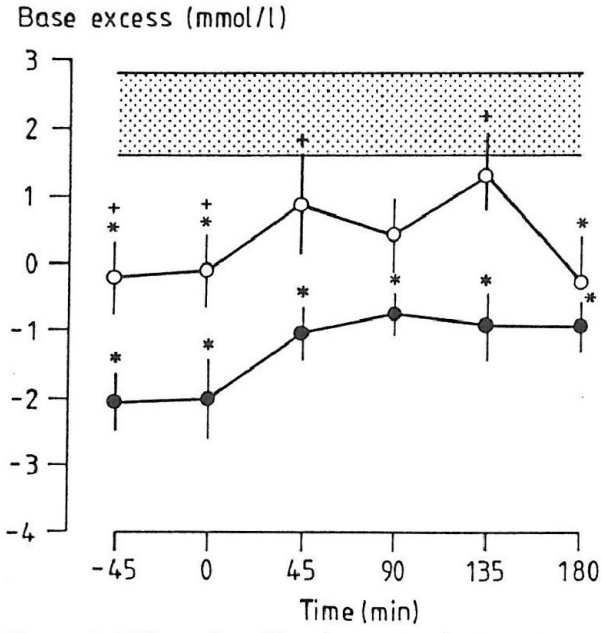

Figure 6. Effect of α-chloralose on calculated base excess. Horizontal lines delineate reference values for conscious animals. Spontaneous respiration (○), artificial respiration (●). (*) indicates values significantly below reference values, (+) indicates significant difference between the two groups. Values are means ± S.E.M.

malize arterial blood pCO_2 and pH was 0.15 l per kg body weight in the weight range 23 to 34 kg (instrument dead space 45 ml).

Fig. 6 shows the calculated base excess. A significant deficit was recorded in spontaneously breathing animals, whereas the artificially ventilated group was only below the reference value before removal of halothane and in the last sample.

DISCUSSION

The observation by *Vincent & Thompson* 1928 that arterial blood pressure in cats remained stable during α-chloralose anaesthesia was confirmed for pigs, whereas the hypertension described by *Brown & Hilton* 1916 and *Bass & Buckley* 1966 in dogs anaesthetized with α-chloralose could not be confirmed. In our experiment spontaneously breathing pigs were hypotensive, presumably due to peripheral vasodilatation, as heart rate remained within the normal range. Artificial ventilation, however, normalized blood pressure, probably by improving cardiac performance, as there was an increase in heart rate and in the rate-pressure product.

Respiratory depression was demonstrated by arterial blood gas measurements. During spontaneous respiration pCO_2 was elevated and respiratory acidosis developed. This condition was reversed by artificial ventilation. The observation by *Dripps & Dunke* 1943 that CO_2 stimulation of the respiratory centre was diminished during α-chloralose anaesthesia in dogs could thus be confirmed in pigs.

The metabolic acidosis in the artificially ventilated animals at the end of the experiment could be explained by the experimental procedure involving removal of HCO_3^- from hepatic and pancreatic secretions.

It is concluded that α-chloralose is a useful anaesthetic in terminal physiological experiments in pigs, provided the animals are intubated and ventilated artificially. Otherwise the animals will develop hypotension and respiratory acidosis. Compared with two

previously described anaesthetic methods in pigs using either halothane and methoxyflurane or metomidate hydrochloride (*Svendsen & Carter* 1989), the present method results in more stable respiratory and cardiovascular conditions.

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Summary
Respiratory and cardiovascular parameters were examined in 47 pigs anaesthetized with α-chloralose 0.25 % (100 mg/kg i.v.). Animals maintained under spontaneous respiration had a stable but subnormal arterial blood pressure. Heart rate was within the normal range. Respiration was depressed, causing elevated pCO_2 and respiratory acidosis.
Artificial ventilation with a minute volume of 0.15 l per kg body weight normalized both cardiovascular and respiratory parameters.
In conclusion α-chloralose can be considered valuable for maintaining anaesthesia in pigs during acute, non-survival experiments demanding minimal cardiovascular and pulmonary disturbance, but only where artificial ventilation is used.

Sammendrag
Der foreligger en undersøgelse af respirations- og kredsløbsparametre hos 47 grise under α-chloralose anæstesi. Under spontan respiration havde dyrene stabilt men subnormalt arterielt blodtryk. Hjertefrekvensen var indenfor normalområdet. Respirationsdepression forårsagede forhøjet pCO_2 og respiratorisk acidose.
Både respirations- og kredsløbsparametre kunne normaliseres ved artificiel respiration med et minutvolumen på 0.15 l pr. minut.
Det kan konkluderes, at α-chloralose er velegnet til vedligeholdelse af anæstesi af grise under akutte, terminale forsøg under forudsætning af, at der anvendes artificiel ventilation.

Yhteenveto / K. Pelkonen
Alfa-kloraloosilla nukutetusta (100 mg/kg laskimonsisäisesti) 47 siasta tutkittiin hengitys- ja verenkiertomuuttujia. Luonnollisesti hengittävillä oli tasainen mutta normaalia alempi valtimopaine. Syketaajuus oli normaalin rajoissa. Hengitys oli heikentynyt, joka aiheutti kohonneen hiilidioksidipitoisuuden ja respiratorisen asidoosin.
Hengityskoneen käyttö (0.15 l/kg min) normalisoi sekä verenkierto- että hengitysmuuttujat.
Yhteenvetona todetaan, että hengityskonetta käytettäessä alfa-kloraloosi on käyttökelpoinen nukutusaine sioille akuuteissa kokeissa, joista eläimen ei tarvitse herätä, kun halutaan pitää verenkierto- ja hengitysvaikutukset mahdollisimman pieninä.

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