EFFECTS IN GOATS OF ACUTE HYPERCARBIA ON BODY OXYGEN STORES

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SUMMARY

Eight anaesthetized and paralysed goats were ventilated for 2 hours with 100% oxygen. By mechanically increasing the deadspace, the level of PaCO₂ was acutely elevated to an average of 62 mm Hg. During the final 30 min of ventilation, the inspired mixture was altered from oxygen to air. The rates at which the arterial and mixed venous oxygen concentrations approached their new steady state values were represented by half-times (t₁/₂) of 0.43 and 1.04 min, respectively. The turnover rate in cisternal spinal fluid proceeded at a considerably slower rate, t₁/₂ = 3.2 min. Acute hypercarbia does not significantly alter the oxygen turnover rate, nor significantly affect the oxygen stores in the cisternal fluid.

Physicians are ministering to increasing numbers of patients who develop acute hypercarbia secondary to lung disease. Many of these patients are treated by mechanical ventilation, which can cause marked changes in arterial blood-gas tensions. These, in turn, are reflected by changes in cerebrospinal fluid (c.s.f.) gas tensions. Data indicate that c.s.f. pH, and presumably c.s.f. Po₂, is remarkably stable in the presence of long-term abnormalities of PaCO₂. However, during acute hypercarbia the relationships between changes in arterial blood-gas tensions and oxygen stores of the body have not been completely established (Mitchell et al., 1965; Cotev, Lee and Severinghaus, 1968).

In previous studies, we documented the oxygen turnover rates (speed of transfer of oxygen from artery to cisternal fluid) in the cerebrospinal fluid of dogs during hypocarbia-hypothermia (Ravin and Sullivan, 1971), normocarbia-normothermia (Sullivan and Ravin, 1968), and hypocarbia-normothermia (Ravin, 1972). The present study extends these observations under the constraints of acute hypercarbia-normothermia, and is undertaken to answer the question: Will acute hypercarbia alter the oxygen turnover rate and/or the oxygen stores in the cisternal fluid?

METHODS

Eight female goats averaging 27 kg (range 19–35 kg) were anaesthetized with intravenous sodium pentobarbitone 15 mg/kg. The trachea of each goat was intubated with a cuffed endotracheal tube, and its ventilation was controlled with a constant volume ventilator. The goats were paralysed with a constant rate intravenous infusion (0.5 mg/min) of 0.1% suxamethionium in 5% dextrose and water to eliminate shivering, muscle movement, or spontaneous respiratory effort. Approximately 400 ml of lactated Ringer’s solution containing 44.6 m.equiv/l. of sodium bicarbonate were infused intravenously each hour to replace the volume of sampled fluid and blood, and to prevent metabolic acidosis from loss of sodium in the copious salivary secretions. Oesophageal temperature was maintained between 37 and 39°C by intermittent surface warming. Teflon catheters were inserted into a carotid artery, jugular vein, and the right heart to permit blood sampling and pressure measurement. An 18-gauge spinal needle was placed percutaneously into the cisterna magna.

The animals were ventilated with 100% oxygen (15 ml/kg body weight at a frequency of 16/min) for 60 min while being prepared for study. Without changing the ventilatory pattern the PaCO₂ was elevated by adding mechanical deadspace (approximately 10 ml/kg). In about 60 min each goat had achieved a new steady state of ventilation, as indicated by a change of less than 2% in PaCO₂ and pH.

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The research described in this report involved animals maintained in animal care facilities fully accredited by the American Association for Accreditation of Laboratory Animal Care.
on three successive samples within a 9-minute period. Carotid, jugular, mixed venous, and cisternal c.s.f. samples were obtained simultaneously. The inspired mixture was abruptly changed to air and additional arterial, venous, and c.s.f. samples were obtained simultaneously at 1, 2, 3, 10, 20, and 30 min after breathing air. Arterial and venous samples were also obtained at 0.5 min. Samples were anaerobically collected over a 30-second period into heparinized syringes and analysed for pH, PaO₂, and PaCO₂ with direct-reading electrodes. Appropriate nomograms (Severinghaus, 1966) were used to correct measured blood-gas tensions for animal-electrode temperature difference. Haemoglobin concentration was determined by spectrophotometry from the first and last arterial samples.

Calculations.

Hellegers' nomogram (Hellegers et al., 1959) for goats was used to derive haemoglobin oxygen saturation from the corrected values of measured Po₂ and pH. The oxygen content of the blood was calculated as:

\[(O_2) = (\text{haemoglobin oxygen saturation} \times \text{oxygen capacity}) + (\text{dissolved oxygen})\]

where dissolved oxygen equals Po₂ × 0.0031. The same Bunsen coefficient was used for cerebrospinal fluid (Christoforides, Laasberg and Hedley-Whyte, 1969). Oxygen capacity was calculated using 1.34 ml O₂/g haemoglobin.

During the period of oxygen washout the changes in CaO₂, CvO₂, and cisternal cerebrospinal fluid oxygen content were analysed in terms of the rate at which each approached its new equilibrium value. A means of expressing the rate of change is the half-time (ti), expressed in minutes for the variable in question to change 50% of its overall change.

The cerebral blood flow equivalent was calculated according to the method of Cotev, Lee and Severinghaus (1968). Since cerebral oxygen consumption (Vo₂), according to the principle of conservation of matter (the Fick equation), must equal cerebral blood flow (Q), times the arteriovenous oxygen content difference, C(a-v)O₂, the equation may be written:

\[\frac{1}{C(a-v)O_2} = \frac{Q}{Vo_2}\]

Therefore, the reciprocal of C(a-v)O₂ is the blood flow in ml per ml of oxygen consumption from that blood. The ratio has been termed the flow equivalent, by analogy with ventilation equivalent (VE/Vo₂). The normal value for cerebral flow equivalent in unanaesthetized man is 14 (c.b.f. 42 ml/min⁻¹.100g⁻¹, Vo₂ 3 ml/min⁻¹.100g⁻¹).

RESULTS

Blood haemoglobin concentration averaged 11.5 ± 1.8 g/100 ml (mean ± SD), with no significant change between the 0- and 30-min samples (P>0.10). Oesophageal temperatures averaged 37.9 ± 1.0°C and remained stable during the experiment. PaCO₂ values averaged 62.2 ± 7.9 mm Hg, and pH values averaged 7.18 ± 0.07 after 90 min of ventilation with 100% oxygen. After 30 min of breathing air the PaCO₂ values averaged 64.0 ± 8.3 mm Hg and the pH value averaged 7.10 ± 0.06.

PaO₂ and PVₐO₂ values decreased abruptly when the goats were changed from oxygen to air breathing. New equilibrium values were reached within 2–3 min. The cisternal c.s.f. Po₂ decreased gradually in 10 min (fig. 1). CaO₂ and CvO₂, half-time values were 0.48 and 1.04 min, respectively, while the changes in cisternal Co₂ proceeded more slowly with a half-time of 3.2 min (fig. 2). Thus, after a change from oxygen to air breathing, arterial equilibration occurred approximately twice as fast as that in the venous pool, and six times as fast as that in the cisternal fluid.

The calculated cerebral blood flow equivalent is 31 (fig. 3), which represents an approximately linear increase with increasing PaCO₂ from previous studies (Ravin and Sullivan, 1971; Sullivan and Ravin, 1968; Ravin, 1972).

DISCUSSION

Acute hypercarbia does not significantly alter the oxygen turnover rate nor significantly affect the oxygen stores in the cisternal fluid. In previous studies during mild hypocarbia (PaCO₂ 30 mm Hg) (Ravin, 1972), and severe hypocarbia (PaCO₂ 15 mm Hg) (Sullivan and Ravin, 1968), the half-time values for oxygen content in the arterial blood were 0.57 and 0.23 min, respectively. The arterial t½ of the present study (PaCO₂ 62 mm Hg) is 0.48 min, a value of similar magnitude. Likewise, the values for cisternal fluid t½ of 3.6 (Ravin, 1972) and 3.2 min are similar.

Why should these values be similar over the sampled range of PaCO₂? Of the known factors the PaCO₂ has the greatest effect on cerebral blood flow (Smith and Wollman, 1972). Within the range of 20–60 mm Hg, cerebral blood flow is a near linear
function of $P_{\text{aCO}_2}$. Each mm Hg increase or decrease in $P_{\text{aCO}_2}$ is associated with an increase or decrease in c.b.f. of about 1 ml.min$^{-1}$.100g$^{-1}$ (Kety and Schmidt, 1948). Our acute studies (Ravin and Sullivan, 1971; Sullivan and Ravin, 1968; Ravin, 1972) corroborate this finding (fig. 3).

Since cerebral blood flow was not measured directly in our experiments, it was expressed in terms of flow per unit oxygen consumption ($Q/\text{Vo}_2$).
Once equilibration with room air occurred the oxygen-venous oxygen content difference \((C(a-v)_{O_2})\) did not change. Since this difference is directly related to \(V_O_2\), this, too, remained steady. Even in the face of a changing \(V_O_2\), however, it is felt that cerebral blood flow per unit of oxygen consumption serves as a useful concept in evaluation of c.b.f. in terms of the demand for oxygen by the tissues.

The mechanism for the effect of \(P_aO_2\) on cerebral blood flow seems to be control of the vascular tone by the pH of extracellular fluid (e.c.f.) near cerebral arterioles (Severinghaus and Lassen, 1967). In the presence of constant \(P_aCO_2\) acute changes in arterial \([H^+]\) or \([HCO_3^-]\) have little immediate effect on blood flow, since these ions enter the extracellular fluid slowly.

In this study, during the adjustment from oxygen to air breathing, mixed venous oxygen tension decreased an average of 38 mm Hg, which represented a change of 3.45 vol\%. If we assume a goat venous blood volume equal to 75\% of the total blood volume, then there would be 60 ml of venous blood per kg of body weight. This would represent a change of 2.07 ml \(O_2\)/kg when changing from oxygen to air breathing \((3.45 \times 0.60)\). When the plotted rate of change in venous blood (fig. 2) is extrapolated to the initial concentration, the intercept is 0 time plus 0.34 min following the alveolar change, and presumably represents the average circulation time. Similarly, it takes about 0.7 min before a change in \(FIO_2\) is followed by the start of the change in the oxygen content of cisternal fluid.

If we assume that cerebrospinal fluid volume in the goat is 1 ml/kg body weight, and that venous blood volume is equal to 75\% of the total blood volume, then the amount of oxygen stored in the c.s.f. represents less than 2\% of that stored in the venous blood, and is negligible in considering total body oxygen stores. At equilibrium the cisternal \(PcO_2\) always fell between the arterial and venous values. However, during periods of change from one \(PcO_2\) level to another, there is no correlation between the arterial and c.s.f. oxygen tensions. Therefore, the suggestion of Gänshirt (1968) that there is clinical application of the measurement of c.s.f. oxygen tension in lieu of the carotid-jugular a-v difference, holds only at equilibrium. The \(PcscfO_2\) is determined by several factors, including \(Pao\), cerebral blood flow, site of cerebrospinal fluid sampling, and \(Po\), of cerebral tissue. Consequently, \(PcscfO_2\) cannot be used as an acceptable approximation of \(Po\) of cerebral tissue.

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**REFERENCES**


**EFFETS SUR LE STOCK CORPOREL D'OXYGENE DE L'HYPERCARBIE AIGUE CHEZ LA CHEVRE**

SOMMAIRE

Huit chèvres anesthésiées et paralysées ont été ventilées durant 2 heures avec 100\% d'oxygène. En augmentant mécaniquement l'espace mort, on éleva le taux de \(Pao_2\), de manière aiguë à une moyenne de 62 mm Hg. Au cours des 30 dernières minutes de la ventilation, on modifia le mélange inspiré d'oxygène en air. Le taux auquel les concentrations oxygéniques artérielles et veineuses mixtes atteignaient leurs nouvelles valeurs steady-state est représenté par des demi-temps (\(t_\frac{1}{2}\)) de respectivement 0.43 et 1.04 min. Le taux de turnover dans le liquide rachidien cisternal était considérablement plus lent, \(t_\frac{1}{2}=3.2\) min. L'hypercarbie aiguë ne modifie pas significativement le taux du turnover d'oxygène, ni les stocks d'oxygène dans le liquide cisternal.
EFFECTS OF ACUTE HYPERCARBIA ON BODY OXYGEN STORES

ÜBER DIE WIRKUNG DER AKUTEN HYPERCARBIE AUF DIE Sauerstoffvorräte des Körpers bei Ziegen

ZUSAMMENFASSUNG
Acht narkotisierte und paralysierte Ziegen wurden zwei Stunden lang mit 100% Sauerstoff beatmet. Durch mechanische Vermehrung des Totraumes wurde die CO₂-Spannung akut bis auf einen Durchschnitt von 62 mmHg angehoben. Während der letzten 30 Minuten der Beatmung wurde die Zusammensetzung des eingatmeten Gases von Sauerstoff auf Luft geändert. Der Zeitraum, innerhalb dessen die arteriellen und gemischten venösen Sauerstoffkonzentrationen ihre neuen Dauerzustandswerte erreichten, wurden durch eine Halbzeit (t₁) von 0,43 bzw. 1,04 min. gekennzeichnet. Die Veränderungsgeschwindigkeit des Liquor in der Zisterne vollzog sich mit einer erheblich geringeren Geschwindigkeit, nämlich t₂ = 3,2 Minuten. Die akute Hypercarbie verändert weder die Geschwindigkeit des Sauerstoffaustausches eindeutig, noch beeinflusst sie eindeutig die Sauerstoffvorräte im Liquor der Zisterne.

EFECTOS DE LA HIPERCAPNIA AGUDA SOBRE LAS PROVISIONES DE OXIGENO CORPORAL EN CABRAS

RESUMEN
Ocho cabras anestesiadas y paralizadas fueron ventiladas durante 2 horas con 100% de oxígeno. Aumentando mecánicamente el espacio muerto, el nivel de la Paco₂ se elevaba de un modo brusco hasta un promedio de 62 mm Hg. Durante los últimos 30 minutos de ventilación se cambiaba la mezcla inspirada, pasando de oxígeno a aire. Las tasas para que las concentraciones de oxígeno arterial y de la mezcla venosa se aproximaran a las de los valores de la nueva situación estable, eran representadas por los tiempos medios (t₁) de 0,43 y 1,04 min. respectivamente. La cuota de retorno en el líquido del espacio espinal se comportaba con unas cifras considerablemente más bajas, t₂ = 3,2 min. La hipercapnia aguda no altera significativamente la cuota del oxígeno de retorno, ni tampoco afecta de un modo importante las reservas de oxígeno en el líquido del espacio espinal.

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