J. Perinat. Med.
13 (1985) 185

Contribution of the BOHR effect to the fall in fetal P_{O_2} caused by maternal alkalosis

A. M. Carter, J. Grønlund

Department of Physiology, University of Odense, Denmark

1 Introduction

Maternal hyperventilation during labour can be detrimental to the fetus [26]. Hyperventilation leads to a fall in fetal P_{O_2} , which is due to a fall in P_{CO_2} and rise in pH of the maternal blood [21]. Recent experimental findings suggest that this may be part of the normal physiological response in moderate to heavy exercise [6, 17], and it is therefore of interest in the general clinical context of pregnancy. The fall in fetal P_{O_2} during respiratory alkalosis has been demonstrated experimentally in the guinea pig [22] and sheep [1, 15, 24] and three mechanisms have been proposed to explain it. Firstly, a rise in pH will increase the oxygen affinity of maternal blood (the BOHR effect), and the closer approximation of the maternal and fetal oxygen dissociation curves may entail that equilibrium between the blood of the mother and the fetus is reached at a lower P_{O_2} . Secondly, the rise in pH, or the fall in P_{CO_2} , could provoke constriction of the vessels supplying the maternal side of the placenta, thereby reducing blood flow and the oxygen supply to the fetus. This has been shown to occur during experiments on the pregnant ewe and her fetus when alkalosis is induced by ingestion of sodium bicarbonate [3] or by hyperventilation due to hyperthermia [25] or exercise [6, 16, 17]. Finally, it has been clai-

Curriculum vitae

ANTHONY M. CARTER, Ph.D., Lecturer in Physiology at the University of Odense, was born in 1942. He was educated at Magdalene College, Cambridge, and the University of Lund, Sweden. He was associate professor at the University of Lund from 1970–1976. His main research interests are the physiology and pharmacology of the placental circulation and the analysis of factors determining the placental exchange of respiratory gases.

med that the effect of alkalosis on fetal P_{O_2} is exerted through the fetal placental circulation. A reduction in umbilical blood flow has been demonstrated experimentally in respiratory alkalosis induced by mechanical hyperventilation [24], but in alkalosis due to hyperthermia [25] or to moderate exercise [17] there was no significant change in fetal placental perfusion.

The present study is a theoretical and experimental analysis of the contribution of the BOHR effect to the reduction in fetal P_{O_2} caused by maternal alkalosis. We measured respiratory

gas tensions in fetal guinea pigs by mass spectrometry [11] during a step change in the pH of maternal blood achieved by infusing an isotonic solution of sodium hydroxide in the descending aorta. The measured response of fetal P_{O_2} was then compared with that predicted by a computer model of placental gas exchange in the guinea pig, given the initial conditions and the extent of the change in maternal arterial pH. The result of this comparison revealed that the leftward shift of the maternal oxygen dissociation curve can account for only a small part of the impact of maternal alkalosis on fetal oxygenation.

2 Materials and methods

Thirteen virgin guinea pigs of outbred stock (Ssc: AL) were mated in our laboratories and used close to term, on the 62nd to 67th days of pregnancy. Maternal body weight was 1.0–1.2 kg and the fetuses studied weighed 62–115 g.

The dam was given atropine (0.05 mg S. C.) and then was anesthetized with diazepam (1.0 mg/kg I. M.) and pentobarbitone sodium (25–30 mg/kg I. P.). Respiration was unassisted but the animals breathed room air enriched with oxygen. Rectal temperature was maintained at 38.1–38.7 °C with the aid of a heating pad.

A polyethylene catheter was inserted by a cut-down in the right carotid artery and advanced into the thoracic aorta. At examination post mortem the tip of the catheter was ca. 0.5–2.0 cm above the level of the diaphragm. A slow infusion of isotonic saline solution (0.03 ml/min) was started in this catheter as soon as it had been tied in place. A second catheter was inserted in a femoral artery to enable the withdrawal of maternal blood samples.

The abdomen was opened by a midline incision and the gravid uterus lifted gently on to a thermostatted table. It was wrapped in plastic foil to restrict evaporation. A transverse incision was made in the uterine wall to expose the

head, neck and forelimbs of one fetus. The cut surface of the uterus was sewn to the fetal skin with a 5–0 silk suture to prevent it from retracting over the fetal abdomen and placenta. A plastic sheath was glued over the fetal snout. The blood gas catheter (see below) was inserted by a cutdown in the right jugular vein of the fetus. It was advanced 20–25 mm and secured in place with silk ligatures. The position of the catheter tip was examined at the end of the experiment.

2.1 Measurement of blood gases

Oxygen and carbon dioxide tensions in the right atrium of the fetus were measured continuously and simultaneously by mass spectrometry [11]. The blood gas catheter [18] was a flexible, stainless steel tube (O. D. 0.8 mm) connected to the high vacuum chamber of the mass spectrometer (MICROMASS SX 200, VG GAS ANALYSIS, Middlewich, England). The catheter tip was covered by a 20 μ m thick polyethylene membrane, supported by a porous plug of sintered bronze. Gases which diffuse across this membrane from the blood are drawn towards the vacuum chamber of the mass spectrometer, and the signal due to diffusive flux is directly proportional to the partial pressure of each gas at the membrane surface. At the start of each experiment, the mass spectrometer was calibrated against a microsystem blood gas analyzer (BMS 3 MK 2, RADIOMETER, Denmark), using a fresh sample of guinea pig blood.

Maternal arterial P_{CO_2} , P_{O_2} and pH were measured in 0.7 ml blood samples obtained from the femoral catheter. The measurements were made at 37 °C with the blood gas analyzer (BMS 3) and the values corrected for maternal body temperature [14]. The hemoglobin concentration and oxygen saturation of the blood were measured in a photometric analyzer (OSM 2 HEMOXIMETER, RADIOMETER, Denmark). Standard bicarbonate and base excess were calculated using the alignment nomogram of SIGGAARD-ANDERSEN. Packed cell volume was measured in glass capillaries centrifuged for 5 minutes in a microhematocrit centrifuge.

2.2 Infusion of base

To investigate the influence on fetal blood gas tensions of an abrupt rise in maternal pH, an infusion of isotonic sodium hydroxide solution (0.15 M) was given in the thoracic aorta. The rate of infusion was 1.24 ml/min (0.19 mmol/min) and its duration was 1 or 2 minutes. The infusion catheter was flushed immediately afterwards with isotonic saline solution, which was given for 1 minute at the same rate of infusion. A sample of maternal arterial blood was withdrawn from the femoral artery between 30–90 sec of a two minute infusion and between 20–60 sec of a one minute infusion. Maternal blood samples were also secured before and after the infusion. The measurement of fetal blood gases was uninterrupted.

2.3 Model predictions

In a separate study [12] we have described a model for the simulation of placental gas exchange in the guinea pig. The model is able to predict the rate of oxygen transfer across the placenta from numerical values of P_{O_2} , P_{CO_2} , pH, hematocrit and the concentration of 2,3-diphosphoglycerate (DPG) in the umbilical and uterine arteries and the blood flow rates on the two sides of the placenta. The calculations require detailed knowledge of the binding of respiratory gases in blood. The comprehensive data available on adult human blood were used to simulate the behaviour of maternal and fetal guinea pig blood. The model thereby takes advantage of the absence in guinea pigs of a fetal hemoglobin [2] and of the close similarity between human and guinea pig blood in such essential features as the hydrogen ion gradient across the erythrocyte membrane, the magnitude of HILL's coefficient and of the BOHR effect factor, and the effect of DPG on oxygen affinity [20, 27]. The model of placental gas exchange is based on the two assumptions that the oxygen and carbon dioxide tensions in the umbilical vein are equal to those in the uterine vein and that the net transfer of acid/base across the placenta is negligible. When the model was tested against experimental data [5], the predic-

ted P_{O_2} , P_{CO_2} , pH and SO_2 of the umbilical venous blood was in good agreement with the measured values [12].

By introducing three additional assumptions, the model can be used to predict the change in P_{O_2} in the fetal heart after the manipulation of maternal pH.

These assumptions are:

1. the rate of oxygen transfer across the placenta two minutes after the start of the base infusion is equal to the preinfusion value,
2. the P_{CO_2} in the umbilical artery is unaffected by the base infusion, and
3. the composition of the blood in the fetal heart is equal to that in the umbilical artery.

Infusion of base causes a primary increase in pH and a secondary decrease in P_{O_2} and P_{CO_2} in the uterine artery. The immediate effect will be to reduce oxygen transfer across the placenta. Oxygen transfer will, however, soon return to its preinfusion value (assumption 1) due to a fall in P_{O_2} in the umbilical arterial blood. The magnitude of the decrease in umbilical arterial P_{O_2} was determined by using an iterative procedure (the secant method), where P_{O_2} in the umbilical artery is decreased until the predicted rate of oxygen transfer across the placenta is equal to the preinfusion value. The decrease in P_{O_2} causes an increase in fetal arterial pH due to the BOHR effect. Therefore, each iteration included an adjustment in pH made by utilizing the conservation equation for the buffer bases in the fetal blood. The same technique was used to predict the fall in umbilical arterial P_{O_2} that would be expected if the base infusion was associated with a reduction of either the maternal or the fetal placental blood flow.

3 Results

3.1 Experimental findings

One experiment failed completely because the catheter tip lodged in the atrial wall. Three others were excluded from further analysis due to a high initial value for P_{CO_2} in the right

atrium, which was taken to indicate fetal distress occasioned by anesthesia and surgical trauma. The remaining nine fetuses had an initial $P_{CO_2} \leq 59$ Torr, which is within one standard deviation of the mean P_{CO_2} measured in fetal blood obtained by cardiac puncture immediately upon laparotomy [5]. In these experiments the tip of the blood gas catheter was entirely within the right atrium of the fetus.

Maternal mean arterial blood pressure was 64.8 ± 10.0 Torr and maternal heart rate was 271 ± 22 beats/min (means $\pm$ S. D.). The blood gas tensions and acid/base status of maternal arterial blood withdrawn from a femoral artery immediately before and during the infusion of sodium hydroxide are given in Tab. I. The mean increase in pH was 0.074 ± 0.037 units.

Tab. I. Blood gas tensions and acid-base status of blood from the maternal femoral artery before and during infusion of sodium hydroxide in the descending aorta of nine pregnant guinea pigs. Values are means $\pm$ S.D.

	Before infusion	During infusion
pH	7.36 ± 0.04	7.43 ± 0.06
P_{CO_2} [Torr]	35.1 ± 2.4	31.5 ± 5.0
P_{O_2} [Torr]	107.7 ± 18.4	104.5 ± 15.3
Base excess [mM]	-4.7 ± 2.4	-2.3 ± 2.6

The mass spectrometer recording from a typical experiment is shown in Fig. 1. There is a rapid fall in P_{O_2} during the infusion of base in the uterine artery with little or no change in P_{CO_2} . The standard procedure adopted was to read the blood gas tensions immediately before the infusion and at 1 minute and 2 minutes from its start. The values given in Tab. II have been corrected for signal drift in order not to overestimate the extent of the changes in blood gas tensions. P_{O_2} fell by a mean of 0.9 ± 0.9 Torr at 1 minute and 3.2 ± 1.6 Torr ($p < 0.001$) at 2 minutes from the start of the infusion. There was a more variable response in P_{CO_2} with a mean rise of 0.2 ± 1.4 Torr at 1 minute and of 1.7 ± 1.8 Torr at 2 minutes after the infusion was started.

Fig. 1. P_{O_2} and P_{CO_2} in the right atrium of a guinea pig fetus during infusion of sodium hydroxide in the maternal descending aorta. Mass spectrometer recording from a typical experiment.

Tab. II. Blood gas tensions in the right atrium of the guinea pig fetus before infusion of sodium hydroxide in the maternal descending aorta and at 1 min and 2 min after the start of infusion. Values are means $\pm$ S.D. ($n = 9$).

	Before infusion	1 min from start of infusion	2 min from start of infusion
P_{CO_2} [Torr]	54.9 ± 3.5	55.1 ± 3.9	56.6 ± 4.4
P_{O_2} [Torr]	12.4 ± 4.6	11.5 ± 4.3	9.2 ± 4.9

3.2 Model predictions

In the simulation of the experiments the model of placental gas exchange was utilized in combination with a complete set of input variables. The P_{O_2} , P_{CO_2} and pH in the uterine artery before and during the base infusion were given as the average of the measured values. The maternal intraerythrocytic DPG concentration

was not measured but was set at 7.0 mM [19]. The preinfusion values for P_{O_2} and P_{CO_2} in the umbilical artery were assumed equal to the average of the values measured in the fetal heart by the mass spectrometer immediately before the start of the base infusion. The pH in the umbilical artery was set at 7.27, which was the value measured in blood obtained by cardiac puncture [5]. The blood flow rates on the fetal and maternal sides of the placenta have been measured under closely similar experimental conditions [4, 11] and were assigned values of 7.5 ml/min and 7.3 ml/min, respectively. The fetal DPG value was set to 1.73 mM [2]. The measured values of fetal and maternal hematocrit were 0.39 and 0.49, respectively.

The simulation predicted a fall in P_{O_2} in the umbilical artery of 0.5 Torr due to the changes in the pH and blood gas tensions in the uterine artery (the BOHR effect). The result of superimposing an alteration in the maternal or the fetal placental blood flow is shown in Figs. 2 and 3. A fall in P_{O_2} of 3.2 Torr is predicted to occur if the maternal placental blood flow is reduced by 8% or the fetal placental blood flow by 17%.

Fig. 2. Predicted change in umbilical arterial P_{O_2} due to a decrease in maternal placental blood flow concomitant with an increase in maternal arterial pH of 0.07 pH-units.

Fig. 3. Predicted change in umbilical arterial P_{O_2} due to a decrease in fetal placental blood flow concomitant with an increase in maternal arterial pH of 0.07 pH-units.

4 Discussion

The aim of this study was to define the contribution of a leftward shift of the maternal oxygen dissociation curve to the fall in fetal arterial P_{O_2} associated with maternal alkalosis. Infusion of base in the descending aorta caused a rise in maternal arterial pH of 0.07 units and a fall in fetal arterial P_{O_2} of 3 Torr. Simulation of the experiments, using a mathematical model for placental gas exchange in the guinea pig, demonstrated that the contribution of altered maternal oxygen affinity per se was only 0.5 Torr. Maternal alkalosis therefore seems to affect fetal oxygenation by other mechanisms that quantitatively are more important. To substantiate this conclusion, it is necessary briefly to consider the premisses upon which the simulation was based.

Firstly, it was assumed that the rate of oxygen transfer across the placenta two minutes after the start of the base infusion was equal to the preinfusion value. This assumption is fulfilled if the fetal oxygen consumption remains constant during the base infusion and if the rate of oxygen transfer is at steady state both before

and two minutes after the start of the infusion. The time constant for the change in the oxygen content of the fetus after a step change in the placental oxygen flux is determined mainly by the mean circulation time, since most of the oxygen binding capacity is in the blood. Assuming a fetal cardiac output of 30 ml/min [4] and a blood volume of 12 ml [8] the mean circulation time is 25 seconds. An interval of two minutes ought therefore to allow complete reestablishment of the steady state oxygen flux across the placenta after the start of the base infusion. We did not measure the rate of fetal oxygen consumption but in a recent study of exercise-induced alkalosis by LOTGERING et al. [17], it was shown that the oxygen consumption of the uterus was unaffected when fetal P_{O_2} fell by about 10%. If a decrease in fetal oxygen consumption occurred during the infusion of base, the model will have overestimated the fall in fetal arterial P_{O_2} .

The second assumption was that P_{CO_2} in the umbilical artery was unaffected by the base infusion. This is to be expected, since the fetus has a large extravascular CO_2 binding capacity. In human adults, the 63% response time of the CO_2 binding capacity is about 40 min [7] and is directly proportional to the ratio between tissue volume and cardiac output, which is about 14 for a 70 kg man. The corresponding ratio for the guinea pig fetus is about 3, assuming a body weight of 100 g and a cardiac output of 30 ml/min. Thus the time constant of the tissue CO_2 stores is about 10 minutes or five times longer than the time interval studied after the start of the base infusion. A small increase in the P_{CO_2} of fetal blood was detected by mass spectrometry. This change was not significant, and a new simulation assuming a rise in fetal P_{CO_2} of 1.7 Torr did not appreciably alter the predicted value of fetal P_{O_2} after base infusion: the absolute value increased by less than 2%.

The model requires a numerical value for pH in the umbilical artery, but this parameter was not measured simultaneously with mass spectrometry. We have therefore used a value of 7.27, which was obtained in a previous study

[5]. The influence of alterations in the initial umbilical arterial pH value was, however, investigated and it was found that an increase in pH of 0.05 units influenced the predicted value of P_{O_2} after base infusion by less than 1%.

The average value of the oxygen tensions measured in situ by the mass spectrometer is about 6 Torr lower than the average value obtained by conventional analysis of blood samples from the fetal heart [5], whereas the average P_{CO_2} value is almost identical to that of the previous study. The difference in P_{O_2} may be due to the existence of an oxygen depletion layer in front of the membrane of the blood gas catheter due to the diffusive oxygen flux across the membrane [13].

In simulating the experiments, it was necessary to assume that the partial pressures of the respiratory gases in the right atrium were similar to those in the umbilical artery, to which the predictions of the model applied. This assumption can be questioned, since preferential streaming of blood is known to occur in the fetal guinea pig heart [9, 10]. Therefore, in separate experiments, we took samples of blood from a catheter placed in a branch of the abdominal aorta, the vitelline artery, and compared blood gas tensions in these samples with those earlier measured in blood obtained by cardiac puncture [5]. P_{O_2} was 16 ± 1 Torr in the vitelline artery ($n = 5$) against 19 ± 4 Torr in the heart ($n = 8$). The corresponding values for P_{CO_2} were 59 ± 7 and 53 ± 10 Torr (means $\pm$ S. D.). There was no significant difference between the group means (Student's t-test for independent observations).

The measured change in fetal arterial P_{O_2} during base infusion was greater than could be accounted for by increased oxygen affinity alone. The difference can probably be ascribed to a concomitant change in placental perfusion. There is a wealth of experimental evidence to suggest that maternal alkalosis is associated with a reduction in maternal placental blood flow. In sheep running on a treadmill, exercise-induced ventilation induces a fall in maternal P_{CO_2} , a rise in pH, decreased maternal placental perfusion, and a fall in fetal arterial P_{O_2} [6, 16,

17]. In the most recent of these studies, it was shown that 40 min of exercise at 70% of maximal maternal oxygen consumption reduced uterine blood flow by 24% and fetal arterial P_{O_2} by 3.0 Torr [16, 17]. During shorter periods of exercise the decrease in blood flow was 13–17% [16]. Maternal alkalosis has also been induced in guinea pigs [22] and sheep [15] by mechanical hyperventilation. These experiments suffer from the disadvantage that positive pressure ventilation itself adversely affects blood flow and fetal P_{O_2} [15, 23]. Controlled experiments in the ewe did, however, indicate that a rise in maternal pH of 0.23 units could precipitate a fall in uterine blood flow of 22% and a fall in fetal arterial P_{O_2} of 3.7 Torr [15]. Metabolic alkalosis arising from the ingestion of sodium bicarbonate also led to a fall in uterine blood flow [3].

It has been shown that umbilical blood flow falls during positive pressure ventilation in

sheep [24]. However, in recent experiments on pregnant ewes exercising at 70% of their maximal oxygen consumption for 10 min, there was a rise in maternal arterial pH without any significant change in fetal placental blood flow [17].

We have simulated the effect on fetal P_{O_2} of superimposing a change in placental perfusion on the increase in maternal oxygen affinity caused by infusion of base. The results indicate that a fall in maternal placental blood flow of 8% could account for the experimental findings. If there were a small compensatory rise in fetal placental perfusion due to hypoxia, the decrease in maternal placental blood flow would have to be correspondingly larger to explain our results. Conversely, assuming maternal placental perfusion to remain constant, the model predicts that a fall in umbilical blood flow of 17% would be needed to explain our findings.

Summary

A decrease in the P_{O_2} of fetal arterial blood is observed in maternal alkalosis caused by hyperventilation in labour or exercise. The contribution of altered blood oxygen affinity to this effect was studied experimentally and by computer simulation of placental gas exchange. Thirteen guinea pigs near term of pregnancy were anesthetized and the right atrium of the fetus was catheterized to enable continuous and simultaneous measurement of P_{O_2} and P_{CO_2} by mass spectrometry. An infusion of base was given through a catheter in the descending aorta of the dam and the effect on fetal respiratory gas tensions observed. The mean change in maternal arterial pH measured in blood taken from a femoral artery was 0.07 ± 0.04 (mean $\pm$ S. D.). There was an immediate decrease in P_{O_2} in the right atrium of the fetus, but no consistent alteration in P_{CO_2} . Two minutes after the start of the infusion, P_{O_2} had fallen by 3.2 ± 1.6 Torr ($p < 0.001$) and P_{CO_2} had risen by 1.7 ± 1.8 Torr (not significant). The experiments were simulated using a mathematical model of placental gas

exchange in the guinea pig. The model was able to predict the change in fetal arterial P_{O_2} , given numerical values for the pH, P_{O_2} and P_{CO_2} of fetal and maternal arterial blood prior to infusion of base and for maternal blood during the infusion of base. These values were obtained from the experimental data. Other input variables of the model were maternal and fetal hematocrit and DPG concentration, and the rates of blood flow on the two sides of the placenta. A simulation in which placental perfusion was assumed to remain constant predicted a fall in fetal P_{O_2} of 0.5 Torr, which is only 15% of that measured experimentally by mass spectrometry. Further analysis showed that the remainder of the effect could be explained by a fall in maternal placental blood flow of 8% or in fetal placental blood flow of 17%. **It is concluded that the BOHR effect makes a small contribution to reduced fetal oxygenation in maternal alkalosis but that other mechanisms are quantitatively more important.**

Keywords: Fetal blood, mass spectrometry, oxygen affinity, placental exchange.

Zusammenfassung

Anteil des BOHR-Effekts bei einem durch eine maternale Alkalose ausgelösten, fetalen P_{O_2} -Abfall

Bei einer maternalen Alkalose, wie sie nach Hyperventilation unter der Geburt oder bei Streß auftritt, kann man

einen Abfall des P_{O_2} im arteriellen Fetalblut beobachten. Inwieweit eine veränderte O_2 -Affinität an diesem Abfall mitbeteiligt ist, wurde experimentell sowie über eine Computer-Simulation des plazentaren Gasaustausches

untersucht. Bei 13 anästhetisierten Meerschweinchen am Termin wurde ein Katheter in den rechten, fetalen Vorhof geschoben und so eine kontinuierliche und simultane Po_2 - und Pco_2 -Messung ermöglicht, die über ein Massenspektrometer erfolgte. Beim Muttertier wurde über einen Katheter in der Aorta descendens eine basische Lösung infundiert und anschließend der Effekt auf die Sauerstoff- und CO_2 -Spannung im Fetalblut untersucht. Die durchschnittliche pH-Änderung betrug im maternalen Blut aus der Femoralarterie 0.07 ± 0.04 . Der Po_2 des Fetalbluts im rechten Vorhof zeigte sofort einen Abfall, während sich der Pco_2 unterschiedlich verhielt. Zwei Minuten nach Infusionsbeginn war der Po_2 um 3.2 ± 1.6 Torr ($p < 0.001$) gesunken, der Pco_2 um 1.7 ± 1.8 Torr (nicht signifikant) gestiegen. Unter Benutzung eines mathematischen Modells über den placentaren Gasaustausch beim Meerschweinchen wurden die Experimente simuliert. Über das Modell war es möglich, die pH-Änderung im arteriellen Fetalblut vorausszusagen, wenn man Werte für den pH, Po_2 und Pco_2 im

fetalen und maternalen Arterienblut, wie sie vor der Infusion der basischen Lösung bestanden, eingab. Ebenso wurden Werte für das maternale Blut, wie sie während der Infusion gefunden wurden, eingegeben. Die Daten selbst wurden aus den Experimenten abgeleitet. Weitere Variablen, die mit dem Modell überprüft wurden, waren der maternale und fetale Hämatokrit, die DPG-Konzentration sowie die Flow-Geschwindigkeiten auf beiden Seiten der Plazenta. Unter der Annahme, daß die placentare Durchblutung konstant bleibt, wurde bei der Simulation ein Po_2 -Abfall von 0.5 Torr vorausgesagt. Das sind lediglich 15% des Po_2 -Abfalls, der experimentell massenspektrometrisch erfaßt wurde. Weitere Analysen zeigten, daß eine Reduktion der Plazentadurchblutung auf der maternalen bzw. fetalen Seite um 8% bzw. 17% den experimentell erfaßten, stärkeren Po_2 -Abfall erklären kann. Wir schließen daraus, daß der BOHR-Effekt einen geringen Anteil an der reduzierten, fetalen Oxygenierung bei einer mütterlichen Alkalose hat und andere Mechanismen von größerer Bedeutung sind.

Schlüsselwörter: Fetalblut, Massenspektrometrie, placentarer Austausch, Sauerstoffaffinität.

Résumé

Rôle de l'effet BOHR dans la chute de la Po_2 fœtale provoquée par l' alcalose maternelle

On observe une diminution de la Po_2 du sang artériel fœtal en cas d'alcalose maternelle provoquée par une hyperventilation au cours du travail ou lors d'efforts. On a étudié, expérimentalement et à l'aide de simulations par ordinateur des échanges gazeux placentaires, le rôle dans ce phénomène d'une altération de l'affinité sanguine pour l'oxygène. On a anesthésié treize cobayes proches du terme de leur gestation et on a cathétérisé l'oreillette droite du fœtus afin de pouvoir mesurer en continu et simultanément, la Po_2 et la Pco_2 par spectrométrie de masse. On a perfusé une solution alcaline à l'aide d'un cathéter situé dans l'aorte descendante de la mère et l'on a observé les effets sur les pressions des gaz respiratoires du fœtus. La variation moyenne du pH artériel maternel mesuré dans le sang artériel fémoral est de 0.07 ± 0.04 (moyenne $\pm$ DS). Il y a une diminution immédiate de la Po_2 dans l'oreillette droite du fœtus, mais pas de modification conséquente de la Pco_2 . Deux minutes après le début de la perfusion, la Po_2 chute de 3.2 ± 1.6 Torr ($p < 0.001$) et la Pco_2 augmente de 1.7 ± 1.8 Torr (non significatif). En se servant d'un

modèle mathématique des échanges gazeux placentaires chez le cobaye, on a simulé des expériences. Ce modèle est capable de prédire les modifications de la Po_2 artérielle fœtale, si l'on donne les valeurs numériques artérielles du pH, de la Po_2 et de la Pco_2 fœtales et maternelles avant la perfusion alcaline ainsi que les valeurs maternelles en cours de perfusion.

On a obtenu ces valeurs à partir des données expérimentales. Les autres variables fournies au modèle sont l'hématocrite maternel et fœtal, la concentration de DPG ainsi que les valeurs du débit sanguin au niveau des deux faces placentaires. Une simulation, au cours de laquelle la perfusion placentaire demeure constante, prévoit une chute de la Po_2 fœtale de 0,5 Torr, ce qui représente seulement 15% de la valeur mesurée expérimentalement par spectrométrie de masse. Une analyse plus poussée montre que l'effet restant peut être expliqué par une chute du débit sanguin placentaire maternel de 8% ou une chute du débit sanguin placentaire fœtal de 17%. On en conclut que l'effet BOHR ne fournit qu'une faible contribution dans la réduction de l'oxygénation fœtale lors de l'alcalose maternelle mais que d'autres mécanismes sont quantitativement plus importants.

Mots-clés: Affinité en oxygène, échanges placentaires, sang fœtal, spectrométrie de masse.

Acknowledgements: This work was supported by The Danish Medical Research Council.

Bibliography

- [1] AARNOUDSE, J. G., B. OESEBURG, G. KWANT, A. ZWART, W. G. ZIJSTRA, H. J. HUISJES.: Influence of variations in pH and P_{CO_2} on scalp tissue oxygen tension and carotid arterial oxygen tension in the fetal lamb. *Biol. Neonate* 40 (1981) 252
- [2] BARD, H., M. SHAPIRO: Perinatal changes of 2,3-diphosphoglycerate and oxygen affinity in mammals not having fetal type hemoglobins. *Pediatr. Res.* 13 (1979) 167
- [3] BUSS, D. D., G. E. BISGARD, C. A. RAWLINGS, J. H. G. RANKIN.: Uteroplacental blood flow during alkalosis in the sheep. *Am. J. Physiol.* 228 (1975) 1497
- [4] CARTER, A. M.: The blood supply to the abdominal organs of the fetal guinea pig. *J. Dev. Physiol.* 6 (1984) 407
- [5] CARTER, A. M., J. GRØNLUND: Blood gas tensions and acid-base status in the fetal guinea-pig. *J. Dev. Physiol.* 4 (1982) 257
- [6] CHANDLER, K. D., A. W. BELL: Effects of maternal exercise on fetal and maternal respiration and nutrient metabolism in the pregnant ewe. *J. Dev. Physiol.* 3 (1981) 161
- [7] CHERNIACK, N. S., G. S. LONGOBARDO: Oxygen and carbon dioxide gas stores of the body. *Physiol. Rev.* 50 (1970) 196
- [8] CONSTABLE, B. J.: Changes in blood volume and blood picture during the life of the rat and guinea-pig from birth to maturity. *J. Physiol. (Lond.)* 167 (1963) 229
- [9] EVERETT, N. B., R. J. JOHNSON: Use of radioactive phosphorus in studies of fetal circulation. *Am. J. Physiol.* 162 (1950) 147
- [10] GIRARD, H., S. KLAPPSTEIN, I. BARTAG, W. MOLL.: Blood circulation and oxygen transport in the fetal guinea-pig. *J. Dev. Physiol.* 5 (1983) 181
- [11] GRØNLUND, J., A. M. CARTER: Continuous measurement of blood gas tensions in the fetal guinea-pig by mass spectrometry. *J. Perinat. Med.* 10 (1982) 226
- [12] GRØNLUND, J., A. M. CARTER: A model of respiratory gas transfer in the guinea-pig placenta. Submitted to publication (1985)
- [13] GRØNLUND, J., H. KOFOED, E. SVALASTOGA: Effect of increased knee joint pressure on oxygen tension and blood flow in subchondral bone. *Acta Physiol. Scand.* 121 (1984) 127
- [14] KELMAN, G. R., J. F. NUNN: Nomograms for correction of blood P_{O_2} , P_{CO_2} , pH and base excess for time and temperature. *J. Appl. Physiol.* 21 (1966) 1484
- [15] LEVINSON, G., S. M. SHNIDER, A. A. DELORIMIER, J. L. STEFFENSON.: Effects of maternal hyperventilation on uterine blood flow and fetal oxygenation and acid-base status. *Anesthesiology* 40 (1974) 340
- [16] LOTGERING, F. K., R. D. GILBERT, L. D. LONGO: Exercise responses in pregnant sheep: Oxygen consumption, uterine blood flow, and blood volume. *J. Appl. Physiol.* 55 (1983) 834
- [17] LOTGERING, F. K., R. D. GILBERT, L. D. LONGO: Exercise responses in pregnant sheep: Blood gases, temperatures, and fetal cardiovascular system. *J. Appl. Physiol.* 55 (1983) 842
- [18] LUNDSGAARD, J. S., B. JENSEN, J. GRØNLUND: Fast responding flow independent blood gas catheter for oxygen measurement. *J. Appl. Physiol.* 48 (1980) 376
- [19] MERLET-BENICHO, C., E. AZOULAY, M. MUFFAT-JOLY: Dependence of 2,3-DPG and oxygen affinity of haemoglobin on sex and pregnancy in the guinea-pig. *Pflügers Arch.* 354 (1975) 187
- [20] MESSIER, A. A., K. E. SCHAEFER: The BOHR effect in chronic hypercapnia. *Respir. Physiol.* 19 (1973) 26
- [21] MILLER, F. C., R. H. PETRIE, J. J. ARCE, R. H. PAUL, E. H. HON.: Hyperventilation during labor. *Am. J. Obstet. Gynecol.* 120 (1974) 489
- [22] MORISHIMA, H. O., F. MOYA, A. C. BOSSERS, S. S. DANIEL.: Adverse effects of maternal hypocapnea on the newborn guinea-pig. *Am. J. Obstet. Gynecol.* 88 (1964) 524
- [23] MORISHIMA, H. O., S. S. DANIEL, K. ADAMSON, L. S. JAMES.: Effects of positive pressure ventilation of the mother upon the acid-base state of the fetus. *Am. J. Obstet. Gynecol.* 93 (1965) 269
- [24] MOTOYAMA, E. K., G. RIVARD, F. ACHESON, C. D. COOK.: Adverse effect of maternal hyperventilation on the foetus. *Lancet* 1 (1966) 286
- [25] OAKES, G. K., A. M. WALKER, R. A. EHRENKRANZ, R. C. CEFALO, R. A. CHEZ.: Uteroplacental blood flow during hyperthermia with and without respiratory alkalosis. *J. Appl. Physiol.* 41 (1976) 197
- [26] SALING, E., P. LIGDAS: The effect on the fetus of maternal hyperventilation during labour. *J. Obstet. Gynaecol. Brit. Cwlth.* 76 (1969) 877
- [27] SCHAEFER, K. E., A. A. MESSIER, C. C. MORGAN: Displacement of oxygen dissociation curves and red cell cation exchange in chronic hypercapnia. *Respir. Physiol.* 10 (1970) 299

Received February 11, 1984. Revised May 25, 1984.
Accepted June 1, 1984.

Dr. Anthony M. Carter
Department of Physiology
Campusvej 55
DK-5230 Odense M, Denmark

Adrenal Steroid Antagonism

Proceedings
Satellite Workshop of the VII. International
Congress of Endocrinology
Quebec, Canada, July 7, 1984

Editor *M. K. Agarwal*

1984. 17 cm x 24 cm. VIII, 399 pages. Numerous illustrations. Hardcover. DM 175,-
ISBN 3 11 010090 8

This volume covers recent advances in the field of gluco- and mineralo-corticoid antagonism. Multifaceted antihormones such as RU 38486, and other derivatives in this series, are reviewed here for the first time. Data suggest that specific antiglucocorticoids and antigestational derivatives may become available to the clinician in the near future.

Also reviewed for the first time in this book are advances in mineralo-corticoid chemistry and the so called glucocorticoid antagonizing factor, produced endogenously, which may represent another aspect of hormone antagonism. Additionally, possible levels of hormone antagonism by inhibition of steroid synthesis or production of antihormone antibody are included.

de Gruyter · Berlin · New York