Fetal Heart Rate and Transcutaneous Monitoring during Experimentally Induced Hypoxia in the Fetal Dog

ALAN G. MONHEIT, MARTIN L. STONE, AND M. MAURICE ABITBOL

Department of Obstetrics and Gynecology, University Hospital, State University of New York at Stony Brook, Stony Brook; and the Jamaica Hospital, Jamaica, New York

ABSTRACT. A model of impaired oxygen delivery, using an acute surgical preparation in the fetal dog, is described. Fetal heart rate, transcutaneous pO_2 and pCO_2 , and tissue pH were simultaneously recorded during hypoxic episodes produced by a series of successive occlusions of the maternal abdominal aorta. Corresponding values were also determined in the arterial blood of the fetus. The following pathophysiologic sequence of events was observed: 1) a latency period with no changes; 2) a drop in pO_2 which stabilized later at a lower pressure; 3) late fetal heart rate deceleration, the pattern of which was not related to the progressively deteriorating fetal condition; 4) a progressive increase in pCO_2 ; 5) a progressive decrease in pH. Abnormal tissue values consistently preceded and were more adversely affected than corresponding blood values. This experimental model demonstrates first that late decelerations of the fetal heart rate are an early sign of fetal hypoxia and second that a fall in fetal blood pH, beyond that level normally seen during labor, occurs relatively late in this pathophysiologic sequence. Between these two, there are intermediary stages that could be continuously monitored in order to identify worsening fetal condition. Continuous tissue pH and transcutaneous pO_2 and pCO_2 recording may potentially be of significant clinical value. (*Pediatr Res* 23:548-552, 1988)

Abbreviations

FHR, fetal heart rate
tc, transcutaneous
t, tissue
UBF, uterine blood flow

Our present knowledge of the pathophysiology of fetal distress is limited by insufficient access to the fetus during labor. Presently only FHR monitoring and intermittent fetal scalp blood sampling (for fetal blood pH determinations) are used. Continuous FHR monitoring is associated with a high false-positive rate approaching 30% (1). The disadvantage of fetal scalp blood sampling is that it is done intermittently and is associated with fetal and maternal complication (2). Continuous recording of pH, pO_2 , and pCO_2 as opposed to intermittent fetal blood sampling may present some benefits (3). Recent progress in tc blood gas and tissue (t) pH monitoring has made this a clinically applicable tool (4). Unfortunately, experience with implantation

of an electrode on the fetal scalp is associated with numerous technical difficulties (2). Additionally, values obtained are different from those obtained by blood sampling. As a result of these shortcomings, such equipment has received very limited use.

In a previous report (5) the relationship between arterial blood pH, pO_2 , pCO_2 , and tpH, tcp O_2 , tcp CO_2 in the fetal dog was examined. It was demonstrated that, under normal physiological conditions, paired values approximated each other; and that, under stressful fetal conditions, they diverged: changes in the skin and subcutaneous values preceded those derived from central blood sampling.

The purpose of our investigation is to study the combined variations of FHR, fetal pH, pO_2 , and pCO_2 (arterial and tc), and their sequential interrelationships, as progressive fetal distress is produced in the pregnant dog. A previously described technique (6), consisting of intermittent occlusion of the abdominal aorta of the pregnant dog in order to reduce UBF, was used herein.

MATERIALS AND METHODS

Herein 12 pregnant dogs were prepared for maternal aortic occlusion and fetal monitoring of different parameters (FHR, tpH, tcp CO_2 , tcp O_2) following a technique previously described (5). Pregnancy in the dog lasts 9 wk and their gestational ages varied from 7 to 9 wk. All 12 dogs had similar anesthesia and surgical preparation, but the intermittent aortic occlusions were performed in only 10 dogs (Fig. 1). The last two dogs had a sham-operation during which the complete procedure on mother and fetus was performed, except there were no occlusions of the maternal abdominal aorta. Anesthesia was induced with 100 to 200 mg of intravenous sodium pentobarbital and maintained with intravenous administration of ketamine hydrochloride (1 mg/kg of body weight) and relaxation with an intravenous succinylcholine drip (500 mg in 500 ml normal saline solution). An endotracheal tube was placed and connected to a Harvard respirator. The abdominal aorta was exposed extraperitoneally following a technique previously described (6, 7), and a vascular occluder (Rhodes, Woodland Hills, CA) and an electromagnetic flow probe were placed around it. A uterine horn was exposed through a laparotomy incision and was incised over the lower back of one of the fetuses. A polyvinyl catheter was inserted into a fetal femoral artery and advanced into the descending aorta. The incised uterine edges were sutured in a circular manner to the back of the fetus, exposing a circle of fetal skin about 5 cm in diameter, onto which tcp O_2 , tcp CO_2 , and tpH electrodes (Kontron, Everett, MA) were implanted. Careful manipulation reduced amniotic fluid loss to a minimum (less than 2 ml). The tcp O_2 , tcp CO_2 , and tpH electrodes, each previously calibrated with two media of known concentration, were implanted on the fetal skin according to previously described protocols (6, 7). Two

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Reprint requests: M. Maurice Abitbol, M.D., Department of Obstetrics and Gynecology, the Jamaica Hospital, 89th Avenue and Van Wyck Expressway, Jamaica, NY 11418.

ECG electrodes were fixed through the uterine wall onto the fetal shoulders, and connected to a cardiograph (6, 7).

The femoral artery catheter was connected through a three-way stopcock to a 0.9% NaCl solution (containing 1 U of heparin/ml) and delivering the solution at a speed of 1 ml/h) and to a Statham pressure transducer. For fetal blood gas analysis, 0.08 to 0.1 ml of fetal blood was drawn before, in the middle, and at the end of each experiment. This represented a negligible amount of blood loss inasmuch as it did not result in any changes in the studied parameters of the sham-operated fetuses. The blood gases and pH were determined on an automatic blood gas analyzer (Instrumentation Laboratory 1302, Lexington, MA) which was calibrated before use and gave accurate measurements with amount of blood as small as 0.08 to 0.1 ml. The experimental procedure was started after tpH, tcpO₂, and tcpCO₂ digital displays remained stable for at least 15 min, and all parameters to be studied were within normal limits. The four sensors (FHR,

tcpCO₂, tcpO₂, and tpH) were connected to a four channel recorder (Sensor Medics, Anaheim, CA).

The maternal aorta was rapidly and totally occluded for successive episodes of 1 min each, these episodes being separated by various periods of rest: 4, 3, 2, and 1 min in each group of two dogs. For the last two dogs the occlusions were extended over a 2-minute period separated by a period of 1-min rest. These occlusions were repeated until the tissue pH reached a value close to 7.05. At this point the fetus was allowed to recover for 1 h during which all variables returned to normal. In three cases, oxygen was added to the inspiratory gas of the dog to facilitate recovery. This entire cycle was repeated twice.

After completion of the experimental protocol (once all values had returned to normal) the fetus with the implanted electrodes was delivered and an Apgar score was determined at 5 min of life. This score was adapted from the original criteria as defined by Virginia Apgar (8), except that the color was evaluated on the neonatal tongue rather than the skin. At the end of each study, the animals were put to sleep with intravenous pentobarbital. All electrodes were removed for recalibration and to determine any drift.

RESULTS

The data are summarized in Table 1. FHR had a mean value of 154 (± 4 SEM) beats/min before the aortic occlusions. It dropped to 104 (± 9 SEM) during the deceleration when tpH was near 7.05 and it was 158 (± 3 SEM) after recovery. With the aortic occlusions, pO₂ and pH went down, whereas pCO₂ went up. The specific relationships between these data will now be described.

Differences between tissue and blood variables (Table 1). Initially the arterial blood pO₂ and pH were slightly higher, and the arterial blood pCO₂ slightly lower than the corresponding t and tc values. The mean blood and t-tc values were, respectively, 35 (± 2 SEM) and 33 (± 2 SEM) mm Hg for pO₂, 41 (± 3 SEM) and 44 (± 2 SEM) mm Hg for pCO₂, and 7.33 (± 0.02 SEM) and 7.30 (± 0.03 SEM) for pH. With increased hypoxic stress, the differences increased markedly and reached their greatest values at the maximum of hypoxia: at this stage, the respective blood and t-tc values were 19 (± 3 SEM) and 10 (± 1 SEM) mm Hg for pO₂, 72 (± 5 SEM) and 112 (± 7 SEM) mm Hg for pCO₂, and 7.18 (± 0.05 SEM) and 7.05 (± 0.07 SEM) for pH. After recovery, all values returned more or less to the original values: 37 ± 2 and 34 ± 2 SEM for pO₂, 37 ± 3 and 40 ± 3 SEM for pCO₂, and 7.32 ± 0.02 and 7.30 ± 0.06 SEM for pH.

Patterns of response to repeated aortic occlusions. Five different

Fig. 1. After exposing the maternal abdominal aorta, a vascular occluder and flow probe are placed around it and connected to a flowmeter (bottom left). The fetal skin is exposed and the following sensors are placed on it (from left top to right bottom): 1) catheter from fetal femoral artery, connected to a pressure transducer; 2) two fetal EKG electrodes (magnified on bottom right); 3) tissue pH electrode; 4) tcpO₂ electrode; 5) tcpCO₂ electrode. All these electrodes are connected to the four-channel recorder on right.

Table 1. Summary of fetal data

Before experiment								Condition when tpH was 7.05								End of recovery					
Dog	FHR	Blood pH	tpH	Blood pO ₂	tc pO ₂	Blood pCO ₂	tc pCO ₂	FHR	Blood pH	tpH	Blood pO ₂	tc pO ₂	Blood pCO ₂	tc pCO ₂	FHR	Blood pH	tpH	Blood pO ₂	tc pO ₂	Blood pCO ₂	tc pCO ₂
1	155	7.34	7.34	38	35	38	39	40	7.18	7.06	21	10	68	108	148	7.28	7.32	43	36	40	40
2	162	7.36	7.34	23	21	42	48	100	7.17	7.06	12	6	54	78	155	7.33	7.29	25	24	39	45
3	159	7.28	7.24	27	25	46	49	112	7.16	7.04	17	9	82	135	164	7.31	7.28	34	34	46	48
4	148	7.38	7.37	41	41	32	34	91	7.19	7.08	22	14	77	113	157	7.37	7.34	42	40	35	37
5	163	7.31	7.28	38	36	44	50	140	7.17	7.03	22	12	98	159	165	7.31	7.30	47	40	22	25
6	149	7.38	7.32	41	40	38	40	105	7.16	7.04	18	9	61	91	149	7.32	7.29	34	31	37	42
7	142	7.32	7.30	42	38	45	45	98	7.15	7.03	16	7	95	132	158	7.35	7.30	46	39	26	31
8	155	7.36	7.34	35	31	45	47	100	7.20	7.11	18	10	61	105	152	7.28	7.28	34	30	39	40
9	151	7.39	7.24	30	26	34	35	130	7.20	7.06	20	12	54	90	153	7.29	7.28	36	35	37	39
10	158	7.29	7.24	33	32	45	50	127	7.17	7.05	19	11	70	105	160	7.36	7.30	32	29	50	55
Mean	154	7.33	7.30	35	33	41	44	104	7.18	7.05	19	10	72	112	158	7.32	7.30	37	34	37	40
±SEM	±4	±0.02	±0.03	±2	±2	±3	±2	±9	±0.05	±0.07	±3	±1	±5	±7	±3	±0.02	±0.06	±2	±2	±3	±3

* Dog 1 is shown in Figure 2; dog 5 is shown in Figure 3; and dog 8 is shown in Figure 4. FHR in beats/min; values in middle column are the deepest drop during late deceleration. pO₂ and pCO₂ in mm Hg. *t* test: *p* < 0.001 when comparing data before experiment to data at tpH 7.05, or when comparing data at tpH 7.05 to data after recovery. When comparing data before experiment to data after recovery, *p* NS.

Table 2. Relationship between patterns of cyclic anoxia and different components of fetal distress*

Dog	Cycling pattern		Time to reach tpH 7.05	Successive time periods for appearance of variation in: recovery					
	Occlusion	Rest		TcpO ₂	Late deceleration	TcpCO ₂	tpH	tpH:7.05	Recovery time
1	1	4	174	66	18	12	18	60	42*
2	1	4	216	54	30	28	16	88	54
3	1	3	202	50	36	28	36	52	82
4	1	3	180	42	32	32	16	58	56
5	1	2	118	30	28	14	18	28	30*
6	1	2	86	22	18	6	10	30	54
7	1	1	66	12	10	12	16	16	28*
8	1	1	42	12	4	4	2	20	32
9	2	1	36	2	0	6	10	18	70
10	2	1	50	4	2	4	12	28	48

* All times are given in min. For dog 1 for instance, with a cycling pattern of one minute occlusion with 4 min rest, it took 174 min to reach tpH 7.05, divided as follows: 66 min for tcpO₂ to start showing a noticeable drop; then another 18 min for the late deceleration to first appear; then another 12 min for tcpCO₂ to start going up; then another 18 min for tpH to start going down; and finally another 60 min for tpH to reach 7.05.

† Recovery time: From tpH = 7.05 to return to original value, without or with (*) oxygenation.

Fig. 2. One-min aortic occlusion with 4 min rest. From left to right: A, TcpO₂ shows cyclic variations with return to normal before the next occlusion (first three occlusions on the left). B, the cyclic variations of tcpO₂ are at a lower level. Note appearance of late deceleration first progressively increasing in severity, then taking on stable pattern (next four occlusions, in the middle). C, in addition to late deceleration, tcpCO₂ demonstrates a temporary rise after each occlusion. TcpCO₂ does not completely return to normal after the occlusion (second occlusion from the right). D, TcpO₂ is now stabilized a low level. There is a progressive drop in tpH almost symmetric and opposite to tcpCO₂ variations (last occlusion on right).

periods were identified in succession (Table 2). 1) A latency period during which none of the four recorded variables (FHR, tpH, tcpO₂, tcpCO₂) showed noticeable changes. 2) TcpO₂ was the first to change. With each aortic occlusion TcpO₂ declined rapidly, and this was followed by a slow recovery when the aortic occlusion was lifted. TcpO₂ did not completely recover by the time the next occlusion occurred, and it eventually reached a lower plateau with a cyclic pattern (Figs. 2 A and B, 3, 4). 3) A FHR late deceleration appeared once tcpO₂ reached a lower level. A lag period of several seconds between the beginning of the aortic occlusion and the beginning of the FHR deceleration was evident. The depth of the deceleration varied from one animal to another and from one occlusion to another (Figs. 2B and 4). 4) TcpCO₂ began to increase after tcpO₂ had reached a lower level. TcpCO₂ variations could also be cyclic. Similar to tcpO₂, recovery was not complete (Fig. 2 C and D); but differently from tcpO₂, there was no plateau achieved, and tcpCO₂ kept increasing as long as the aorta was repeatedly occluded (Figs. 3 and 4). 5) TpH was the last variable to show deterioration, decreasing until the aortic occlusions were discontinued when tpH reached 7.05. The drop in tpH was straight or irregular (Figs. 3 and 4).

Severity of responses. Whereas the five successive patterns were seen in all fetuses, each episode was shorter when aortic occlu-

Fig. 3. One-min occlusion, with 2 min rest. TcpO₂ decreases cyclically to a lower level with each occlusion. FHR shows a mild late deceleration followed by a reactive tachycardia with each occlusion. After a delay in relation to tcpO₂ drop, tcpCO₂ goes up continuously. After a delay in relation to tcpCO₂ rise, tpH begins to fall continuously. TcpCO₂ was rescaled after fourth occlusion because it went off scale.

Fig. 4. One-min occlusion with 1 min rest. tcpO_2 stabilizes at a lower level with minimal variations and FHR late decelerations increase in severity. The delayed rise in tcpCO_2 and further delayed drop in tpH are almost symmetrically opposite. The recovery follows a reverse pattern.

Table 3. Range of maternal parameters during protocol*

Dog	BP (mm Hg)	Pulse (min)	Blood pH (mm Hg)	Blood pO_2 (mm Hg)	Blood pCO_2 (mm Hg)
1†	100/70–113/75	68–79	7.30–7.42	42–60	34–39
2	102/71–105/74	68–72	7.34–7.37	40–43	38–42
3	108/65–111/72	64–67	7.30–7.32	35–38	40–40
4	95/61–104/70	80–85	7.38–7.42	39–41	36–39
5†	100/72–110/75	65–76	7.29–7.39	45–54	35–45
6	93/60–97/65	72–77	7.40–7.44	38–41	37–40
7†	95/64–104/70	64–82	7.35–7.44	42–57	34–42
8	104/70–105/72	75–76	7.32–7.33	42–44	38–39
9	105/70–108/70	67–70	7.30–7.33	34–38	43–44
10	93/60–98/66	71–74	7.28–7.32	40–41	42–46
Mean	100/66–106/71	69–76	7.32–7.38	40–46	38–42

* *t* test: *p* NS.

† O_2 , maternal oxygenation during recovery.

sions were divided by shorter intervening rest periods (4, 3, 2, and 1 min) (Table 2). It took 216 and 174 min to reach a tpH of 7.05 for the two dogs stressed by a 1-min occlusion with 4-min rest. In contrast only 42 and 66 min were necessary in the two dogs where the pattern was a 1-min occlusion and 1-min rest.

Recovery and delivery. The recovery period after the last aortic occlusion was characterized by a reversal of previously noted patterns; this was similar in all cases (Fig. 4). The FHR returned to normal immediately after the last deceleration. Five to 10 min later, tcpO_2 started to rise slowly and then more rapidly. When it neared its original value, tcpCO_2 started to fall. Two to 3 min later, tpH started its upward return to normal. The recovery curve of tcpO_2 , tcpCO_2 , and tpH seemed to be both steady and regular. Maternal administration of oxygen, when added to the inspiratory gas through the Harvard respirator, consistently enhanced the recovery.

After the aortic occlusions were discontinued and all the values had returned to normal, the fetus under study was delivered and all the electrodes were removed. All such fetuses started to breathe spontaneously and were given an Apgar score at 5 min of life which varied between 7 and 10. Recalibration of the continuous electrodes after removal showed minimal drift (less than 10%) as in our the previous report (5).

Sham operation. In the two control dogs with sham operation, only minimal variation in FHR, pO_2 , pCO_2 , and pH (arterial blood as well as tc) were noted over 4 h of continuous observation, indicating no fetal deterioration during these studies.

Maternal status during the experiments. All parameters of

maternal condition including blood pressure, heart rate, pH, pO_2 , and pCO_2 , were found to remain stable and within normal limits throughout each experiment. These are summarized in Table 3.

DISCUSSION

From the observations previously reported (5) and from those reported herein it may be concluded that alterations in pO_2 , pCO_2 , and pH appear first and are more accentuated with the tc sensors, and appear later in blood drawn from the abdominal aorta. The other conclusion is that, with repeated aortic occlusions in the pregnant dog, the fetus will display a progressive state of compromise characterized by the following sequence. 1) An initial fall in tcpO_2 , then in arterial pO_2 ; 2) FHR decelerations; 3) tcpCO_2 , then arterial pCO_2 rise; 4) TpH , then arterial pH fall.

The presence of hypoxia before hypercarbia and the appearance of both first in tc tissues then in arterial blood can be explained the following way: O_2 variations are not buffered, whereas CO_2 variations are, and buffer mechanisms are more sophisticated in blood than in tissues. Physiological variations in oxygenation are therefore wider and become manifest more rapidly. When the lower limit of these physiological variations has been reached, FHR may have already responded with a deceleration which, in this early stage, is of limited clinical significance. On the contrary, CO_2 and pH variations appear much later after they have exceeded buffer mechanisms. Consequently they indicate a greater severity of distress.

How much of these observations can be applied to human

conditions? It is very difficult to compare the effect of occlusion of the abdominal aorta in the pregnant dog to the effect of the contracting uterus in pregnant women because the experimental conditions and the clinical situation are too dissimilar. However, it is well known that FHR late deceleration is a relatively rapid and early response to hypoxia and is not associated initially with acidosis (9). The drop in arterial pH beyond that seen during normal labor is an advanced sign of fetal distress, as it is the final component of the previously described sequence. The clinical observation that some late decelerations are not associated with a pH drop, whereas others are, now becomes clear: the former precede the latter. It is difficult to differentiate fetal "stress" from "distress" solely on the appearance of the late deceleration (10, 11).

Another logical conclusion that can be applied to the human condition is that fetal hypoxia initially affects nonvital organs such as skin and subcutaneous tissue, then vital organs such as the heart: this may explain the late aspect of the FHR deceleration, but other mechanisms are likely (12).

Several researchers have studied fetal distress in pregnant animals, using different modalities to interrupt uterine blood flow. Wilkening and Meschia (10) and other authors have generally used chronic preparations. The acute surgical preparation presented herein was done under general anesthesia, raising the question of how much the insults of surgery and anesthesia may have affected the physiological responses of the fetal dog.

There is a vacuum of information about that interval between the earliest (late FHR deceleration) and the more advanced (fall in blood pH) sign of fetal compromise. The application of continuous monitoring of pH, pO_2 , and pCO_2 on the fetal scalp may be useful in filling this void. Tc electrodes are commonly used in neonatal intensive care units but their use in obstetrics has been associated with technical difficulties yet to be solved.

Hopefully, a more complete surveillance of fetal metabolism during labor will become possible, a result of which may be a

reduction in the rate of cesarean section for fetal "distress," too often solely based on the earliest appearance of a FHR deceleration. However, this type of monitoring may allow appropriate intervention before serious acidemia develops. In this way a fetus born in the best possible condition will result while maternal operative intervention is kept to the necessary minimum. The ultimate goal of a healthy mother and baby will be one step closer.

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