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Transcutaneous PO_2 and cardiovascular observations in the sheep fetus following the reduction of uterine blood flow

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The transcutaneous PO_2 ($tcPO_2$)-electrode has been widely used in the intensive neonatal care and has been proved to be a valuable method for the indirect continuous recording of the arterial PO_2 [4]. Recently it was also applied to monitor the PO_2 of the fetus during labor [4]. Information concerning the comparison of the $tcPO_2$ and the PO_2 in the fetal aorta and carotid artery and its alteration during fetal hypoxia are still lacking. The relationship of the cardiovascular response of the fetus and the $tcPO_2$ to fetal hypoxia has not been examined, too. It was therefore important to investigate the changes of the $tcPO_2$ and the fetal cardiovascular parameters simultaneously. For this purpose a sheep preparation was used to study the response of the $tcPO_2$-electrode, the PO_2 in the fetal aorta and fetal heart rate to acute alterations of uterine blood flow. It could be shown that the $tcPO_2$ responded with a delay to the alterations of the arterial PO_2. In addition it could be shown that the $tcPO_2$ was influenced by a peripheral vasoconstriction that took place as a response to fetal hypoxia.

1 Material and methods

The experiments were performed on 11 near term pregnant sheep (fetal weight: range 1800–4800 g, mean 3390 g (SD 1120 g). Prior to operation the sheep was kept in a seperate room for 24 hours where it had free access to water.

1.1 Anaesthesia

Pentobarbital was given intravenously followed by a single injection of Alloferin® (ROCHE) (Alcuroniumchlorid) for relaxation. The ewe was then intubated and mechanically ventilated by an ENGSTROM respirator which maintained a positiv endexspiratory pressure ventilation and so preventing pulmonary atelectasis. Anaesthesia was maintained with 0.5% halothane in 30% oxygen balanced with nitrogen oxide. The maternal femoral artery was exposed and a catheter with an inflatable balloon advanced into the maternal aorta (Fogarty 30 F).

1.2 Preparation and instrumentation of the animal

The uterine horn was delivered by a midline abdominal incision and opened in an avascular area. The fetal leg was then delivered and the left femoral artery was isolated. Two catheters were advanced into fetal aorta, one for blood sampling, the other for the continuous measurement of fetal arterial blood pressure (FA BP) and fetal heart rate (FHR). Over the right femoral artery a fiber glass optic system was introduced into the fetal aorta. It served for the continuous measurement of the oxygen saturation (Hämoreflektometer, SCHWARZER-Corporation, Germany). The system was calibrated by the blood samples at control and at zero. After shaving the fetal head the precali-

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brated $tcPO_2$ electrode (HELLIGE. Germany) was glued to the hairfree area with Histoacryl® (BRAUN/ Melsungen).

In four additional experiments the fetal carotid artery was isolated. A T-tube was inserted so that a free flow was guaranteed. Blood samples could be drawn at the same time from the aorta and the carotid artery while the $tcPO_2$ was measured.

Uterine blood flow was reduced for three minutes to zero by an inflatable balloon which was located about 10 cm above the bifurcation of the aorta. The complete reduction of flow could be assured by the blood pressure which was measured in the aorta below the occlusion and in four experiments by measuring uterine blood flow of the right and left uterine artery, respectively, with an electromagnetic flow probe (STATHAM-Corporation).

2 Results

2.1 The transcutaneous PO_2, the arterial PO_2 in the aorta ($PO_{2,a}$) and the oxygen saturation ($SO_{2,a}$) determined continuously and by sampling

Fig. 1. shows the course of the $tcPO_2$, the arterial PO_2 and the oxygen saturation in the aorta as a response to the reduction of uterine blood flow. It is apparent that the fall of the SO_2 measured by blood sampling and by direct continuous recording shows a good correlation. The SO_2 at control was 53.4% (SD 13.4) (N = 13) and fell within 2 to 3 minutes to 5.6% (SD 3.1) and 4.1% (SD 1.9), respectively.

The $tcPO_2$ and the $PO_{2,a}$ indicate at control a difference of about 4–5 mmHg. Following the reduction of uterine blood flow the $tcPO_2$ responded after 26.6 (SD 7.9) sec, whereas the SO_2 fell after 12.3 (SD 3.1) sec. The $PO_{2,a}$ approached zero after 2 min (0.9 mmHg (SD 2.0)) whereas the $tcPO_2$ was zero after 3 min (0.4 mmHg (SD 0.7)). After the occlusion of the maternal aorta was released and uterine blood flow increased, the SO_2 rose after 23.9 (SD 14.4) sec. The rise of the $tcPO_2$ after the release of UBF was extremely delayed and occurred after 72.6 (SD 41.9) sec.

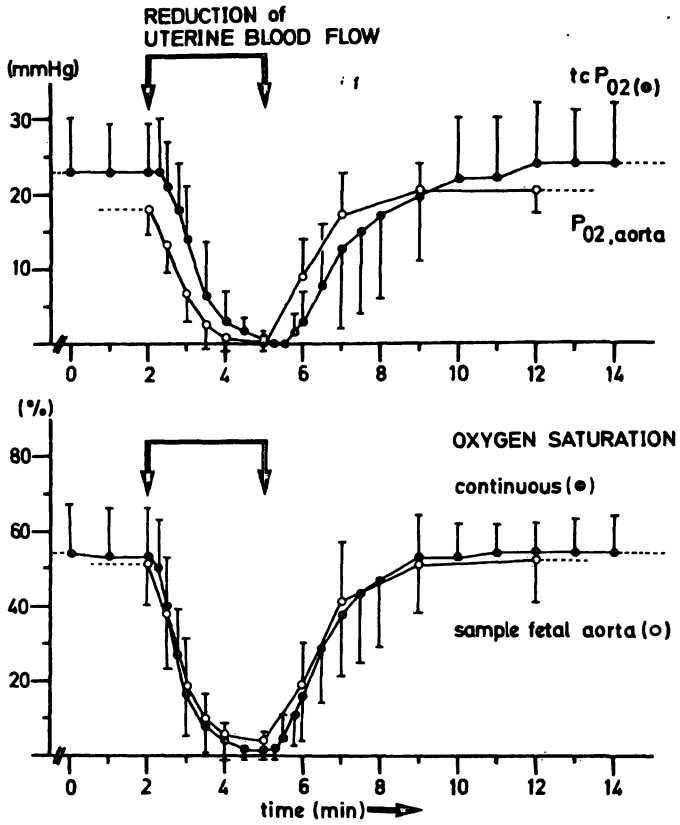

Fig. 1. The course of the transcutaneous PO_2 ($tcPO_2$), the PO_2 in the blood sample from the fetal aorta (upper part of the fig.), the continuously measured oxygen saturation in the fetal aorta and in the sample (lower part of the fig.) before, during and following the complete reduction of uterine blood flow. (Number of observations: 13; mean ± standard deviation). Note the difference between the $tcPO_2$ and the PO_2 in the fetal aorta, the delayed response of the electrode to hypoxia and during recovery.

2.2 The cardiovascular response of the fetus to the reduction of uterine blood flow

The fetal cardiovascular response to the reduction of UBF is shown in Fig. 2. The systolic blood pressure (BP) and the diastolic BP were at control 62 (SD 10) mmHg and 43 (SD 7) mmHg, respectively. Fetal heart rate (FHR) was 175 (SD 28) beats per minute. Following the reduction of uterine blood flow (UBF) the BP started to rise after 23.2 (SD 8.2) sec accompanied by an increase of the puls pressure after 31.5 (SD 10.2) sec and fetal heart rate fell after 31.3 (SD 17.3) sec. Three minutes after UBF had been completely reduced fetal heart rate was 81 (SD 30) b/min and the BP 81 (SD 22) mmHg and 51 (SD 17) mmHg, respectively. With the release of UBF FHR showed

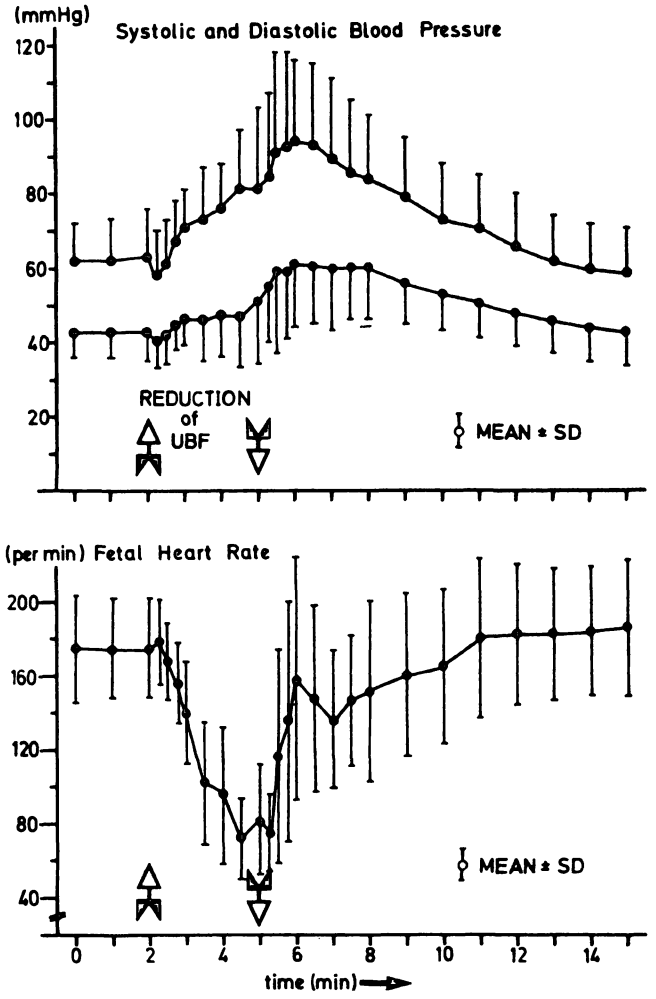

Fig. 2. Systolic and diastolic blood pressure and fetal heart rate as a response to the complete reduction of uterine blood flow. (Number of observations: 13; mean ± standard deviation). Fetal heart rate fell and the blood pressure rose at a response to the reduction of uterine blood flow. During recovery the increase of fetal heart rate was related to the decline of the systolic and diastolic blood pressure.

an immediate rise which was accompanied by an increase of the systolic and diastolic BP. During the further course the BP fell again accompanied by a normalisation of the FHR. The previous control values were achieved 7–8 min after UBF was released.

2.3 Analysis and discussion of the $tcPO_2$ measurements

Concerning the $tcPO_2$ readings three facts became apparent.

a. The delay of the $tcPO_2$-response compared to changes of the arterial PO_2.

b. the delay of the $tcPO_2$-response after fetal hypoxia during the recovery period
and

c. the difference that exists between the $tcPO_2$ and the PO_2 in the fetal aorta.

2.4 To a. The delay of the $tcPO_2$ to fetal hypoxia

The reduction of uterine blood flow (UBF) to zero interrupts the transfer of oxygen from the mother to the fetus so that the oxygen requirement of the fetus has to be covered by the oxygen which is stored in the fetal blood and in the maternal placental blood. If the oxygen consumption of the fetus remains constant a continuous fall of the PO_2 and SO_2 should occur. Compared to the continuously measured SO_2 in the fetal aorta the $tcPO_2$ fell with a delay of about 15 sec. Provided that the cutaneous blood flow is not altered during the initial 20 sec following the reduction of UBF the delay may be caused by the response time of the electrode itself and by the equilibration time between the fetal tissue and the arterialized cutaneous blood.

2.5 To b. The delay of the $tcPO_2$ after fetal hypoxia during the recovery period

The cause of the delayed response of the $tcPO_2$ after fetal hypoxic episodes is clearly indicated by the additional experiments in Fig. 3. Uterine blood flow was reduced for 2 min to zero. Fetal blood pressure rose and fetal heart rate fell as a response to the declining PO_2. A normalization of the arterial PO_2 took place within 2 to 3 min after the reduction of flow was released. The $tcPO_2$ however reached the range of the control 5 min late.

It is well known that during hypoxia catecholamines are released [2] and that this may account for a vasoconstriction that takes place in the peripheral circulation. The reduced blood flow under the $tcPO_2$-electrode may then be responsible for the delayed $tcPO_2$ normalization after hypoxic episodes.

To prove the influence of the catecholamines on the $tcPO_2$ Norepinephrine was given intravenously

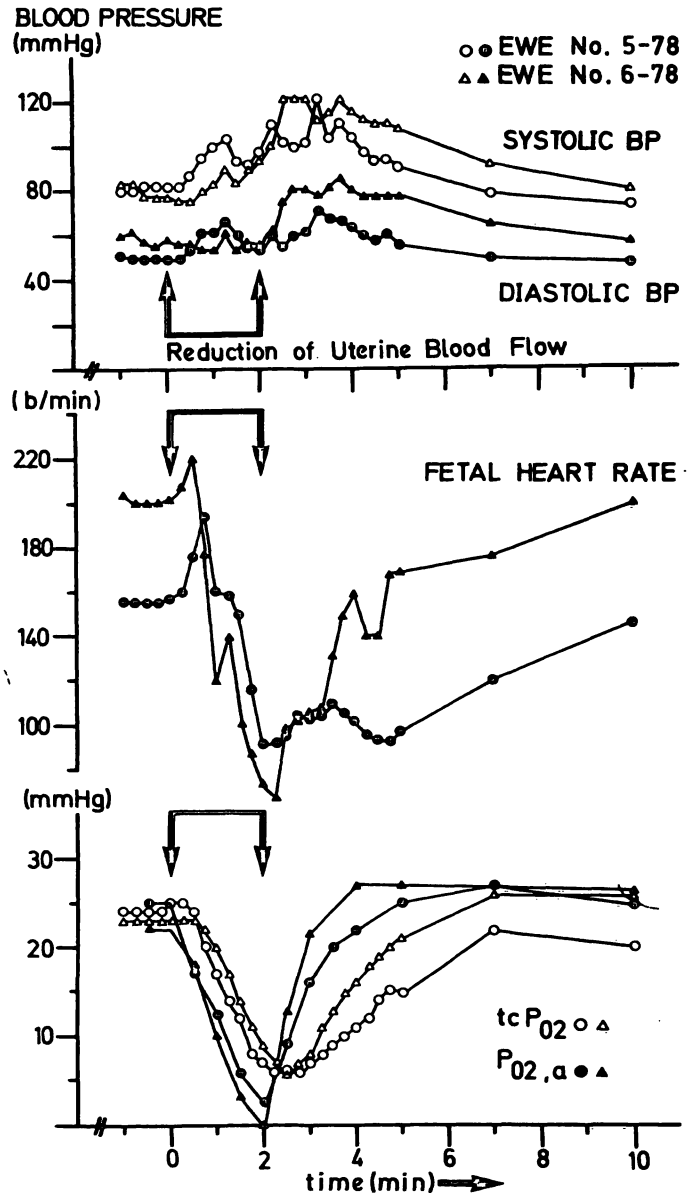

Fig. 3. Systolic and diastolic blood pressure, fetal heart rate and the transcutaneous PO_2 ($tcPO_2$) and the PO_2 in the carotid artery as a response to the reduction of uterine blood flow for 2 min in ewe Nr. 5/78 and ewe Nr. 6/78. Note, that after uterine blood flow was restored, the FHR is still low, whereas the $PO_{2,a}$ is in the normal range. The $tcPO_2$ recovers simultaneously with the normalization of the blood pressure and FHR.

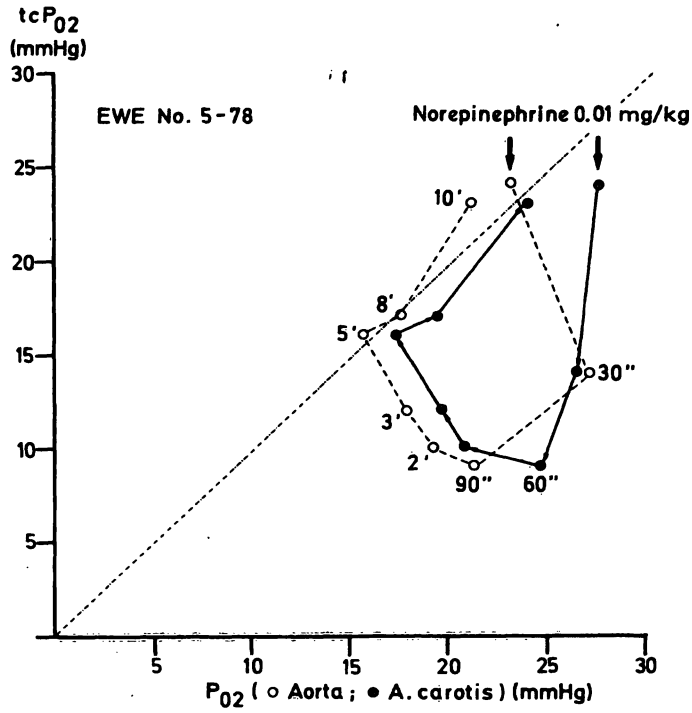

Fig. 4. The transcutaneous PO_2 versus the PO_2 in the fetal aorta (open circles) and in the carotid artery (closed circles), respectively, following a Norepinephrine-injection (0.01 mg/kg). The numbers indicate the time in sec and min following the injection. As a response to the injection of NE into the fetal vena cava the $tcPO_2$ fell without any significant change of the arterial PO_2 during the initial 60 sec. During the further course the PO_2 in the aorta and carotid artery fell, whereas the $tcPO_2$ rose. This effect was induced by the reduction of uterine blood flow which was simultaneously measured and by the release of the vasoconstriction under the electrode. With increasing utrine blood flow after 5 min the $tcPO_2$ and the PO_2 in the artery rose.
The dotted line is the line of identity.

into the fetus. In Fig. 4 the response of the PO_2 in the carotid artery and in the aorta was compared with the $tcPO_2$.

0.01 mg/kg Norepinephrine given intravenously was followed by a fall of the $tcPO_2$ without any significant alterations of the arterial PO_2 during the initial 60 sec. The delayed fall of the arterial PO_2 was due to a reduction of uterine blood flow. Despite of the fall of the arterial PO_2 the $tcPO_2$ rose again and the arterial PO_2 was 5 min after injection equal with the $tcPO_2$. During the further sequence the $tcPO_2$ as well as the arterial PO_2 rose again caused by a normalization of uterine blood flow.

2.6 To C. The $tcPO_2$-arterial PO_2 difference

It is well known for a long time that the carotid arterial blood contains more oxygen than does that in the descending aorta of the fetus (reviewed by DAWES 1968 [3]). This difference may account for the observed $tcPO_2$–$PO_{2,a}$-difference in the sheep fetus. In four preparations in addition a T-tube was inserted into the left carotid artery so

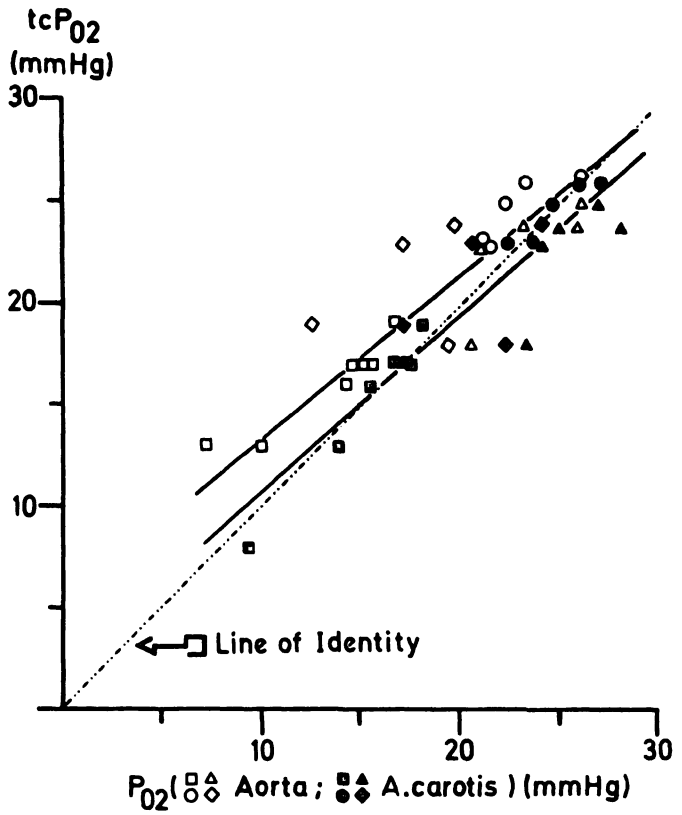

Fig. 5. The correlation of the $tcPO_2$ and the PO_2 in the aorta (open symbols) and in the carotid artery (closed symbols). Each symbol represents one animal. The broken line is the line of identity. There exists a very good correlation between the $tcPO_2$ and the arterial PO_2 (aorta and carotid artery), respectively, in the PO_2 range of 10–30 mmHg.
The calculated regression lines are:
$tcPO_2 = 2.04 + 0.87 \cdot PO_{2,a.carotis}$, ($r = 0.923$; $N = 21$, $2\alpha < 0.001$); $tcPO_2 = 5.22 + 0.81 \cdot PO_{2,aorta}$, ($r = 0.8972$; $N = 21$, $2\alpha < 0.001$).

that free passage of blood to the brain was guaranteed. Blood was sampled from the carotid artery and the descending aorta simultaneously while the $tcPO_2$ was measured. In Fig. 5 the $tcPO_2$ is plotted against the PO_2 in the carotid artery. It is obvious that the $tcPO_2$ is very close correlated to the PO_2 in the aorta by about 2 mmHg and that may be the reason for the observed $tcPO_2$–$PO_{2,a}$-difference.

3 General discussion

For fetal surveillance each tool is appreciated that delivers more information concerning the fetal condition during labor as at the present state available. The $tcPO_2$-electrode, applied by HUCH and others (reviewed by HUCH et al., 1977 [4]) to the fetus during parturition seems to give such additional information.

That the PO_2 of the fetus falls during labor especially during the second stage is known since it was possible to analyze the blood from the fetal scalp [1,6,7]. The $tcPO_2$ recording has however evidenced that during contraction the PO_2 falls. In this context two questions should be discussed more extensively:

a. Which additional information do we have in hand by recording the $tcPO_2$ compared to fetal heart rate
b. Which errors may be created by concluding from the $tcPO_2$ reading to the pathomechanism of fetal heart rate deceleration.

To a.:
Uterine blood flow is reduced during each uterine contraction and parallel to the reduced blood supply to the uterus the fetal PO_2 falls.
In Fig. 1 it is demonstrated that the reduction of flow is followed by the decline of the arterial PO_2 and $tcPO_2$. Heart rate fell and blood pressure rose simultaneously indicating the reduced fetal O_2 supply. Despite the delayed response of the $tcPO_2$ the fall of fetal heart rate reflected the fall of the PO_2 in the fetal circulation.
Even during recovery the increase of the heart rate was related to the rise of the oxygen saturation. After the reduction of flow was released, the SO_2 started to rise after 23.9 (SD 14.4) sec and heart rate after 31.6 (SD 17.3) sec. The increase of the $tcPO_2$ was however extremely delayed: 72.6 (SD 41.9) sec. **If the course of the $tcPO_2$ however is compared with the course of the blood pressure it can be seen that the $tcPO_2$ is reflected by the blood pressure and similar to the fetal heart rate.** That seems to prove that at normal "central" arterial oxygenation the peripheral circulation is still reduced and this may be also valid for other organs. So far, **the $tcPO_2$ measurement shows very clearly that the delayed recovery of the fetal heart rate is related to the extreme secretion of catecholamines during hypoxia resulting in peripheral vasoconstriction and elevated blood pressure.** Despite the restored central oxygenation it may be

suggested that fetal heart rate, fetal blood pressure and also $tcPO_2$ come back to control values if the response of the catecholamines in the peripheral circulation disappears. The additional information we obtain by $tcPO_2$ monitoring will be to get an insight into the fetal peripheral circulation which allows us to appreciate the stress condition of the fetus.

To b.:

The fall of fetal heart rate as a response to acute hypoxia is closely related to the decline of the oxygen in the fetal blood and bound to a critical fall of the SO_2. In this context **the time at which the SO_2 falls is dependent on the fetal oxygenation before hypoxia was induced and on the oxygen consumption of the fetus** [5]. These parameters interfere with the delayed response time of the electrode.

In addition during the recovery time the increase of the heart rate is paralleled by the rise of the arterial PO_2. At this time the $tcPO_2$ is still low because it starts to rise if the vasoconstriction in the peripheral circulation changes. From this point **it may be misleading to conclude from the peripheral oxygenation that heart rate alteration are not related to fetal oxygenation.**

In summary, the $tcPO_2$ electrode applied to the fetal head is reflecting the PO_2 of the carotid artery. Under hypoxic conditions, however, the $tcPO_2$–$PO_{2,a}$-difference rises indicating the reduced blood flow and the poor oxygenation in the cutaneous tissue and probably of other organs. Fetal heart rate reflects the changes of the $tcPO_2$. This may be also valid for the human fetus. More simultaneous measurements of the $tcPO_2$ and FHR in the human are, however, necessary to find out if the $tcPO_2$ offers additional information and whether the $tcPO_2$-monitoring is a valueable tool for fetal surveillance during labor.

Summary

On 11 near term pregnant sheep the response of the fetal transcutaneous oxygen partial pressure ($tcPO_2$) was compared with the alteration of the oxygen saturation (SO_2) and the PO_2 in the fetal aorta (FA), fetal heart rate (FHR) and fetal arterial blood pressure (FA BP) following the reduction of uterine blood flow (UBF).

The FA SO_2 changed 12.3 (SD 3.1) sec and the $tcPO_2$ 26.6 (SD 7.9) sec after UBF was reduced. The $tcPO_2$ response was also delayed after UBF was restored: 72.6 (SD 41.9) sec compared to the SO_2 response: 23.9 (SD 14.4) sec. **The reduction of UBF was paralleled by a rise of the FA BP and a fall of FHR.** They were at control within 10 min after the reduction of UBF was released reflecting the normalization of the $tcPO_2$.

There was a $tcPO_2$–FA PO_2-difference which was due to the difference that exist between the carotid artery PO_2 and the PO_2 in the fetal aorta.

The delayed response of the $tcPO_2$ electrode was due to the response time of the electrode itself. The delay during the recovery period however was predominantly due to the peripheral vasoconstriction as proved by Norepinephrine injection. The $tcPO_2$ reflects very close the fall of the FA BP and the rise of the FHR during the recovery period and vice versa. The importance of the $tcPO_2$–$PO_{2,a}$ difference for the fetal condition during labor has still to be worked out.

Keywords: Cardiovascular system, fetal heart rate, fetal shock, transcutaneous-arterial PO_2 difference, transcutaneous PO_2.

Zusammenfassung

Transcutaner PO_2 und kardiovaskuläre Beobachtungen am Schaf-Feten bei Reduktion der uterinen Durchblutung
Bei 11 trächtigen Schafen wurde am Ende der Tragzeit der fetale transcutane Sauerstoffpartialdruck ($tcPO_2$) gemessen und die Änderung des $tcPO_2$ auf die Reduktion der uterinen Durchblutung mit dem Abfall der Sauerstoffsättigung (SO_2) und dem PO_2 in der fetalen Aorta (FA), der fetalen Herzfrequenz (FHR) und der Reaktion des fetalen Blutdrucks verglichen.

Durch vollständige Drosselung der uterinen Durchblutung fiel die FASO_2 in 12,3 (SD 3,1) sec. ab. Der $tcPO_2$ zeigte einen Abfall nach 26,6 (SD 7,9) sec. Nach dem Anstieg der Uterusdurchblutung war die Normalisierung des $tcPO_2$ ebenfalls gegenüber dem FA SO_2 verzögert: Nach Freigabe der Durchblutungsdrosselung stieg der $tcPO_2$ nach 72,6 (SD 41,9) sec. an, während der Anstieg der Sauerstoffsättigung bereits nach 23,9 (SD 14,4) sec. erfolgte.

Die Reduktion der uterinen Durchblutung verursachte einen Anstieg des fetalen Blutdrucks und einen Abfall der fetalen Herzfrequenz. 10 Min. nach Normalisierung der uterinen Durchblutung hatten Blutdruck und Herzfrequenz den Ausgangswert annähernd wieder erreicht. Die Normalisierung des Blutdrucks reflektierte die Normalisierung des $tcPO_2$.
Es bestand eine $tcPO_2$-FA PO_2-Differenz, deren Ursache in der Differenz des PO_2 zwischen der Arteria carotis und der Aorta bestand.

Die verzögerte Reaktionszeit des $tcPO_2$ zu Beginn der Durchblutungsreduktion ist bedingt durch die Reaktionszeit der Elektrode, während die verzögerte Normalisierung des $tcPO_2$ nach der Hypoxie in erster Linie durch periphere Vasokonstriktion hervorgerufen wurde. Dies konnte durch Injektion von Norepinephrin nachgewiesen werden.
Der Verlauf der $tcPO_2$ gibt daher einen Einblick in die kardiovaskuläre Reaktion des Feten. Es gilt daher zu prüfen, welche Bedeutung die transkutan-arterielle PO_2-Differenz für Zustand der Feten während der Geburt hat.

Schlüsselwörter: Fetale Herzfrequenz, fetaler Schock, kardiovaskuläres System, transkutan-arterielle PO_2-Differenz, transkutaner PO_2.

Résumé

Po_2 transcutanée et observations cardio-vasculaires chez le foetus de mouton a la suite de la réduction du flux sanguin uterin.
La préssion partielle transcutanée d'oxygène ($tcPO_2$) a été mesurée chez 11 moutons gravides en fin de grossesse et les variations de la $tcPO_2$ consécutives à la réduction de l'irrigation utérine ont été mises en corrélation avec la chute de la saturation d'oxygène (SO_2) et la PO_2 dans l'aorte foetale (AF), ainsi qu'avec la fréquence cardiaque foetale (FCF) et la réaction de la tension artérielle foetale.
Sous l'éffet de l'abolilion de l'irrigation utérine, la AF SO_2 chuta en l'espace de 12,3 sec. (SD 3,1). La chute de la $tcPO_2$ se produisait après 26,6 sec. (SD 7,9). Après rétablissement de l'irrigation utérine la normalisation de la $tcPO_2$ était également décalée par rapport à la AF SO_2: après libération de l'irrigation utérine la $tcPO_2$ s'élevait après 72,6 sec. (SD 41,9) alors que l'augmentation de la saturation d'oxygène se produisait déja après 23,9 sec. (SD 14,4).

La réduction de l'irrigation utérine avait pour conséquence une élévation de la tension sanguine foetale et une chute de la fréquence cardiaque foetale. 10 minutes après la normalisation de l'irrigation utérine la tension sanguine et la fréquence cardiaque avaient retrouvré leurs valeurs de départ. La normalisation de la tension sanguine reflêtait celle de la $tcPO_2$.
L'on notait une différence entre la $tcPO_2$ et la AF PO_2, dont la cause résidait en la différence de PO_2 entre l'artère carotide et l'aorte.
La réaction retardée de la $tcPO_2$ au début de la réduction de l'irrigation est liée au temps de latence de l'électrode, alors que la normalisation retardée de la $tcPO_2$ après l'hypoxie est liée avnt tout à la vasoconstriction périphérique. Ceci a pu être prouvé par l'administration de norépinéphrine.
L'évolution de la $tcPO_2$ permet ainsi une approche de la réaction cardio-vasculaire du foetus. Il s'agit donc de déterminer l'importance de la différence de PO_2 transcutanéo-artérielle sur status foetal.

Mots-clés: Différence transcutanéo-artérielle de PO_2, fréquence cardiaque foetale, PO_2 transcutanée, schock foetal, système cardiovasculaire.

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