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Uterine blood flow, oxygen uptake, and vascular resistance of pregnant sheep near term

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Reduced uterine blood flow may be caused by a reduced arterial blood pressure and by an increased uterine vascular resistance [2, 3, 4]. In addition, reduced uterine blood flow seems to occur normally during vigorous uterine contraction in the expulsive stage of labor [1].

In pregnant rhesus monkeys and in pregnant guinea pigs **uterine O_2-uptake decreases when uterine blood flow falls below about 80 ml min^{-1} kg^{-1}** [5, 7].

We were interested to know whether similar relations between uterine O_2-uptake and uterine blood flow occur in sheep, the fetal weight of which is similar to that in human. As the available data do not allow to draw conclusions on this relation we measured uterine O_2-uptake, uterine blood flow, and uterine vascular resistance in the sheep. The data should give further indications on the effect of reduced uterine blood flow on the fetus.

1. Methods

1.1 Material

11 Merino-sheep near term were used. The maternal weight was 66.6 kg (SD = 7.3 kg). The weight of the uterus was 10.3 kg (SD = 5.0 kg). The mean fetal weight was 4.4 kg (SD = 1.6 kg) and 6 sheep had one and 5 sheep had two fetuses.

1.2 Anesthesia

The sheep were anesthetized with pentobarbital (initial dose 20 mg/kg i. v.; additional infusion at a rate of 5 mg/kg/h).

Curriculum vitae

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Dissertation entitled: Uterine blood flow, uterine O_2-uptake and uterine resistance. Chief areas of interest: Fetal and neonatal physiology; in particular, gas exchange between mother and fetus.

1.3 Surgical manipulations

The animals were tracheotomized and ventilated by a Starling pump. For relaxation Alloferin was given. An electromagnetic cuff flowmeter with an inner diameter of 5 mm was put around the uterine artery. In order to prevent spasms the wall of the uterine artery and the surrounding tissue were infiltrated with a local anesthetic (Scandicain). In spite of this manoeuvre local constriction did occur. Therefore in some sheep uterine blood flow was reduced even at the beginning of the experiment. However we did not intend to present normal values of blood flow and oxygen consumption but the relation between these two parameters.

Tab. I. Uterine blood flow, oxygen uptake (both related to the combined weight of the fetus, myometrium and placenta), the arterial venous oxygen difference across the uterus, the perfusion pressure (arterial-venous blood pressure), and uterine vascular resistance.

No. of sheep / No. of measurement	Uterine blood flow	Uterine O_2-uptake	Arterio-venous oxygen difference	Perfusion pressure	Uterine vascular resistance
	$ml \cdot min^{-1} \cdot kg^{-1}$	$ml \cdot min^{-1} \cdot kg^{-1}$	ml/100 ml	mmHg	$10^4 \cdot dyn \cdot s \cdot cm^{-5} kg^{-1}$
5.1	59	3.2	5.4	55	7.45
5.2	97	4.2	4.3	89	7.34
9.1	91	4.7	4.2	123	10.81
10.1	36	1.8	5.0	51	11.33
10.2	151	8.0	5.3	104	5.51
11.1	108	7.2	6.7	90	6.66
12.1	139	6.5	4.7	97	5.58
12.2	124	4.8	3.9	100	6.45
13.1	65	5.2	7.9	101	12.43
13.2	92	6.1	6.7	111	9.65
13.3	137	6.1	4.4	119	6.95
14.1	62	2.5	4.0	111	14.31
14.2	91	2.9	3.2	113	9.93
14.3	103	5.0	4.8	105	8.15
15.1	28	1.9	6.8	97	27.71
15.2	55	3.0	5.5	110	16.00
15.3	83	3.7	4.5	102	9.83
15.4	85	4.0	4.7	105	9.88
16.1	142	4.0	2.8	91	5.13
16.2	204	5.9	2.9	91	3.57
17.1	51	3.4	6.6	105	16.47
17.2	82	4.7	5.8	106	10.34
20.1	50	2.6	5.2	97	15.52
20.2	109	3.8	3.5	96	7.05

1.4 Measurements and calculations

The blood pressure in the cannulated vessels was continuously monitored with strain gauge transducers. The O_2-concentration of the blood samples were determined with the manometric apparatus of VAN SLYKE.

The oxygen uptake of the uterus was calculated from the uterine blood flow and the O_2-concentration difference between the arterial blood and the uterine venous blood. This procedure is based on the assumption that the blood drawn from the main uterine vein is representative for the uterine venous blood. This assumption is not necessarily true and may result in some errors in determining uterine O_2-uptake.

Uterine blood flow was measured with an electromagnetic flowmeter, placed around a single uterine artery. If both uterine horns were pregnant, the measured value was related to the weight of the horn where the flowmeter was placed. X-ray photographs after injections of opaque medium into the uterine vessels have shown that the uterine arteries supply only the horn on the respective side in twin pregnancies [6]. When only one horn was pregnant (sheep Nos. 11, 12, 14, 17, and 20) the flowmeter was placed successively around the left and the right uterine artery, and the blood flow ratio of both uterine arteries was determined. During the main part of the experiment the blood flow in only one uterine artery was continuously recorded. The fetal uterine blood flow was calculated from this record, assuming a constant flow ratio of both uterine arteries.

2. Results

The data of uterine blood flow, O_2-uptake, arterial-venous O_2-concentration difference ($AVDO_2$), and vascular resistance are listed in Tab. I.

In Fig. 1 uterine O_2-uptake of pregnant sheep is related to uterine blood flow. **When the uterine blood flow was 140 ml min^{-1} kg^{-1} or more the uterine O_2-uptake was about 6 ml min^{-1} kg^{-1}.** When the **uterine blood flow was decreased below 100 ml min^{-1} kg^{-1}, uterine O_2-uptake was reduced to a nearly proportionate extent.** In Fig. 2 the $AVDO_2$ across the uterus is related to the uterine blood flow. The $AVDO_2$ was about 4.5 ml/100 ml when the uterine blood flow was between 100 and 150 ml min^{-1} kg^{-1}.

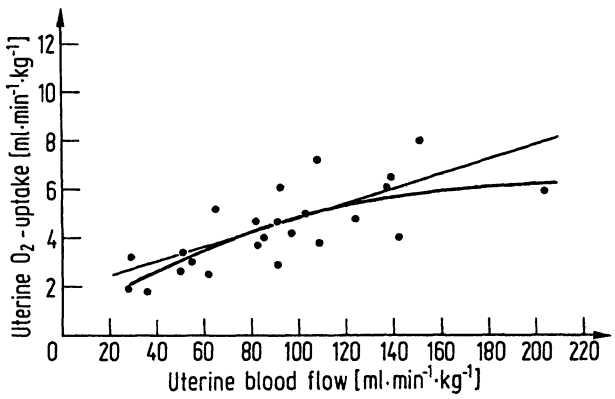

Fig. 1. Uterine O_2-uptake related to uterine blood flow in the pregnant sheep near term. The linear regression line shows that uterine O_2-uptake was significantly decreased when the uterine blood flow was reduced ($V_{UT,O_2} = 1.8 + 0.03 \cdot Q_{UT}$) ($2\alpha < 0.001$). The parabolic regression line shows the best approximation to the measured values, but there is no significant difference between these two.

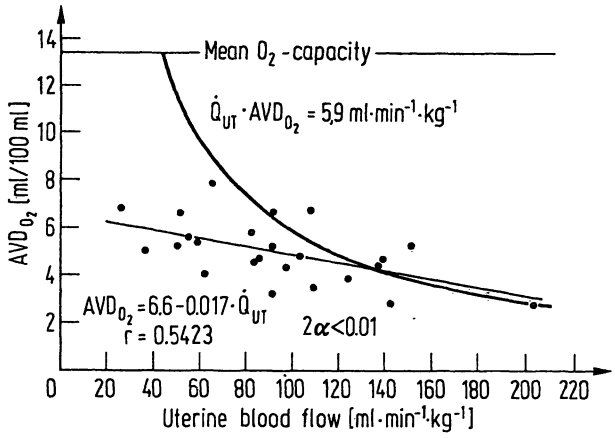

Fig. 2. $AVDO_2$ across the uterus related to uterine blood flow. The thin full line is the linear regression line adapted to the data (points). The thick full curve shows a theoretical line for the $AVDO_2$ we would expect when the uterine O_2-uptake remains 5.9 ml min^{-1} kg^{-1}. The regression line and the theoretical line deviate from each other when the uterine blood flow is below 100 ml min^{-1} kg^{-1}.

There was an inverse linear relationship between the $AVDO_2$ and the uterine blood flow. The thick line in Fig. 2 indicates the theoretical line for the $AVDO_2$ we would expect with a constant uterine O_2-uptake of 5.9 ml min^{-1} kg^{-1}. This theoretical line seems to fit the experimental data when the uterine blood flow is above 100 ml min^{-1} kg^{-1}. However, the data at flow rates between 80—100 ml min^{-1} kg^{-1} differ significantly from the line. The same is true for the values at even lower flow rates. In other words: at **flow rates above 100 ml min^{-1} kg^{-1} the uterus seems to extract the amount of O_2 from the maternal blood needed for a constant rate of O_2-uptake,** whereas at **lower flow rates the extraction becomes less;** i. e. the O_2-uptake drops.

In Fig. 3 uterine O_2-uptake is related to uterine vascular resistance. The uterine O_2-uptake was 6 ml min^{-1} kg^{-1} when the uterine vascular resistance was $2 \cdot 10^4$ dyn s cm^{-5} kg. **The O_2-uptake was reduced by 50% when the vascular resistance increased threefold.** The curve reflects the fact that those changes of uterine blood flow, that are due to changes of uterine vascular resistance, play an **important role in reducing uterine O_2-uptake.**

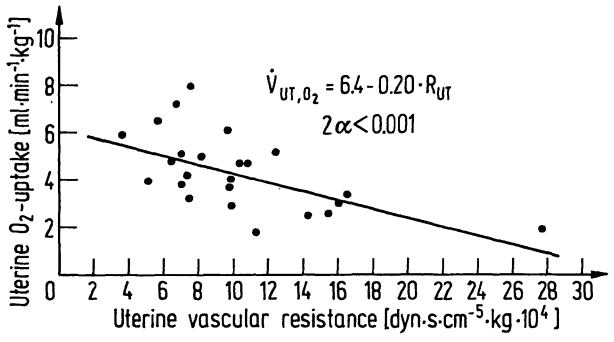

Fig. 3. Uterine O_2-uptake related to uterine vascular resistance.

3. Discussion

The present results indicate that in the sheep the uterine O_2-uptake is reduced when the uterine blood flow falls below 80—100 ml min^{-1} kg^{-1}. This finding is similar to that obtained in the rhesus monkey by PARER et al. [7] and in the guinea pigs by KÜNZEL and MOLL [5].

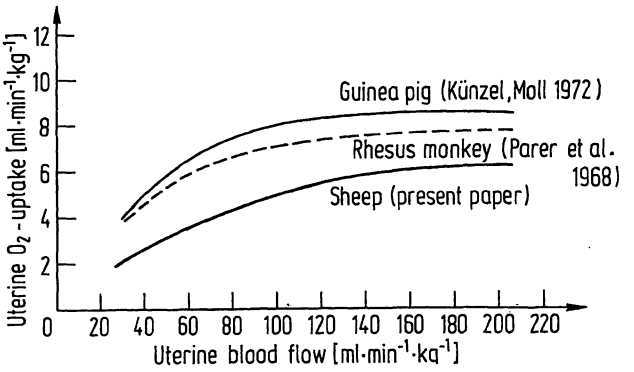

Fig. 4. Uterine O_2-uptake related to uterine blood flow in the guinea pig [5], the rhesus monkey [7], and in sheep (present paper). Parabolic regression lines are shown which were adapted to the respective data.

Fig. 4 shows the regression lines which are calculated for the data obtained in the three species mentioned above. For the sake of comparison the respective parabolic regression lines are drawn, even if only in the guinea pigs the sum of squares around the regression line was significantly reduced by replacing the linear lines by parabolic lines. It can be seen that in **all three species** uterine O_2-uptake is reduced when uterine blood flow falls below 80—100 ml min^{-1} kg^{-1}. In the view of this similarity between species differing in fetal weight as well as in placental structure **it seems likely that a similar relation between uterine O_2-uptake and uterine blood flow occurs also in man.**

Fig. 4 allows to compare uterine O_2-uptake of the three species at the same uterine blood flow per uterine weight (weight of the uterine muscle and its content, i. e. the placenta, and the fetus). The uterine O_2-consumption seems to be inversely related to the fetal weight. The sheep have the highest fetal weight and the lowest O_2-consumption per weight. On the other hand, the guinea pig and the rhesus monkey have the lowest fetal weight and the highest O_2-consumption ($2P < 0.02$). Thus we find in the fetus a similar relation between body weight and oxygen consumption per weight as in the adult.

Summary

Materials and Methods

11 pregnant sheep near term (fetal weight 4.4 kg, SD = 1.6 kg) were anesthetized with pentobarbital. Electromagnetic cuff flow meters were put around one uterine artery and the blood flow was measured. The brachial artery and the uterine vein were cannulated. The blood pressure was measured in these vessels. Blood samples were drawn, the oxygen concentrations were measured in the manometric apparatus of VAN SLYKE. From the uterine blood flow and the $AVDO_2$ across the uterus the uterine O_2-uptake was calculated.

Results and Conclusions

Uterine O_2-uptake was related to uterine blood flow **(Fig. 1). At flow rates above 140 ml min^{-1} kg^{-1} uterine O_2-uptake had a value of about 6 ml min^{-1} kg^{-1}. A reduction of uterine blood flow below 100 ml min^{-1} kg^{-1} resulted in a proportionate fall of uterine O_2-uptake.**

Uterine O_2-uptake was correlated with uterine vascular resistance **(Fig. 3).** This indicates that **flow reduction caused by an increased vascular resistance plays an important role in fetal hypoxia.**

Comparing the data obtained in guinea pigs, rhesus monkeys and sheep **(Fig. 4)** we find a similar relation between the uterine O_2-uptake and the uterine blood flow. The maximum uterine O_2-uptake per weight, however, seems to be inversely related to the fetal weight.

Keywords: Blood flow, fetus, hypoxia, oxygen uptake, uterus, vascular resistance.

Zusammenfassung

Uterusdurchblutung, Sauerstoffaufnahme und Gefäßwiderstand beim trächtigen Schaf am Ende der Tragzeit.

Untersuchungsgut und Methodik

11 trächtige Schafe am Ende der Tragzeit (Fetalgewicht 4,4 kg SD = 1,6 kg) wurden mit Pentobarbital anästhesiert. Um die A. uterina wurde ein elektromagnetisches Cuff-Flowmeter angebracht und die Durchblutung gemessen. Die A. brachialis und die V. uterina wurden kanüliert. In diesen Gefäßen wurde der Blutdruck gemessen. In den Blutproben wurde die Sauerstoffkonzentration manometrisch nach VAN SLYKE bestimmt. Aus der Durchblutung des Uterus und der $AVDO_2$ am Uterus wurde die uterine Sauerstoffaufnahme berechnet.

Ergebnisse und Schlußfolgerungen

Es bestand eine Beziehung zwischen der uterinen O_2-Aufnahme und der Uterusdurchblutung **(Fig. 1). Bei einer Durchblutung über 140 ml min^{-1} kg^{-1} betrug die uterine O_2-Aufnahme 6 ml min^{-1} kg^{-1}. Nahm die uterine Durchblutung unter 100 ml min^{-1} kg^{-1} ab, so erfolgte auch eine Abnahme der uterinen O_2-Aufnahme.**

Die uterine O_2-Aufnahme war zum uterinen Gefäßwiderstand korreliert **(Fig. 3).** Diese Beziehung zeigt, daß eine **Reduktion der Durchblutung als Folge eines erhöhten Gefäßwiderstandes eine wichtige Rolle bei der Entstehung einer fetalen Hypoxie** spielt.

Vergleicht man die Ergebnisse von Meerschweinchen, Rhesusaffen und Schafen **(Fig. 4),** so findet sich eine ähnliche Beziehung zwischen uteriner O_2-Aufnahme und uteriner Durchblutung.

Das Maximum der uterinen O_2-Aufnahme bezogen auf das Gewicht scheint jedoch eine inverse Beziehung zum Fetalgewicht zu haben.

Schlüsselwörter: Durchblutung, Fet, Gefäßwiderstand, Hypoxie, Sauerstoffaufnahme, Uterus.

Résumé

Irrigation sanguine de l'utérus, absorption d'oxygène et vasorésistance de moutons pleins à terme.

Sujets et méthodique

11 moutons pleins arrivant à terme (poids foetal 4,4 kg, SD = 1,6 kg) ont été anesthésiés au pentobarbital. On a placé un Cuff-Flowmeter électromagnétique autour de l'A. uterina et mesuré l'irrigation sanguine. Puis on a canulé l'A. brachialis et la V. uterine pour pouvoir mesurer la pression sanguine dans ces vaisseaux. Dans les épreuves de sang, on a déterminé la concentration d'oxygène selon le procédé manométrique de VAN SLYKE. On a calculé l'absorption d'oxygène utérine à partir de l'irrigation sanguine de l'utérus et l'$AVDO_2$ à l'utérus.

Résultats et conséquences

On a constaté alors une relation entre l'absorption O_2 utérine et l'irrigation sanguine de l'utérus **(Fig. 1). Pour une irrigation sanguine supérieure à 140 ml · min^{-1} · kg^{-1}, on a observé une absorption O_2 utérine de 6 ml · min^{-1} · kg^{-1}. Une diminution de l'irrigation sanguine utérine inférieure à 100 ml min^{-1} kg^{-1} entraînait une baisse de l'absorption O_2 utérine.**

On a également relevé une corrélation entre l'absorption O_2 utérine et la vasorésistance utérine **(Fig. 3).** Cette relation montre qu'une **réduction de l'irrigation sanguine consécutive à une vasorésistance élevée joue un rôle important dans la genèse d'une hypoxie foetale.**

Si on compare les résultats obtenus après examens de cochons d'Inde, de singes rhésus et de moutons **(Fig. 4),** on trouve une relation similaire entre l'absorption O_2 utérine et l'irrigation sanguine utérine.

Le maximum d'absorption O_2 utérine relative au poids semble, cependant, avoir une relation inverse avec le poids foetal.

Mots-clés: Consommation d'oxygène, foetus, hypoxie, irrigation du sang, utérus, vasorésistance.

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