Scalp Blood Flow Measured by the Xenon Clearance Technique and Transcutaneous PO₂ in the Fetal Lamb

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Summary

Scalp blood flow and transcutaneous (tc) PO₂ were measured in four fetal lambs at 130–135 days of gestation. Scalp blood flow was measured by the xenon clearance technique using a technetium source to correct for changes in distance from the detector. The effect of circular pressure, the so-called “tonsure effect” on scalp flow and tcPO₂, was evaluated by pressing a ring on the scalp. A circular pressure between 20–30 mmHg markedly reduced local scalp blood flow and was sufficient to reduce tcPO₂ to zero. We found evidence of significant recirculation of xenon in the fetal circulation indicating right-left shunting. This study showed that the tonsure effect seriously affected scalp blood flow and tcPO₂ in the fetus.

Abbreviations

OD, outer diameter
tc, transcutaneous

During labour, the presenting part of the fetus, usually the fetal scalp, offers the only direct access to fetal blood for measurement of pH and gas tensions. The validity of information obtained from that accessible capillary circulation has been questioned, because any reduction in local blood flow will result in a discrepancy between the central and peripheral parameters (12). The results of certain studies comparing scalp pH in a capillary sample taken shortly before, and cord pH values directly after delivery do not suggest a marked reduction in local scalp blood flow (2), but recently published work on tcPO₂ suggests that there is a fall in local scalp blood flow due to mechanical factors (12, 13). One of these, the so-called “tonsure effect,” is the pressure exerted by the cervical ring on scalp tissue (12). Apart from mechanical effects, other factors like hypoxemia, in particular when combined with acidemia, were found to reduce peripheral blood flow in the ovine fetus (1, 4). If the fetal scalp shares in that effect, it might reduce its value as a source of pH and blood gas values, either from a capillary sample or from tissue measurements.

To date, no reliable information on scalp blood flow has been available, though scalp blood sampling is now widely used for fetal monitoring during labour. This paper describes preliminary experience with the Xenon clearance technique for measurement of scalp blood flow in the fetal lamb. Using this method, variations in local scalp blood flow and tcPO₂ as a result of a simulated “tonsure effect” were studied.

MATERIALS AND METHODS

Four pregnant ewes of mixed breed with a gestational age of 130–135 days were used for this study. The animals were sedated

with an intramuscular injection of diazepam (2 mg/kg) and ketamine (4 mg/kg) and, after this, were placed in left lateral recumbancy and oxygen administered by face mask. Diazepam (1 mg/kg) and ketamine (2 mg/kg) were administered intravenously, and a tracheal tube inserted and connected to a McGill ventilation circuit. The spontaneously ventilating ewe received a gas mixture consisting of 5 vol % CO₂, 47.5 vol % O₂, and 47.5 vol % N₂O. If necessary, 0.1–1 vol % methoxyfluorane was added. Anaesthesia was further maintained by ketamine intravenously (2 mg/kg) every 2 h.

After local infiltration with 1% lignocain of the abdominal wall, a paramedian incision was made and the uterus was exposed. The fetal head was localized and delivered by a small uterine incision. The fetal mouth and nose were covered with a glove filled with warm saline solution. The skin and subcutaneous tissues overlying the left carotid artery were infiltrated with 1% lignocain and the vessel was catheterised. The catheter was connected to a Statham pressure transducer for measurement of the fetal arterial blood pressure, and was also used for collection of fetal blood samples. An area of the fetal scalp was shaved with a small razor and a tc electrode (Radiometer E 5241) was placed on the scalp by gluing the electrode fixation ring with Loctite. The electrode was prepared and calibrated according to the manufacturer's instructions and the electrode was heated to 44°C. Contact gel was applied between the electrode membrane and the skin. The tcPO₂ electrode was connected to an oxygen monitoring system (Radiometer TCM 1).

A catheter was placed in the carotid artery of the ewe and maternal arterial blood pressure was monitored using a Statham pressure transducer. Fetal and maternal arterial blood samples were taken at regular intervals, and pH, PCO₂, and PO₂ measured using an IL 613 blood gas analyser.

Scalp blood flow was locally reduced by pressing a rubber covered brass ring (OD, 5 cm) on the skin surrounding the site of injection of the Xe and the tcPO₂ electrode. This ring was pressed on the scalp by an elastic band attached to the ring and placed under the jaws. Care was taken that the ring did not compress the jugular veins and carotid arteries. The pressure exerted by the ring on the scalp was determined by passing a thin silastic tube between the ring and the skin and measuring the pressure required to establish a flow of water in the tube. The accuracy of this method was checked by placing known weights on the ring and calculating the pressure. Local pressure on the scalp varied in this experiment between 20–30 mmHg. Cooling of the skin was prevented by covering the scalp with insulating towels.

Xenon clearance technique. About 0.05 ml of isotonic saline containing 2–8 MBq (50–200 μ Ci) of [¹³³Xe] was injected into the scalp of the fetus close to the electrode using a small hypodermic needle (OD, 0.4 mm). A small capsule containing about 2 MBq (50 μ Ci) of [^{99m}Tc] was attached to the scalp near the site

of injection. A sodium iodide scintillation detector with a crystal 5 cm in diameter was placed over the site of injection and the output was taken through amplifiers to pulse height analysers selecting the 80 KeV peak of [^{133}Xe] and the 140 KeV photopeak of [$^{99\text{m}}\text{Tc}$]. The two outputs were recorded with a dwell time of 1 min digitally on C60 cassettes and were also taken to a small computer (Commodore PET), which corrected for cross-over between the two energy windows and used the [$^{99\text{m}}\text{Tc}$] count rate to correct the [^{133}Xe] count rate for variations in distance between the fetal head and the detector (3). The rate of xenon wash out (k) was also calculated, and the corrected [^{133}Xe] count rate (C) and k were recorded on a four pen recorder together with the output from the transcutaneous oxygen electrode. The ^{133}Xe wash out rate k is given by:

$$k = \ln C_B/C_A$$

where C_A and C_B are the count rates in successive minutes. Because k is of the order of 0.01, the values were multiplied by 1000 before being printed out as relative blood flow. Data stored on cassettes were transferred to a PET computer and used to derive k for any selected series of points on the washout curve by finding a least squares fit for a straight line through points on a plot of $\ln C$ against time.

In order to eliminate the transient effects of injection trauma or vasoactive additives in the tracer solutions (11), the first 10 min immediately after the injection were not included in the studies. Repeated injections of Xenon in one animal were always carried out at different sites of the fetal scalp; moreover, to minimize the possible influence of background activity of a previous injection, the interval between subsequent injections was at least 60 min and the amount of Xenon always exceeded the previous dose by a factor of 2. On one occasion, after a series of measurements involving three injections of [^{133}Xe], fetal and maternal arterial blood samples were counted in order to estimate the level of recirculating [^{133}Xe].

RESULTS

The ring was applied to the fetal scalp with a pressure of 20–30 mmHg for 10 min in four cases. This always resulted in a

marked reduction of scalp blood flow in the area within the ring. In one case, blood flow fell to zero. The reduction in local blood flow was in all cases accompanied by a local fall in tcPO_2 to almost zero. After releasing the pressure on the ring, an initial steep rise in local scalp blood flow was observed for 5–10 min, reaching values much higher than the stabilized flow.

A representative example of the tonsure effect on blood flow and tcPO_2 is shown in Figure 1. Table 1 shows the mean values for blood flow and tcPO_2 during and after the tonsure effect together with fetal arterial pH and blood gas values. Mean values for tcPO_2 were calculated by taking samples at 1-min intervals from the tracings. In two cases the ring was applied on the scalp with a pressure of 10–15 mmHg. This did not result in any detectable reduction in local blood flow, but tcPO_2 fell initially to approximately 25% of the baseline level.

It was noticed, however, that under steady state conditions, the blood flow curve hardly ever reached a definite horizontal plateau. This observation was confirmed in one experiment where an undisturbed Xe blood flow study was obtained (Fig. 2). It is obvious that there is a slight but continuous, almost linear fall in the flow when the first 10 min are excluded. This finding cannot invalidate the observations obtained during the tonsure experiments because of the marked differences that were found.

DISCUSSION

The xenon clearance technique is widely used for blood flow studies (9), but has not proved useful for absolute measurements of skin blood flow. The blood-tissue partition coefficient is dependent upon the amount of adipose tissue, so it not only varies widely between individuals but also varies between regions of the skin on a single individual (14). Its main value is its ability to demonstrate acute changes in skin or subcutaneous blood flow.

The most striking observation of this study was the marked reduction in scalp blood flow that was found when a ring was pressed with a pressure of 20–30 mmHg on the scalp and caused tcPO_2 readings of 0. Our results corroborate the findings of Jansen and Nathanielsz (7), who used a similar technique to simulate

Fig. 1. Local scalp blood flow and transcutaneous (tc) PO_2 in the course of one experiment in an area surrounded by a ring that is pressed on the skin during a period indicated by I—I. Note the initial steep rise of the flow after the pressure is released.

Table 1. Mean ($\pm$ S.D.) values of scalp blood flow (arbitrary units) and transcutaneous (tc) PO_2 in an area surrounded by a ring pressed on the scalp and after releasing pressure. Fetal arterial acid base and blood gas values during this procedure are given on the right side. Mean tc PO_2 values were calculated by taking samples at 1-min intervals

Exp. no.		Scalp		Arterial			BE ²
		Flow	tc PO_2	pH	PO_2 ¹	PCO_2 ¹	
1	Pressure	0	0	7.27	17	51	-4.8
	Release 1st 10 min	77 $\pm$ 17	15 $\pm$ 2				
	Release 2nd 10 min	52 $\pm$ 7	17				
	Release 3rd 10 min	40 $\pm$ 6	16	7.25	15	57	-4.2
2	Pressure	15 $\pm$ 5	0	7.29	19	61	0
	Release 1st 10 min	120 $\pm$ 39	18 $\pm$ 1				
	Release 2nd 10 min	60 $\pm$ 9	21 $\pm$ 1				
	Release 3rd 10 min	46 $\pm$ 6	21	7.33	18	56	+1.1
3	Pressure	45 $\pm$ 32	0				
	Release 1st 10 min	117 $\pm$ 36	21 $\pm$ 2	7.31	23	54	-1.8
	Release 2nd 10 min	66 $\pm$ 12	21 $\pm$ 1	7.35	22	48	-0.3
4	Pressure	8 $\pm$ 3	0				
	Release 1st 10 min	59 $\pm$ 19	16 $\pm$ 3	7.37	21	51	2.4
	Release 2nd 10 min	45 $\pm$ 9	17	7.39	19	49	2.9

¹ mmHg.

² (mmole/liter).

the tonsure effect in the fetal lamb. They found that pressure on a ring reduced tc PO_2 to zero, but local blood flow was not measured in their experiments.

Blood supply to scalp tissue is unique in that it cannot be provided from underlying tissues, but has to cross the bony plate and therefore is much more susceptible to the effects of compression. The circular pressure exerted by the cervix and the birth canal on the human fetus during labour is reported to be approximately three times the intra-amniotic pressure (10). Normal blood pressure exerted on the small arteries and arterioles supplying the capillary network of the scalp is not exactly known, but will be lower than the carotid mean arterial pressure, which was about 50 mmHg in our normoxemic fetuses. Even at normal basal intraamniotic pressures of 10–15 mmHg, a considerable reduction in blood flow might occur, assuming that fetal intravascular blood pressure in the scalp is not influenced by an increase in intrauterine pressure.

The latter assumption, however, seems unlikely with the fetus *in utero* because the rise in fetal central arterial blood pressure is of the same order as the increase in intrauterine pressure and is likely to be followed by an increase in intravascular scalp pressure as well. The cervix is usually not as rigid as the ring used in this experiment, and is unlikely to exert an equally strong pressure all around. It would be unwise to extrapolate the results from these experimental studies directly to the clinical studies during labour.

The results of the present study indicate that the xenon clearance technique, when applied to the fetus, has its limitations. Although the double isotope technique of Bülow and Madsen (3) has been used with success in this laboratory (5, 8), during the present experiment there were periods of variability of flow often associated with active or passive fetal movements. This may have been due to material such as the ring used for compression scattering gamma rays from the [^{99m}Tc] into the [¹³³Xe] energy window. Movements near the detector when taking blood samples may also have caused changes in recorded flow, as well as movements of the insulating towels which may have produced changes in scalp temperature. Changes in skin temperature can be an important factor in the measurement of skin blood flow (6). The oxygen electrode has its temperature stabilised, but an experiment on the forearm of one of the authors (J.C.W.C.) showed that when xenon is injected under the electrode, some of it is absorbed by the electrode. When the animal was left

Fig. 2. Undisturbed flow pattern in the fetal scalp measured with the xenon clearance technique over a period of 30 min. As in all other experiments in this study, the first 10 min after the injection were excluded.

undisturbed for 30 min, a smooth curve of blood flow against time was obtained (Fig. 2).

One advantage of xenon as a tracer for blood flow experiments is due to its low solubility in blood. Most of the tracer is lost in a single passage through the lungs, almost eliminating recirculation. We observed that the flow curve never reached a plateau, suggesting significant recirculation. This was confirmed by taking fetal and maternal arterial blood samples after an experiment involving three injections. The fetal blood sample has a significant level of xenon activity whilst the maternal sample did not. Exchange in the placenta is via a blood/blood interface rather than a blood/air interface of the lung, whilst mixing of arterial and venous blood is a characteristic of fetal circulation, so recirculation of xenon is likely to occur in the fetus. The xenon clearance technique does not therefore provide a suitable method for the detection of smaller variations in skin blood flow in the fetus.

In conclusion, this study revealed that blood flow in the fetal scalp can markedly be reduced when a circular pressure between 20–30 mmHg is exerted on the skin and that this is sufficient to reduce tc PO_2 to zero.

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The Influence of Age on Acute Renal Toxicity of Uranyl Nitrate in the Dog

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Summary

The influence of age upon uranyl nitrate (UN) induced acute renal failure (ARF) was evaluated in 30 canine puppies 1–2 wk and 3–5 wk old. Renal function and morphologic studies were performed 2 h (initiation phase) and 24 h (maintenance phase) after UN administration. Age-matched controls received vehicle alone. Administration of UN to 1–2-wk-old puppies produced no changes in whole kidney glomerular filtration rate (GFR), despite a significant reduction in renal plasma flow (RPF) ($P < 0.01$). In contrast, during the maintenance phase, GFR was 60% lower than in the control group ($P < 0.02$) whereas values for RPF were nearly identical to control values. In 3–5-wk-old puppies the magnitude of response to the heavy metal was much greater and GFR was nearly completely suppressed during the maintenance phase. This major alteration of GFR was independent of changes in RPF, because RPF remained similar to control values.

Morphologic alterations consistent with the nephrotoxic effects of UN were observed in the proximal tubules of the most differentiated nephrons. These age-related morphologic alterations correlated well with the functional response (GFR) observed after UN administration, *i.e.*, a proportionately greater degree of both morphologic and functional alterations followed the administration of the heavy metal in the oldest group of puppies.

Abbreviations

ABG, arterial blood gas
ARF, acute renal failure
5% D in 1/3 NS, 5% dextrose in 1/3 normal saline solution
FENa, fractional excretion of sodium

FF, filtration fraction
GFR, whole kidney glomerular filtration rate
MAP, mean systemic arterial pressure
RBF, renal blood flow
RPF, renal plasma flow
UKV, urinary potassium excretion
UN, uranyl nitrate
UNaV, absolute urinary sodium excretion
V, urinary flow rate

Abundant experimental evidence on the pathogenesis of nephrotoxic forms of acute parenchymal renal failure has been obtained mainly from studies using mature mammals. These studies have examined the mechanisms by which antibiotics and heavy metals induce ARF (4, 7, 10, 11, 24); however, little attention has been given to the pattern and pathogenesis of nephrotoxic ARF in the developing mammal. There is some clinical and experimental evidence suggesting that the immature kidney is more tolerant to the nephrotoxic effects of aminoglycosides than its adult counterpart (9, 19).

It is well established that during the period of maturational growth, developmental changes occur in the perfusion of superficial glomeruli, distribution of renal blood flow, and in tubular transport (1, 2, 13–16, 20, 21, 25). Age-related differences in sensitivity to nephrotoxic agents could arise from the normally occurring differences in renal function in the developing mammal. UN-induced ARF has been well characterized in the mature mammal (7, 10, 11, 24). The present investigation, therefore, was undertaken to further explore and delineate the influence of age upon UN-induced ARF in the immature dog.