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Cortical Blood-flow in the Porcine Kidney

A Radioactive Microsphere Study

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Summary. Renal cortical blood-flow distribution was measured by means of radiolabeled microscopheres in eight kidneys from 4 pigs of mixed Yorkshire and Danisk landrace. We found a pronounced intracortical variation in the perfusion pattern of 28 sections of outer cortex. Three consequetive flow determinations with an interval of 45 minutes showd that the heterologous perfusion pattern was plastic, changing between the flow-determinations. In addition, we found a significantly reduced perfusion in the renal poles, compared to the rest of the outer cortex. It is speculated that the reduced polar perfusion is a contributing aetiological factor to the increased incidence of polar scar formation secondary to reflux nephropathy.

Key words: Renal blood flow – Radiolabelled microspheres – Porcine kidney

Introduction

In clinical practice kidney perfusion and to some extent kidney function is considered to be equally distributed across the parenchyma. The uneven distribution of lesions due to vesico-ureteral reflux (VUR) and/or obstruction suggests that the susceptibility of the parenchyma may vary from area to area, and in preliminary studies we found that the perfusion may vary across the parenchyma as detected by gamma scintigraphy, and may change from time to time in repeated investigations. We undertook the present study using radioactive microspheres in order to see whether such variations in perfusion across the cortical parenchyma occur within a short range of time, and whether systematic regional variations are present.

Materials and Methods

Eight kidneys from 4 pigs of mixed Yorkshire and Danish landrace breed weighing between 25 and 29 kg were investigated. The animals were anaesthetized with intramuscular Midazolam (15 mg) and ketamine hydrochloride (Ketalar) 300 mg, and anaesthesia was maintained by a continuous infusion of Ketamine, Midazolam and pancuronium. After intubation controlled ventilation was obtained using a respirator. Volume, frequency and admixture of oxygen were guided by arterial gas analysis. Catheters were introduced into the abdominal aorta and into the left ventricle via the femoral arteries using X-ray control.

After the surgical preparation the animals were equilibrated for 45 min wrapped in thermofoil.

The blood flow measurements were performed using styrene-divinyl benzene ion-exchange 15 ± 1.5 micron microspheres (MS) uniformly labeled with either Ruthenium-103, Scandium-46 or Cerium-141, coated with polymeric resin (New England Nuclear), and suspended in 10% Dextran (MW 70,000) with 1% Tween-80 added. After vigorous shaking for 5 min a vial containing 300 μCi equal to 12×10^6 MS was injected into the left ventricle catheter within 15 s. Then the catheter was perfused with bodywarm saline. Through the catheter in the abdominal aorta reference blood sampling was performed using a roller pump.

Each animal underwent 3 isotope injections. The first was performed 45 min after the surgical preparation followed by the second and the third with an interval of 45 min.

Immediately after the experiment the animal was sacrificed and the kidneys were removed, frozen and sectioned. Each kidney was divided into 28 pieces from outer cortex. The inner cortex and medulla were likewise sectioned and analyzed. After cutting, the pieces were weighed and analysed in a gamma-counter (Packard Auto Gamma 5650). Blood flow distribution was calculated using the formula

$$F_i = N_i \times RF/A_t$$

where F_i is the flow in the investigated region (ml/min/g) and N_i the activity of the isotope in the investigated region (counts/min/g), RF the aspirated volume in the reference sampling and A_t the total activity in RF (counts/min).

Statistics

The blood flow in each piece of kidney cortex was calculated for each isotope. Intra-cortical variation and variation from left to right was calculated for each animal and each isotope by way of computerized analysis of variance

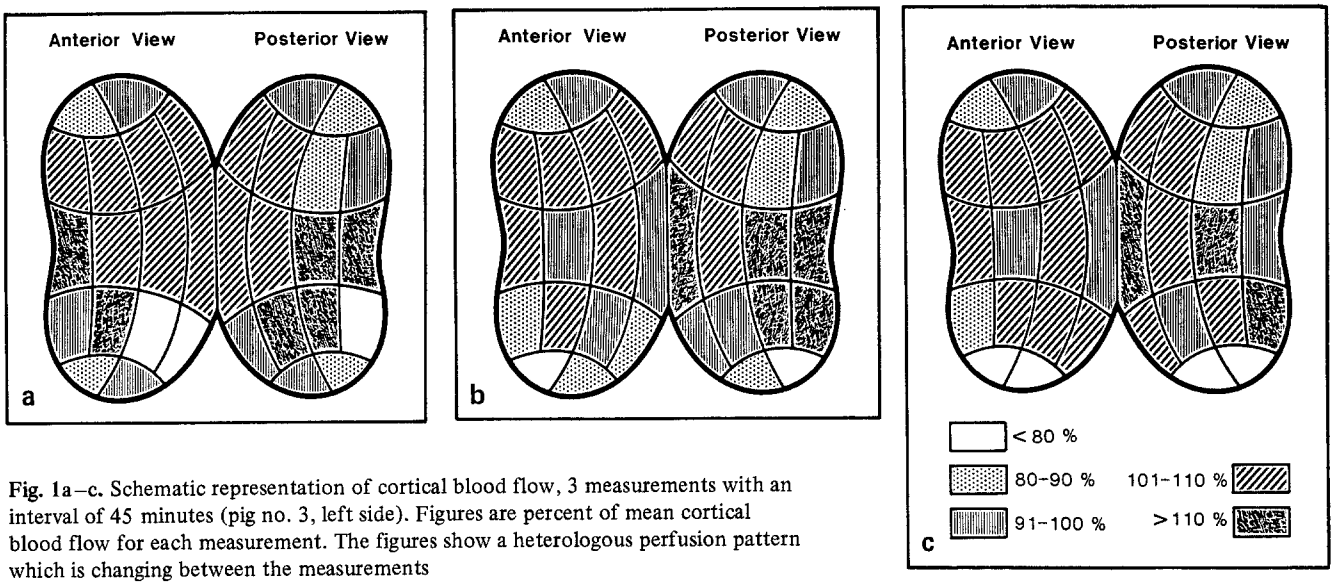

Fig. 1a–c. Schematic representation of cortical blood flow, 3 measurements with an interval of 45 minutes (pig no. 3, left side). Figures are percent of mean cortical blood flow for each measurement. The figures show a heterologous perfusion pattern which is changing between the measurements

Table 1. Renal cortical blood flow in pole-area (a) versus rest of outer cortex (b). Figures are ml/min/g tissue weight, mean of left and right side together, standard deviation in parenthesis

Pig no.		Isotope no.		
		1	2	3
1	a:	2.59 (0.17)	2.73 (0.18)	2.84 (0.21)
	b:	2.89 (0.13)[a]	3.02 (0.10)[a]	3.08 (0.13)[a]
2	a:	2.21 (0.14)	2.54 (0.10)	2.69 (0.11)
	b:	2.33 (0.20)	2.67 (0.33)	2.84 (0.32)
3	a:	2.42 (0.12)	2.84 (0.16)	2.83 (0.09)
	b:	2.79 (0.21)[a]	3.36 (0.24)[a]	3.36 (0.22)[a]
4	a:	1.23 (0.13)	1.79 (0.11)	1.88 (0.18)
	b:	1.44 (0.28)[a]	2.16 (0.14)[a]	2.28 (0.21)[a]

[a] denotes statistically significant difference between a) and b)

(ANOVA) using the GENSTAT V program (Lawes Agricultural Trust, Rothamsted Experimental Station).

The perfusion of the polar cortex was tested with reference to the rest of the outer cortex using Student's *t*-test on log-transformed data.

The level of significance was chosen to 5%.

Results

Mean kidney weight was 67.47 g (SD 4.41), and mean weight of the single piece for analysis was 1.26 g (SD 0.51).

Analysis of all flow values showed a significant systematic difference between the three total cortical flows, with an increase from flow no. 1 to 3. This difference was not related to particular individuals nor to the side studied.

There was a significant variation in the perfusion within the 28 pieces from each kidney cortex. This inhomogeneous perfusion pattern showed significant variation for each of the three isotopes, i.e. changed as a function of time (Fig. 1).

All measurements clearly demonstrated a lowered flow in the kidney poles, and in 3 out of 4 pigs this difference was significant for all flow measurements, Table 1.

One flow determination from one pig showed marked deviations from the rest of the values, since the total cortical perfusion in this particular measurement was diminished by a factor of 10 compared to the rest, and in addition the perfusion pattern was far more inhomogenous. The two additional flow measurements of that kidney did not show this differing result.

Discussion

The validity of blood flow measurements using radio-labelled microspheres (MS) is well established through a variety of experimental models which have studied the regional blood flow in different organs [1, 3, 11].

Several investigators have applied this technique to evaluate the renal blood flow under various conditions [2–6]. Since the medullary perfusion is predominantly postglomerular it is not possible to evaluate this part of the organ using the discribed technique. In contrast the method can be used for the estimation of cortical blood flow, and especially for the detection of relative changes in perfusion within the same region. It has been claimed that in the cortex a certain skimming of MS takes place so that the concentration of MS should be lower in blood supplying the deep glomeruli than the superficial [2, 5]. The present study, however, deals entirely with the superficiel cortex, and accordingly this source of error is ruled out.

We found for all pigs a significant increase in total renal perfusion as a function of time during the investigations.

This finding must be ascribed to anaesthesia although blood pressure readings and other metabolic data were constant.

Further, there was as a constant finding a significantly lower blood flow in the polar areas. This might be due to a different caliber of the microcirculation in those areas so that mechanical trapping of the microspheres did not take place to the same extent as in the rest of the outer cortex. There were, however, no data to support this assumption, and the possible significance of this finding will be discussed later.

Apart from these systematic flow variations we found a significant intra-cortical variation in the perfusion within the same kidney, which appeared to be completely random. This finding is similar to reports from dog kidneys after ureteral obstruction [4], but the present study suggests that this is a spontaneous phenomenon in the normal multicalyceal kidney. Furthermore, the inhomogeneous pattern of cortical perfusion changed within the time of investigation so that blood flow and thereby kidney function might vary across the parenchyma from time to time. This is in accordance with previous unpublished renographical data from human material, which showed pronounced variation in the uptake pattern in repeated gamma-camera renography. In one flow measurement in one particular kidney we found values of total cortical blood flow 10 times lower than the rest and with a far more inhomogeneous distribution. The contralateral kidney did not show a similar deviating result and a probable explanation is the occurrence of arterial spasm in the preglomerular capillaries. It is therefore conceivable that the result for that particular case may be an extension of the mechanism generally responsible for the uneven perfusion of the kidney cortex.

It was previously shown that intrarenal reflux (IRR) firstly occurred through the compound papillae [7], which are found predominantly in the kidney poles [9]. Further investigation showed that the underlying factor is the architecture of the openings of the collecting ducts on the papillary surface, so that IRR occurs where open orifices are found regardless of the shape of their papillae [8, 9]. Furthermore, it has been shown that intrarenal backflow is enhanced by ischaemia so that it may take place at low intrapelvic pressures in the presence of low intrarenal blood flow [10]. Bearing in mind the predominance of reflux nephropathy in the kidney poles we suggest, based on the present findings, that reduced polar blood flow may be a contributory factor in the occurence of scar formation secondary to VUR in this region.

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