GLOMERULAR HAEMODYNAMICS IN PREGNANT RATS

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Introduction

A marked rise in glomerular filtration rate during pregnancy is well documented both in man and in the rat [1, 2]. However, the reasons for this phenomenon are not clear. Bayliss [3] found a rise in single nephron glomerular filtration rate (SNGFR) proportional to an increase in glomerular plasma flow, with no change in the other determinants of glomerular ultrafiltration. However, others have not found an increase in renal plasma flow during pregnancy [4]. In this condition, the rise in GFR is due to an enhanced filtration fraction, suggesting an increased filtration pressure as the primary change in glomerular dynamics [5]. The present study was undertaken to clarify the mechanism by which filtration increases during pregnancy.

Methods

Studies were performed in 12 pregnant and 13 non-pregnant female rats (control), with glomeruli on the kidney surface (Munich-Wistar strain). Pregnant rats were studied 15–16 days after mating. All animals were anaesthetised by intraperitoneal injection of sodium pentobarbital (Nembutal, 60mg/kg body weight), placed on a temperature-regulated table and prepared for micropuncture as previously described [6]. Briefly, a tracheostomy was performed and indwelling polyethylene catheters inserted into the left jugular vein, the left femoral vein and the left femoral artery. The left kidney was exposed through a midline laparotomy and was gently separated from the adrenal gland and perirenal fat. The kidney was then placed in a Lucite cup and its surface covered with heated saline (37°C) during micropressure measurements or mineral oil during collections from tubules and peritubular capillaries. After the surgical preparation, an IV infusion of bicarbonate-saline solution (Na 138mmol/L, HCO₃ 28mmol/L, Cl 115mmol/L) containing chemical (non-isotopic) inulin (7%) was commenced at an infusion rate of 0.02ml/min, and was maintained thereafter. After 60 minutes of stabilisation, three to ten timed complete collections of tubular fluid were performed.
with sharpened micropipettes (5 to 8μm, OD), filled with coloured mineral oil. Three to five blood samples were collected from the welling point of superficial efferent arterioles utilising heparinised oil-filled micropipettes (12–15μm OD). Details about the procedure of these collections have been previously described [6]. Coincident with tubule fluid and peritubular blood collections, femoral arterial blood samples, 100μl in volume, were obtained for determination of haematocrit, plasma inulin and protein concentration. Hydrostatic pressure was measured in surface glomerular capillaries (P_G), in proximal tubules (P_T) and in the largest peritubular capillaries (so-called efferent arteriole pressure, EAP) by a servo-nulling device. Micropipettes with outer tip diameter of 2–4μm and containing 1.5M NaCl solution were used. Cortical pressures were registered simultaneously with mean arterial pressure from the femoral artery (BP) in a dual-channel Hewlett-Packard recorder (7702 B).

Analytical determinations and calculations

The volume of tubule fluid collected from individual nephrons was estimated from the length of the fluid column in a calibrated constant-bore quartz tubing of approximately 70μm ID (Friedrich and Dimmock, Millville, NJ, USA). The concentration of inulin in tubular fluid was measured by the microfluorescence method of Vurek and Pegram. Plasma inulin concentration was determined by the diphenylamine method. Plasma protein concentration was measured by Lowry’s method in femoral arterial blood and by a microadaptation of the same method in blood collected from efferent arterioles [6].

Single nephron GFR (SNGFR), single nephron filtration fraction (SNFF), blood flow across single afferent arteriole (AABF) and single efferent arteriole (EABF), plasma flow across single afferent arteriole (AAPF) and single efferent arteriole (EAPF), oncotic pressure at the afferent end (π_a) and at the efferent end (π_e) of the glomerulus, effective filtration pressure at the afferent end (EFP_a) and at the efferent end of the glomerulus (EFP_e), vascular resistance across single afferent arteriole (R_a) and single efferent arteriole (R_e) were calculated as previously described [6]. The ultrafiltration coefficient (K_f) was calculated according to a differential equation elaborated by Deen and associates [7], that gives the true value of K_f in the presence of a filtration pressure disequilibrium. In the presence of filtration pressure equilibrium, only the minimal numerical value of K_f was calculated.

Statistical

Unpaired t test was used for comparison of the means. Student’s t value was used to test the null hypothesis EFP_e = 0.

Results

In pregnant rats, SNGFR was markedly increased, both as an absolute value (35.5 ± 2.2 versus 22.5 ± 1.3nl/min, p < 0.0005) and when the value was adjusted for kidney weight (37.2 ± 2.4 versus 26.2 ± 1.6nl/min/g kidney weight, p < 0.0005).
PG rose from a control value of 44.8 ± 0.9 mmHg to 50.6 ± 1.0 mmHg (p < 0.0005). This rise in PG was not associated with any change in PT, πa or πe. Therefore, the enhanced PG accounted for a similar rise in EFPa and in EFPe. The latter, in control rats was not statistically different from zero, indicating a filtration pressure equilibrium. In pregnant rats, instead, EFPe averaged 9.7 ± 1.4 mmHg; this value was significantly greater than zero (p < 0.0005), indicating pressure disequilibrium at the end of glomerular capillaries (Table I). Minimal possible Kf in control rats was greater than the true value of Kf in pregnant rats (0.0475 ± 0.0050 versus 0.0379 ± 0.0022 nl/s/mmHg, p < 0.05).

<table>
<thead>
<tr>
<th></th>
<th>PG</th>
<th>PT</th>
<th>πa</th>
<th>πe</th>
<th>EFPa</th>
<th>EFPe</th>
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<tbody>
<tr>
<td>Control Rats</td>
<td>44.8</td>
<td>14.0</td>
<td>14.9</td>
<td>29.3</td>
<td>16.0</td>
<td>1.7</td>
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<tr>
<td>±0.9</td>
<td>±0.7</td>
<td>±0.4</td>
<td>±1.1</td>
<td>±1.0</td>
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<tr>
<td>Pregnant Rats</td>
<td>50.6</td>
<td>14.0</td>
<td>14.2</td>
<td>26.9</td>
<td>22.4</td>
<td>9.7</td>
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<tr>
<td>±1.0</td>
<td>±0.4</td>
<td>±0.5</td>
<td>±1.4</td>
<td>±1.1</td>
<td>±1.4</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>&lt; 0.0005</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>&lt; 0.0005</td>
<td>&lt; 0.0005</td>
</tr>
</tbody>
</table>

Results are means ± SEM

During pregnancy, SNFF was unchanged. Hence, AAPF rose parallel with SNGFR, averaging 105.5 ± 9.2 nl/min versus 63.0 ± 3.3 nl/min in control rats (p < 0.0005). Similar rises occurred also in AABF, EAPF and EABF. Ra was markedly reduced from 4.056 ± 0.321 to 2.045 ± 0.151 dyne/s/cm⁻⁵ (p < 0.0005). Also Re was significantly decreased (Table II).

<table>
<thead>
<tr>
<th></th>
<th>AABF</th>
<th>AAPF nl/min</th>
<th>EABF</th>
<th>EAPF</th>
<th>Ra dyne/s/cm⁻⁵</th>
<th>Re dyne/s/cm⁻⁵</th>
<th>SNFF</th>
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<tr>
<td>Control Rats</td>
<td>120.8</td>
<td>63.0</td>
<td>99.6</td>
<td>40.4</td>
<td>4.056</td>
<td>2.478</td>
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<td>±7.1</td>
<td>±3.3</td>
<td>±6.0</td>
<td>±2.6</td>
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<td>±0.172</td>
<td>±0.01</td>
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<tr>
<td>Pregnant Rats</td>
<td>200.2</td>
<td>104.5</td>
<td>164.7</td>
<td>69.0</td>
<td>2.045</td>
<td>1.768</td>
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<tr>
<td>±18.0</td>
<td>±9.2</td>
<td>±16.2</td>
<td>±7.4</td>
<td>±0.151</td>
<td>±0.152</td>
<td>±0.02</td>
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</tr>
<tr>
<td>p</td>
<td>&lt; 0.0005</td>
<td>&lt; 0.0005</td>
<td>&lt; 0.0005</td>
<td>&lt; 0.0005</td>
<td>&lt; 0.0005</td>
<td>NS</td>
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</tr>
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</table>

Results are means ± SEM
Discussion

The present study confirms that SNGFR is markedly enhanced during pregnancy. According to a recent model of glomerular ultrafiltration [7], this rise in SNGFR is mainly due to an increase in glomerular plasma flow. In fact, SNGFR is highly flow-dependent, this dependence being particularly strict when a filtration pressure equilibrium is achieved [8]. During pregnancy, SNGFR rose proportionally to AAPF, as witnessed by the constancy of SNFF, despite a filtration pressure disequilibrium taking place, due mainly to a reduction in the ultrafiltration coefficient. The decline in SNFF expected from the fall in $K_f$, however, was opposed by a rise in $P_G$, i.e. in effective filtration pressure, that contributed in this way to the increase in SNGFR.

Both the augmented glomerular blood flow and the increased filtration pressure occurring in pregnancy are accounted for by a fall in afferent arteriole resistance. The reasons for this reduction in $R_a$ are not apparent in the present study. A possible cause is the extracellular fluid volume expansion documented in pregnancy [9]. Alternatively, the decline of $R_a$ may be due to circulating vasodilating substances, like prostaglandins, the excretion of which is known to increase during gestation. Increased circulating PGE$_2$ may account for the reduction in $K_f$ [10].

References

1 Davidson JM, Dunlop W. Kidney Internat 1980; 18: 152
3 Baylis C. J Physiol 1979; 295: 101
4 Lindheimer MD, Katz AI. J Lab Clin Med 1971; 78: 633
5 Dunlop W. Postgrad Med J 1979; 55: 329
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Open Discussion

STRUYVENBERG (Chairman) Could you speculate on the mechanisms both of the increase in glomerular plasma flow, and the decrease in ultrafiltration coefficient caused by pregnancy, because I think they are not related? They might probably be the result of an increase in one or more prostaglandins.

DAL CANTON Yes, I do believe that one possible mechanism is just a rise in prostaglandin secretion during pregnancy because prostaglandins have a renal vasodilating property, and it has also been shown that prostaglandins cause a reduction in the ultrafiltration coefficient. This is one possible mechanism. However, renal vasodilatation and particularly a dilatation of arterioles that accounts both for the rise in effective filtration pressure and in glomerular blood and plasma flow may be due also to the extracellular or plasma volume expansion that occurs during pregnancy.