Circulatory changes during pregnancy in spontaneously and renal hypertensive rats

Y. LUNDGREN, K. KARLSSON AND U. LJUNGBLAD
Department of Physiology and Department of Gynecology and Obstetrics, University of Göteborg, Göteborg, Sweden

Summary

1. Mean arterial pressure, heart rate, cardiac output (dye-dilution technique), stroke volume, total peripheral resistance (TPR), utero–placental blood supply (microsphere technique) and foetal weights were determined 2 days before expected birth in normotensive control (NC) rats, spontaneously hypertensive (SH) rats, rats with short-standing renal hypertension induced early in pregnancy and rats with established renal hypertension induced 4 weeks before pregnancy. Non-pregnant rats in comparable states served as controls.

2. In normal pregnancy cardiac output increased by 33% and blood pressure and TPR decreased by 17 and 38% respectively. The same principal changes were noted in SH rats and those with short-standing renal hypertension, but no changes were found in rats with established renal hypertension during pregnancy.

3. Myometrial and placental blood supply was lower in all hypertensive groups compared with NC rats, the reduction being 46 and 36% in SH rats and in rats with established renal hypertension as much as 74 and 68% respectively.

4. In SH rats foetal weights were reduced compared with NC rats, but despite the 68% reduction of placental blood flow in rats with established renal hypertension foetal weights were here unchanged.

Key words: haemodynamics, pregnancy, renal hypertension.

Abbreviations: TPR, total peripheral resistance; SH, spontaneously hypertensive; NC, normotensive control; ERH, established renal hypertensive; SRH, short-standing renal hypertensive.

Introduction

Normal pregnancy is characterized by increased cardiac output and decreased total peripheral resistance (TPR), whereas established hypertension, on the other hand, is associated with increased TPR and a largely unchanged cardiac output (cf. Chesley, 1978).

The effects of hypertension on central haemodynamics and utero–placental blood flow during pregnancy and on birth weights have been debated in recent years but still very little is known (cf. Chesley, 1978).

The aim of the present study was to explore in rats whether spontaneous and renal hypertension interferes with haemodynamics and foetal weights during late pregnancy.

Methods

Mean arterial blood pressure, heart rate, cardiac output, stroke volume, TPR and organ blood flow were determined 2 days before expected birth in Wistar normotensive control (NC) rats, spontaneously hypertensive (SH) rats, rats with short-standing renal hypertension induced early in pregnancy (SRH rats) and ERH rats (renal hypertension induced 4 weeks before pregnancy). Matched non-pregnant NC, SH, SRH and ERH rats served as controls. Body weight was 180–200 g at mating in NC, SH and SRH rats and at induction of hypertension in ERH rats.

Renal hypertension was induced by a silver clip on the left renal artery, leaving the right kidney intact, and mean pressure had to be 130 mmHg or more. Pressure and heart rate during awake rest
were measured in the caudal artery before induction of hypertension, before mating and immediately before acute experiments.

Cardiac output was measured during Nembutal anaesthesia with a cardiogreen dye-dilution modification in pregnant and non-pregnant groups (8–13 rats in each group), and mean pressure and heart rate were recorded in the caudal artery.

The utero-placental blood supply (5–13 rats in each group) was then determined with the microsphere technique (Rudolph & Heymann, 1967). Radioactive 'carbonized' microspheres (25 ± 5 μm) were injected into the left ventricle via the carotid artery and reference blood was withdrawn from the right femoral artery. After each experiment organs of interest were analysed for gamma activity, together with the reference blood, and foetal weights were measured.

Means ± se values were calculated. The Fisher and the Wilcoxon tests were used for statistical evaluations.

Results
During pregnancy awake mean blood pressure decreased significantly in NC and SH rats (from 112 ± 2 to 100 ± 3 mmHg and from 144 ± 5 to 111 ± 5 mmHg respectively), but no significant change occurred during pregnancy in SRH or ERH rats (from 145 ± 5 to 137 ± 3 mmHg and from 149 ± 5 to 154 ± 5 mmHg respectively).

Cardiac output (ml/min) increased significantly (33%) during pregnancy in NC rats, entirely due to increase in stroke volume, and TPR (mmHg min/ml) decreased by 38%. The same principal changes, though less pronounced, occurred in SH rats, where cardiac output increased 19% (due to a 10% increase in heart rate and 8% increase in stroke volume) and TPR decreased by 27%.

Also in SRH rats cardiac output increased with pregnancy (29%), due to equal heart rate and stroke volume increases, and TPR fell by 19%. In contrast, no increase in cardiac output or decrease in TPR was found in ERH rats during pregnancy.

In all hypertensive groups cardiac output was significantly lower and TPR higher compared with NC rats during pregnancy, the TPR increase being most pronounced in ERH rats, which did not show any changes in central haemodynamics during pregnancy.

Myometrial and placental blood flows were reduced in all 'hypertensive' groups compared with NC rats, myometrial blood flow being 90 ± 16, 49 ± 6, 42 ± 6 and 24 ± 5 ml min⁻¹ 100 g⁻¹ in NC, SH, SRH and ERH rats respectively. Placental blood flow was 158 ± 32, 101 ± 14, 76 ± 17 and 51 ± 12 ml min⁻¹ 100 g⁻¹ in NC, SH, SRH and ERH rats respectively. Thus the reductions in myometrial and placental blood flow were most pronounced in ERH rats, being 74 and 68% respectively.

Concerning placental weight, no significant difference was found in any of the hypertensive groups compared with NC rats. Foetal weights were reduced in SH rats compared with NC rats, being 2·5 ± 0·2 and 2·9 ± 0·2 g respectively. In contrast, foetal weights were normal in SRH and ERH rats, despite considerable reductions in placental blood flow.

Discussion
Hypertension in pregnancy is probably the most important factor causing foetal growth retardation and predisposing for asphyxia and other complications during delivery. Different opinions have been presented concerning the effects of hypertension on haemodynamics during pregnancy and on placental and foetal weights, and results are contradictory (cf. Chesley, 1978).

Several studies of normal pregnancies demonstrate increased cardiac output and decreased TPR during pregnancy compared with non-pregnant controls (cf. Chesley, 1978), in good agreement with the present results on NC rats. The same principal changes in central haemodynamics were seen in primary as well as short-standing renal hypertension as in normal pregnancy, i.e. increased cardiac output and decreased TPR. Cardiac output during pregnancy was, however, decreased in both SH and SRH rats compared with pregnant NC rats, and did not differ significantly from that of non-pregnant NC rats. Further, despite the reduction in TPR during pregnancy, TPR was still increased in pregnant SH and SRH rats compared with pregnant NC rats. In contrast, pregnant ERH rats showed similar cardiac output and TPR values as non-pregnant ERH rats, i.e. a significantly increased TPR and unchanged cardiac output even when compared with non-pregnant NC rats.

The question arises whether the relative reduction in nutritional blood supply found in all hypertensive groups affects predominantly the utero-placental region. This was the case in all the hypertensive variants, placental blood flow being 36% lower in SH rats than in NC rats even if mean pressure was almost normalized in SH rats during pregnancy. The reduction in placental blood flow was most pronounced in ERH rats, being here 68%
compared with 52% in SRH rats. The regional resistance increase probably reflects vasoconstriction associated with structural changes in the utero-placental vascular bed, present also in SRH rats.

Despite the considerable reduction of placental blood flow in ERH rats and SRH rats this did not reduce either placental or foetal weights, suggesting that the placental blood supply normally has a considerable over-capacity. This represents a good safety margin for the foetus to manage the circulatory demands associated with delivery. In SH rats both the elevation in TPR and the placental blood flow reduction were much less pronounced, but foetal weights were here reduced compared with NC rats, which was not the case in SRH and ERH rats. For such reasons the reduced birth weights in SH rats are unlikely to be due to insufficient placental blood supply but may rather reflect genetic influences.

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References