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Structural Changes in Umbilical Vessels in Pregnancy Induced Hypertension

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Abstract

Background: Pregnancy Induced Hypertension (PIH) is associated with placental morphological changes, alterations in the blood flow patterns in the umbilical vessels and adverse fetal and maternal outcome. Studies have demonstrated changes in the structure of the umbilical vessels but these have not been described across the length of the cord or correlated with the severity of disease.
Study design: A case control study.
Setting: Kenyatta National Hospital.
Materials and methods: Thirty six umbilical cords from newborns of women with and without PIH (18 cases, 18 controls) were obtained and studied with light microscopy. Of the cases 9 women had severe PIH and 9 had mild PIH. Means and standard deviations for the various parameters of the various groups were obtained. Student's *t*-test and ANOVA were used to compare means, a p value of <0.05 being significant.
Results: The structure of the umbilical vessels changes from the placental end to the fetal end. The umbilical vein in PIH had a greater wall thickness and a smaller luminal area than in the controls. The vein's wall-luminal ratio increased from the placental to the fetal end. Duplication of the elastic subintimal lamina (ESL) was higher in the cases. The ESL was more commonly duplicated in the fetal end. There were no structural differences between the umbilical arteries in PIH and in the controls.
Conclusion: PIH is associated with structural changes in the umbilical vessels. These changes are more predominant in the vein than in the artery and in the vein, they are more obvious in the fetal end. The observed increase in wall-luminal ratio from the placental to the fetal end suggests that the fetal end of the umbilical vein has a more refined role in the regulation of blood flow to the fetus.

Keywords: Umbilical vessels; Pre-eclampsia; Pregnancy

1. Introduction

Pregnancy Induced Hypertension (PIH) is a common pathological syndrome affecting pregnancy [1] and is associated with adverse fetal and maternal outcome of variable severity [2,3]. The effects on the fetus are as a result of a reduction in placental perfusion [4,5] subsequent to reduced maternal blood flow and relative volume depletion. Altered haemodynamics in the umbilical blood vessels have been documented using Doppler Ultrasound velocimetry [5–7]. The altered haemodynamics are associated with some structural changes of the umbilical vessels [8–10].

Studies have shown variations between the extracellular matrix composition in PIH and in normotensive umbilical vessels [8,11,12]. Junek et al. [8] reported increased thickness of the tunica media and intima in the arteries and an increased rate of duplication of the internal elastic lamina in preeclamptic cords. Inan et al. [9] reported reduced luminal areas and reduced vessel wall thickness in both artery and vein in preeclampsia compared to normal pregnancies and pregnancies complicated with chronic hypertension.

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There have been no studies on the sequential structural changes along the length of umbilical vessels and how these are related to the severity of PIH. This work was undertaken to study the structure of the umbilical vessels in normotensive and hypertensive patients.

2. Materials and methods

Umbilical cords were obtained from newborns of women who delivered at Kenyatta National Hospital during the period May to August 2005 after approval from the Hospital's ethical and review board and with written consent from the patients.

Cases were defined as women diagnosed with PIH defined as de novo hypertension with proteinuria (Blood Pressure, BP, Systolic $\geq$140 mmHg, Diastolic $\geq$90 mmHg) in second trimester. The cases were further divided into two groups (A, BP $\geq$140/90 mmHg and B, BP $\geq$160/100 mmHg) based on blood pressure [13]. The control group (C) was comprised of women with no evidence of elevated blood pressure (Systolic $<$140 mmHg, Diastolic $<$90 mmHg) either before or during pregnancy. Patients with a history of chronic hypertension and Diabetes Mellitus were excluded from the study. Cases of single umbilical artery were also excluded.

Specimens were fixed with 10% formalin solution. Umbilical cord was divided into 3 segments of equal length from the placenta at its insertion point: the placental, middle and fetal. Length was measured using a non-extensile tape. Standard histological techniques for light microscopy was used and sections stained with Masson's trichrome, Weigert's Van Gieson stain and Haematoxylin-eosin stains [14]. The slides were viewed under a Leica BME light microscope.

Measurements were taken by projecting the image onto a video monitor. A transparent grid was placed onto the screen and measures of area and thickness taken in arbitrary units. Photographs were taken from the microscope eyepiece using a Sony DSC P9 digital camera. The luminal area, wall area and wall thickness of the umbilical vein and arteries were obtained. The ESL was also observed for duplication defined as presence of more than one layer of elastic fibre lamellae at any point in the circumference of the vessel.

The data was analysed using the Statistical Package for Social Sciences (SPSS) version 11.5. Means and standard deviations were obtained for the various parameters in the different groups. Student's *t*-test was used to compare the characteristics of the case and control groups while one-way ANOVA was used to compare various parameters among the three groups. A p value of $<$0.05 was considered significant.

3. Results

A total of 36 women were enrolled in the study. Eighteen women had PIH while the other 18 were normotensive. The mean blood pressure for the controls was $118.3 \pm 8.9/70.3 \pm 9.9$ mmHg, mild PIH $156.3 \pm 20.7/100.3 \pm 8.2$ mmHg and severe PIH $170.3 \pm 8.8/113.0 \pm 13.9$ mmHg. Socio-demographic characteristics and clinical findings of the patients are shown in Table 1. Gestational age in weeks, birth weight and placental weight were significantly lower in cases than in controls. There were no significant differences in maternal age, and cord length between cases and controls. Mild PIH were younger women than those with severe PIH (24 ± 6 years, 31 ± 7 years, $p = 0.044$). There were no differences in gestational age $p = 0.715$, birth weight $p = 0.980$, placental weight $p = 0.980$ and cord length $p = 0.108$ between mild and severe PIH.

Table 1
Socio-demographic characteristics and clinical findings

Characteristic (Mean $\pm$ SD)	Controls	Cases	p-Value
Maternal age (years)	24.6 ± 5.6	27.7 ± 7.4	0.171
Gestation (weeks)	39.1 ± 2.5	36.8 ± 3.4	0.027
Birth weight (grams)	3023.1 ± 581	2180.6 ± 397	$<$0.001
Placental weight (grams)	435.2 ± 107	371.4 ± 62	0.032
Cord length (cm)	33.1 ± 8.5	28.3 ± 9.9	0.125

SD, standard deviation.

In women with normal blood pressure, the umbilical vein tunica media was predominantly muscular and it's wall thickness smaller than that of the artery at corresponding levels. Unlike the artery the vein had occasional duplication of the ESL. In women with pregnancy induced hypertension, there were no structural differences observed in the arteries compared to the controls. However, the vein wall was markedly thicker in cases (Fig. 1B), than in controls (Fig. 1A). The apparent increase was due to the tunica media and the tunica intima. The media showed thicker muscle bundles with increased trabeculations and more prominent connective tissue septae. The medial smooth muscle often displayed different orientations as opposed to the predominantly circular orientation seen in the vein of normotensive women (Fig. 1B).

The tunica intima was thicker and rich in collagen. The ESL was more prominent in the veins in PIH than in the controls. The thicker ESL was often duplicated and folded in PIH (Fig. 1C).

Table 2 shows structural changes in the umbilical veins. The vein's wall-luminal ratio increased from controls to mild and severe hypertensive groups significantly, $p = 0.000$. The most marked increase was in the fetal end, about 12 times as compared to 5 times at the placental end. The wall-luminal ratio of the umbilical vein increased from the placental to the fetal end significantly in all groups Table 2. Within the groups, the largest increase was in the severe PIH about 10 times as compared to 4 times in the control group. The umbilical artery showed an insignificant progressive reduction in size from the placental to the fetal end in the cases and the controls, $p > 0.05$, data not shown.

In the vein, presence of trabeculations in the tunica media was also more prominent in the fetal segment compared to the other segments. In the placental segment, the orientation of the smooth muscle in the tunica media was predominantly circular. With progression from the placental to the fetal segment there was increased presence of smooth muscle taking oblique and longitudinal directions.

The vein showed an increasing rate of ESL duplication from controls to mild and severe hypertensive groups, Table 2. The ESL changes were observed in both cases and control, though not statistically different within the groups, $p > 0.05$ (Table 2). The highest rate of ESL duplication was observed in the fetal segment of the severe hypertensive group while the lowest rate was observed in the placental segment of controls (Table 2). Though there were significant differences in gestation age between control and cases (Table 1), these differences did not appear to explain the observed differences in umbilical vein morphology (Fig. 2). Fig. 2 is a scatter plot showing that at each gestation, umbilical cords from PIH patients were thicker than those of controls.