Doppler velocimetry of the materno-fetal circulation in preterm delivered pregnancies complicated with hypertension

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Submitted: 2008-12-15 Accepted: 2009-05-09 Published online: 2009-09-02

Key words: **foetal hypotrophy; IUGR; gestational hypertension; preterm delivery; preeclampsia; cerebral-to-placental resistance ratio (CPR)**

Neuroendocrinol Lett 2009; **30**(3): 403–408 **PMID:** 19855368 NEL300309A14

Abstract

BACKGROUND: Hypertension is one of the most frequent complications of pregnancy. Due to high risk of morbidity and mortality in both mothers and children, it is necessary to continuously monitor the pregnancy, principally with biophysical methods. Particularly, doppler velocimetry of the materno-fetal circulation proves useful.

THE AIM of the study was to assess the usefulness of doppler test in monitoring the condition of the foetus in preterm delivered pregnancy complicated with hypertension.

MATERIAL AND METHODS: The retrospective analysis comprised the data of 116 women who delivered prematurely at the Clinics of the Department of Gynaecology and Obstetrics at the Collegium Medicum of the Jagiellonian University in the years 2006–2007, resulting in creation of Group I involving 38 pregnant women with preeclampsia, and Group II of 36 women whose pregnancy was complicated with gestational hypertension. Control group was formed of 42 women with correct arterial blood pressure. When describing the groups, the differences in the birth weight and Apgar score were indicated.

RESULTS: A significant statistical difference was found in the area of pulsation rate in the umbilical artery and *cerebro*-placental ratio (*CPR*). In the case of preterm delivery complicated with arterial pressure disorders, the foetus is characterised with worse organic perfusion and slower somatic growth than if no concomitant hypertension is present. Hypertension forms an additional risk factor in the course of preterm delivery, and doppler velocimetry is a good method for monitoring the condition of the foetus, as it allows for detection of irregularities and for implementation of relevant treatment to improve the newborn's condition at birth.

ORIGINAL ARTICLE

INTRODUCTION

Hypertension in pregnant women is one of the greatest problems of contemporary obstetrics, as despite many years of studies no satisfactory treatment methods have been established. Presently, it is one of most frequent causes of morbidity and mortality in both mothers and newborns [Duley 2003; Ghoghoberidze *et al.* 2008; Leeman & Fontaine 2008; Liu 2008]. The problem is that apart from effective reduction in arterial blood pressure in the mother (which is not always the best solution for the foetus) and preterm delivery, no effective treatment has been developed that would improve

the intrauterine condition of the baby. Improvement in obstetric results is therefore more related to the progress in neonatological treatment that permits even very little children to survive, as many attempts to improve the intrauterine condition of the foetus, e.g. by application of L-arginine [Report of the National High Blood Pressure Education Program 2000; Rytlewski *et al.* 2005; Rytlewski *et al.* 2006], are still in the phase of clinical trials.

Due to the fact that basic lesions are related to pathological implantation (in the first trimester of gestation), which with pathology in the mother's organism leads to the development of preeclampsia, treatment may only be symptomatic. Therefore, it is broadly accepted that the only effective procedure upon diagnosis of a severe preeclampsia is to delivery the pregnancy. This raises no objections after completion of the 37th week of gestation. In the earlier period of gestation, risks related to prematurity must be juxtaposed to the risk for the mother and the child in the case of continuing the pregnancy for too long [Duley 2003; Norwitz & Funai 2008]. It has been shown that the condition of the premature infants and the prognoses for newborns from pregnancies complicated with preeclampsia (hypertension and albuminuria) were much worse than in the case of children whose mothers had no gestational hypertension, but also delivered preterm [Banias *et al.* 1992]. Another pathology is the low birth weight of premature infants (IUGR – Intrauterine Growth Restriction), particularly observed in preeclampsia, which is probably related to pathology within the placenta resulting from incorrect implantation [Kuriak & Chervenak 2006]. The developing placental insufficiency results in reduction of blood flow in the utero-placental unit, which leads to foetal undernutrition and anoxia. A compensatory mechanism is launched, comprising increase in blood flow through vital organs, with reduced flow through other body parts [Peeters *et al.* 1979], which as a consequence results to asymmetrical foetal IUGR.

Owing to the development of state-of-the-art techniques, in particular doppler ultrasonography, it is possible to precisely and non-invasively monitor the condition of the foetus [Goldenberg *et al.* 2008]. The analysis of doppler velocimetry in cerebral vessels of the foetus and in umbilical cord is a very useful method to assess anoxia. The umbilical artery is normally a low-resistance vessel, increasing blood flow with the time of gestation, while reducing the resistance. In turn, the middle cerebral artery is characterised with greater resistance, and although initially growth and then drop in the resistance value is observed, it should always be higher than in umbilical artery. Information about the operation of the placenta is obtained from doppler measurements in the umbilical artery. For the purpose of a more precise analysis of foetal response to the incorrect blood flow in placental vessels, the CPR (Cerebro-Placental Ratio) ratio was introduced, calculated according to the formula: CPR = PI MCA / PI UA. In a correct situation, in the period from week 20 to week 42 of gestation, the ratio's value ranges between 1.08 and 2, maintaining a relatively constant value between week 27 and week 37 [Arias 1994]. In a pregnancy complicated with IUGR, incorrect reduction in blood flow in the uterine artery is observed, and compensatory growth in the flow in the middle cerebral artery, which is defined as centralisation of the blood circulation (the value of CPR drops below the norm 1–1.07) [Arbeille *et al.* 1987]. It has been shown that CPR ratio correlates well with the condition of the foetus, and its incorrect value is significantly related to a worse perinatal result in pregnancies complicated with intrauterine growth restriction [Bahado-Singh *et al.* 1999], preeclampsia and arterial hypertension [Simanaviciute & Gudmundsson 2006]. For the purpose of early detection of the risk to the foetus, it is necessary to continuously monitor of the foetus and the mother in order to adjust further treatment to the clinical situation.

The purpose of the paper was to assess the usefulness of doppler test in monitoring the condition of the foetus in preterm delivered pregnancy complicated with hypertension.

MATERIAL AND METHODS

The retrospective analysis comprised the data of 116 women who delivered prematurely at the Clinics of the Department of Gynaecology and Obstetrics at the Collegium Medicum of the Jagiellonian University in the years 2006–2007, resulting in creation of Group I involving 38 pregnant women with preeclampsia, according to the NHBPEP WGHBPiP classification of 2000 [Report of the National High Blood Pressure Education Program. Working Group on High Blood Pressure in Pregnancy. 2000], and Group II of 36 women whose pregnancy was complicated with gestational hypertension. Control group was formed by 42 women with physiological course of pregnancy.

Apart from standard parameters, such as age, parity, duration of gestation upon hospitalisation, method of delivery, obstetric condition on admittance (shortening and dilation of the cervix, condition of the amniotic sac), indications of inflammation (leucocytosis, CRP), use of antibiotics, tocolytic drugs and hospitalisation period of patients, also the data regarding the newborn were analysed (birth weight, Apgar score [Apgar 1953] on the fifth minute after birth) and hospitalisation period at the newborn ward.

A separate analysis involved the results of doppler velocimetry (pulsatility ratio) in the uterine artery and middle cerebral artery, CPR ratio, and amniotic fluid index), as an important factor impacting on the intrauterine comfort of the child.

The data were subjected to a statistical analysis. Populations of women enrolled in the study were characterised in the descriptive manner. Variables of continuous nature were presented by providing minimum and max-

Table 1. Group characteristics

	Group I [n = 38]	Group II [n = 36]	Group III [n = 42]	Significance
Characteristics of the patients				
Average age of women [years], average SD <min – max>	29.84 (4.56) <22–40>	29.69 (4.64) <20–38>	28.36 (4.56) <18–37>	p = 0.281
Duration of gestation on admission [week] average, SD <min – max>	30.61 (3.40) <24–36>	33.36 (3.15) <27–37>	31.57 (3.40) <23–36>	p = 0.002
Pregnancy median (quartile interval) <min – max>	1 (1) <1–6>	1 (1.5) <1–6>	2 (1) <1–5>	p =0.355
Delivery median, (quartile interval) <min – max>	1 (0) <1–4>	1 (1) <1–5>	2 (1) <1–5>	p = 0.210
Characteristics of the newborns				
Birth weight [g] median, (quartile interval) <min–max>	1325 (630) <390–2310>	1950 (1605) <600–3970>	1840 (970) <650–3200>	**p = 0.004**
Apgar scor median, (quartile interval) <min–max>	7 (3) <1–9>	8 (2) <3–10>	9 (3) <3–10>	p = 0.003
Period of hospitalisation at the newborn ward [days] median, (quartile interval) <min–max>	29 (37) <0–89>	8 (45) <0–113>	20 (29,5) <0.5–168>	p = 0.477
Period of patients' hospitalisation				
Period of patient's hospitalisation [days] median, (quartile interval) <min – max>	9.5 (8) <5–26>	7 (6.0) <5–38>	11.5 (17.0) <1–63>	p = 0.067
Period of hospitalisation before delivery [week] median, (quartile interval) <min – max>	5.5 (7.0) <0–32>	2 (6.5) <0–32>	7 (19.0) <0–59>	p = 0.024

* – ANOVA test
 # – ANOVA rang Kruskal Wallis test

imum values, arithmetic mean and standard deviation. Categorised variables were presented by providing the median, minimum and maximum values, number and percentage values. To compare the variables with distribution similar to normal, after meeting the assumption of variance uniformity in 3 study groups, single-factor variance analysis (ANOVA) was applied. In the event where the assumptions listed were not met, the differences were tested for significance with non-parametric ANOVA rang Kruskal-Wallis test. On comparison of the variable values, the level of statistical significance was set as $p<0.05$. The calculations were made using STATISTICA statistical suite.

RESULTS

Patient characteristics has been presented in Table 1. The groups of pregnant women were not statistically different as regards age, parity and past deliveries. Only the period of gestation on admission in the group of women with preeclampsia was the shortest.

Premature infants featured statistically significant differences as regards birth weight and Apgar score, depending on the group. In the post-hoc tests, it was determined that in Group I, where mothers were diagnosed with preeclampsia, newborns were characterised with a significantly lower birth weight, and score in Apgar score (Fig.2). Differences between Group II and III (gestational hypertension and preterm delivery) are not statistically significant. The period of newborns' hospitalisation at the neonatological ward as well as patients' hospitalisation period did not differ between the groups. It was, however, concluded that the period of hospitalisation before the delivery in patients with gestational hypertension (Group II) was statistically significantly shorter.

The analysis of the outcomes of obstetric examination on admission (Table 2) revealed that the groups featured statistically significant differences as regards shortening and dilation of the cervix and the condition of amniotic sac. Patients in Group III (without hypertension) were characterised with greater advancement of preterm delivery and outflow of amniotic fluid was more frequently observed, while in post-hoc tests no differences were found in examinations between Group I and II. No statistically significant differences were observed between the groups as regards the observed leucocytosis and positive CRP (>7.0 mg/dl).

It has been observed that statistically more frequently tocolysis was applied (with magnesium sulphate and/or phenoterol) in Group III, while antibiotic therapy was administered with similar frequency in the groups

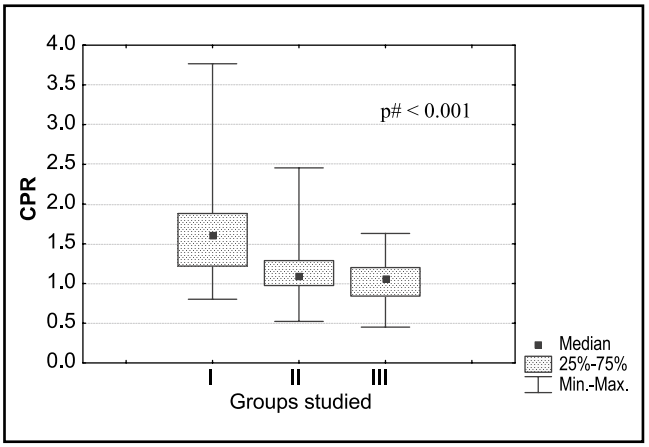

Fig. 1. Cerebro - Placental Ratio depended on the groups..

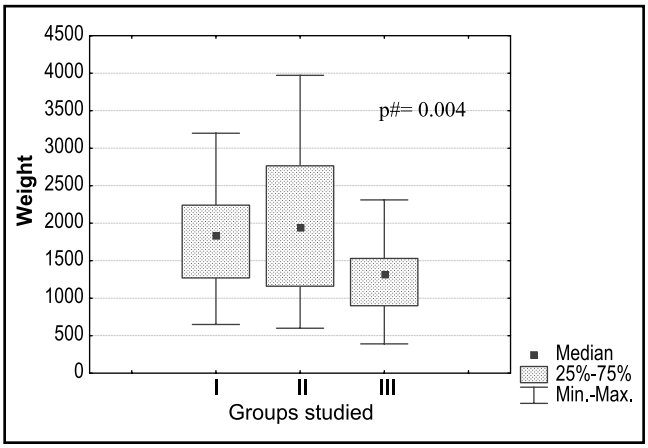

Fig. 2. Birth weight of children in the groups.

analysed. All patients in Group I and 94.44% of patients in Group II had delivery with caesarian section, significantly more frequently than in Group III, where the percentage of caesarian sections amounted to 66.66%.

The analysis of the outcomes of ultrasonographic doppler test showed that the studied groups of patients featured statistical differences in the area of pulsation rates in the middle cerebral artery and umbilical artery, as well as CPR. It was observed that in Group III, where patient had correct blood pressure, CPR was higher than in Groups I and II (Fig. 1). In turn, in the post-hoc tests, no statistical differences were found between Groups I and II. It was also pointed that the amniotic fluid index (AFI) is statistically significantly lower in Group III, where more frequently than in Group I and II amniotic fluid outflow was observed (Table 3).

DISCUSSION

Hypertension induced by pregnancy is the most frequent form of gestational hypertension, as it occurs with the frequency of 6–17% in primigravidas and 2–4% of multiparas, while preeclampsia is diagnosed in the range of from 2 to 7% in the first pregnancy [Jasovic-Siveska & Jasovic 2008; Rytlewski *et al.* 2008]. Both these conditions are related to high perinatal morbidity and mortality in children and mothers, particularly when these are revealed before completion of week 34 of gestation [Sibai 2003]. Many reports show a strong impact of preeclampsia on the impairment of the correct foetal development, causing intrauterine growth restriction [Odegård *et al.* 2000], and this occurs more frequently as compared to patients with pregnancy-induced hypertension [Manning *et al.* 1982]. In this study, newborns of mothers with preeclampsia were characterised with statistically significant lower birth weight as compared to the groups: with normal tension and gestational hypertension, which remains in line with the results of other studies [Banias *et al.* 1992; Martínez *et al.* 2008]. Buchbinder *et al.* observed differences in the perinatal outcomes depending on the severity of hypertension, indicating that regardless of concomitant albuminuria hypertension forms a predisposition to preterm delivery and lower birth weight [Buchbinder *et al.* 2002].

High-risk pregnancies require enhanced monitoring using the state-of-the-art diagnostic techniques. Doppler ultrasonography allows for assessment of velocimetry parameters in foetal and placento-uterine circulation, providing precious information about the intrauterine condition of the foetus and possible irregularities. Among the available doppler flow parameters, greater clinical usefulness of the calculated cerebro-placental ratio (CPR) was found, which is a ratio of PI values of the middle cerebral and umbilical arteries, as compared to these arteries analysed separately [Hnat *et al.* 2002; Arduini & Rizzo 1992]. The value of CPR ratio below 1 allows to isolate the group with high risk of IUGR and severe complications in the newborn. When analysing the results of mean CPR value between the groups in the study performed, a statistically significant difference was found between the groups with hypertension (Groups II and III), and the group of patients without hypertension, while observing the mean CPR value below 1 in the group of patients with diagnosed preeclampsia. When assessing the impact of gestational hypertension on the condition of the foetus and the premature infant using doppler ultrasonography of intravascular flows in the umbilical artery and middle cerebral artery, in one group a clear relation was found between the incorrect CPR value (mean CPR value = 1.06) and the low birth weight of newborns (average body weight – 1325g) and Apgar score (average score – 7), which conforms to the data available in literature [Arias 1994; Simanaviciute & Gudmundsson 2006].

The work of Gudmundsson *et al.* compares the cerebral-uterine ratio (ratio of PI of middle cerebral artery and PI of uterine artery) to CPR ratio in pregnancy with preeclampsia complication. A comparative prediction value of the newborn's condition was found for both ratios [Sibai 2006].

Table 2. Clinical assessment of the groups analysed, treatment and delivery method

	Group I [n = 38]	Group II [n = 36]	Group III [n = 42]	Significance
Obstetric examination on admission				
% of cervical shortening median, (quartile interval) <min – max>	25 (100) <0–100>	55 (90) <0–100>	50.0 (50.0) <0–100>	p = 0.038
cervical dilation (cm) Median, quartile interval <min – max>	0 (0) <0–1>	0.5 (1.0) <0–2>	1 (0.50) <0–3.5>	p < 0.001
Premature rapture of membranes, (%)	2 (5.2%)	6 (16.66%)	23 (54.76%)	p < 0.001
Presence of non-specific indications of inflammation				
Leucocytosis [000/ml] average, SD <min – max>	12.32 (4.40) <5.0–21.9>	11.85 (3.10) <6.6–19.0>	12.15(3.41) <5.9–21.2>	p = 0.862
positive CRP (>7.0 mg/dl), n(%)	18 (47.36)	12 (33.3)	16 (38.1)	p = 0.455
Application of tocolysis and antibiotic therapy				
Tocolysis n, (%)	27 (71.05)	9 (25.0)	38 (90.47)	p< 0.001
Antibiotic therapy n, (%)	19 (50.0)	14 (38.88)	27 (64.28)	p = 0.08
Delivery method				
Number of caesarian sections n, (%)	38 (100)	34 (94.44)	28 (66.66)	p < 0.001

Table 3. Results of ultrasonographic test.

	Group I [n = 38]	Group II [n = 36]	Group III [n = 42]	Significance
Results of doppler ultrasonographic test				
Pulsation index (PI) at umbilical artery (UA) median, (quartile interval) <min – max>	1.25 (0.48) <0.79–2.95>	1.10 (0.30) <0.59–2.4>	0.97 (0.27) <0.6–2.56>	**p < 0.001**
Pulsation index (PI) at middle cerebral artery (MCA) median, (quartile interval) <min – max>	1.34 (0.360) <0.82–1.99>	1.21 (0.400) <0.71–1.94>	1.67 (0.630) <0.91–2.41>	**p = 0.003**
CPR median, (quartile interval) <min – max>	1.06 (0.358) <0.45–1.63>	1.1 (0.313) <0.52–2.46>	1.61 (0.662) <0.8–3.77>	**p < 0.001**
Amniotic fluid index (AFI) [mm] average, SD <min – max>	98.55 (31.24) <11–166>	101.19 (28.65) <36–190>	73.55 (47.88) <10–209>	**p =0.002**

Preterm delivery can be clinically divided into: spontaneous delivery, caused by preterm labour (with ineffective tocolysis) with preserved amniotic sac and premature rapture of membranes (PROM), and induced delivery, where the pregnancy is terminated due to indications for the mother or the foetus [Gramellini *et al.* 1992]. This division was applied in our material. The comparative group (Group III) was formed by patients with spontaneous preterm delivery, where statistically significant differences were observed both as regards the extent of shortening and dilation of the cervix, and the condition of amniotic sac and the quantity of amniotic fluid as compared to other groups. Group I and II included pregnant women undergoing caesarean section due to the maternal-foetal risk caused by hypertension. The decision on invasive or procrastination approach was dictated with the clinical condition of the patient and the foetus based on additional examination, in line with the principles presented by Norwitz *et al.* [Norwitz & Funai 2008]. The average hospitalisation period from admission to the delivery in the studied group with preeclampsia (5±5 days) is comparable to the time recorded in the study by Chammas *et al.* (6±5 days), where the impact of procrastination procedure on the perinatal outcome was analysed in patients with severe preeclampsia [Chammas *et al.* 2000].

Because the condition at birth is impacted by the time of delivery, it is worth quoting the results of the study by Bombrys et al., who pointed to very low percentage of survivals in premature infants born before completion of week 27 (57%) in pregnancies with complications from week 24 of gestation with severe preeclampsia, despite the implementation of the procrastination procedure [Bombrys *et al.* 2008]. Thus achieved prolongation of the pregnancy to increase the survival opportunities in premature infants may,

however, impact on bad overall condition and health complications in the mothers [Ghoghoberidze *et al.* 2008]. Chang *et al.* pointed to the lower risk of early and late death of newborns in incomplete pregnancies complicated with gestational hypertension as compared to those without hypertension [Chen *et al.* 2006].

To conclude, it must be stated that gestational hypertension, with special consideration to preeclampsia, constitutes an important risk factor and clearly impacts on deterioration of obstetric outcomes in preterm deliveries. Doppler test allows for diagnosing the risk for the foetus, hence it is a very useful method of monitoring complicated pregnancies, particularly in simultaneous hypertension and preterm delivery.

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