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Rational control of arterial pressure during labor in women with arterial hypertension

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ABSTRACT

Objectives: Were to identify the advantages and disadvantages of different protocols of antihypertensive therapy in women with arterial hypertension during the process of labour and their effects on the labour progressing and perinatal complications.

Material and methods: 228 women who had childbirth in 2013–2018 in the Ternopil perinatal centre "Mother and Child" were surveyed. The study included full-term singleton pregnancies in cephalic presentation. According to the treatment program, women were divided into 4 groups: Group 1: 58 pregnant women who neglected treatment or had insufficient compliance; Group 2: 57 pregnant women who used methyldopa and classic beta-blockers during pregnancy and labor; Group 3: 57 pregnant women who received high selective beta-blocker with vasodilating properties nebivolol in addition to methyldopa; Group 4: 56 healthy pregnant women with normal blood pressure and without other somatic pathology.

Results: Hypertension and inadequate hemodynamic control can become risk factors for higher incidence of low birth weight, prolonged or discoordinated labour, excessive blood loss during and after delivery. The program of treating hypertension in pregnant women with nebivolol hydrochloride provides sufficient control of blood pressure and helps to avoid blood pressure spikes or an excessive increase of systolic and diastolic blood pressure and heart rate during childbirth, which could endanger the mother's health.

Conclusions: The treatment with nebivolol hydrochloride for women with chronic arterial hypertension during pregnancy and delivery allows to normalize the progress and duration of labour, decrease the incidence of low birth weight and the percentage of excessive blood loss during labour.

Key words: delivery; arterial hypertension; rational control; nebivolol hydrochloride

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INTRODUCTION

The hemodynamics of a pregnant woman undergoes a significant burden during pregnancy, culminating in childbirth [1, 2]. In women with the uncompromised cardiovascular system, heart rate, systolic blood pressure and cardiac output increase significantly (by 35–45%) due to the elevated circulating blood volume during delivery and directly in the postpartum stage [3, 4]. With the healthy course of pregnancy and childbirth, these changes are accompanied by decreased peripheral vascular resistance, which makes it easier for the maternal cardiovascular system to adapt to complex physiological requirements and hemodynamic conditions [5, 6].

It should be noted that for women with preexisting arterial hypertension before pregnancy their cardiovascular system has already been functioning in conditions of excessive hemodynamic demands to the heart muscle and blood vessels; and pregnancy /labour/ postpartum stage causes an additional significant load to the heart and blood vessels, so childbirth for women with arterial hypertension is an extremely dangerous process [7]. In this regard, a significant amount of research is devoted to controlling blood pressure during pregnancy, as well as the identification of the benefits and disadvantages of certain treatment programs in pregnancy [8, 9], and a smaller amount of research is devoted to the actual course of arterial hypertension during childbirth. The work of Eva Martin, (2016) [10], on the treatment of the rise of arterial pressure during childbirth, draws attention. According to this report, women who had high blood pressure during childbirth (more than 2.500 birth histories were analyzed) had a 4-fold higher number of disabling complications, namely the thrombotic and hemorrhagic

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complications (cerebral stroke and myocardial infarction), angina attacks, convulsive states, sepsis, blood transfusion. This study also compared methods of emergency care for sudden high blood pressure spikes during labour and the correlation of each method with the number of debilitating complications. However, the aforementioned study did not aim to consider methods for controlling blood pressure during pregnancy and the effect of controlling arterial hypertension during pregnancy on the course of labour, but only the urgent „spikes" and severe range hypertension during labor and its urgent care, that allows to continue the scientific research in this direction.

Objectives

Were to identify the advantages and disadvantages of different protocols of antihypertensive therapy in women with arterial hypertension during the process of labour and their effects on the labour progressing and perinatal complications.

MATERIAL AND METHODS

Participants

During 2013–2018, 228 women were surveyed in Ternopil regional perinatal centre „Mother and Child", and their charts were analyzed. Arterial hypertension was verified in 172 women, 56 women were healthy and formed a control group. The study included labouring women on 40 ± 2 weeks of gestation.

The criteria for inclusion of pregnant women in the trial were: 1) singleton pregnancy; 2) the onset of labour in the anterior occipital presentation; 3) the presence of the arterial hypertension of the I-II stage or episodes of hypertension in the history; 4) the possibility of observing all the patients from the 12th week up to the childbirth and within 90 days of the postpartum stage; 5) the absence of previous myocardial infarction or cerebral haemorrhage; 6) the absence of clinical manifestations of preeclampsia at the start of observation; The exclusion criteria were: 1) severe concomitant somatic pathology (diabetes mellitus, hypo/hyperthyroidism, cardiac failure, renal failure, severe anaemia etc.) or severe obesity; 2) infectious pathology (pneumonia, pyelonephritis); 3) traumatic injuries during pregnancy.

According to the treatment protocol during pregnancy and childbirth, the laboring women were divided into 4 groups: the 1st group — 58 pregnants who neglected the treatment of arterial hypertension before pregnancy and had insufficient compliance during pregnancy; the 2nd group — 57 pregnants with arterial hypertension, who used methyldopa and classic beta-blockers, (atenolol, metoprolol, bisoprolol) during pregnancy; the 3rd group — 57 pregnants who received high selective beta-blocker with vasodilating effect nebivolol hydrochloride (5–10 mg orally per day) in addition to methyldopa; the 4th group — 56 healthy pregnants without hypertension or other somatic pathology.

Interventions

Arterial pressure was monitored using the Holter system for surveyed women from the beginning of labour and within 48 hours after childbirth to analyze the effectiveness of different therapy protocols. Measurement of the basic parameters of central hemodynamics and respiration rate was performed at the beginning of the 1st stage of labour; at the start of an active phase of labour (cervical dilatation more than 3 cm), in the 2nd stage of labour, in the 3rd stage of labour and 2 hours after delivery.

Statistical analysis

Quantitative variables were expressed as mean ± SD and categorical variables as number and percentage.

Ethical approval

Informed consent was obtained from the all pregnant women after notified verbally and in writing about the detailed plan, assumptions and scope of the study. The research project was approved by the Ethics Committee of the Ternopil State Medical University, Ternopil, 2014.

RESULTS

In the 1st group, the highest spikes of systolic blood pressure (SBP) and diastolic blood pressure (DBP) that exceeded the rates in pregnancy by 20–45% were present. At the onset of labour, there was a sustained high blood pressure with a maximum peak of 168.2 ± 5.82 mm Hg in the 2nd stage and a moderate decrease to 140.2 ± 1.26 mm Hg in the 3rd stage of labour (Tab. 1).

Patients of the 2nd group, who received methyldopa and beta-blockers without vasodilating properties had insignificant spikes of systolic pressure at the onset of labour, SBP differed from the weekly values by over 12%, and rigidity of DBP was observed.

Comparing heart rate in the Group 2 and Group 4, the increase in heart rate of Group 2 women does not correspond to the rate of increase in healthy women, and ranges by only 4 beats per minute, that is 20% less than in healthy pregnant women. The insufficient compensatory increase of heart rate was accompanied by shortness of breath while in healthy childbirths respiratory rate grew smoothly, changing to slow deep breathes during pushes.

In women belonging to Group 3, the SBP and DBP did not exceed the values determined as normal blood pressure. The increase in heart rate and respiratory rate were close to the same in the control healthy group. These parameters indicate that adequate control of blood pressure during

Table 1. Parameters of arterial pressure and heart rate in the labouring women (M ± m)

Groups (n = 88)	Labour progress	SBP, mm Hg	DBP, mm Hg	Heart rate, per min.	Respiratory rate, per min.
1 group	Onset of labor	136.2 ± 1.78*	108.8 ± 1.08*	92.0 ± 1.88	18.8 ± 1.15
	First stage	139.2 ± 3.11*	110.4 ± 4.24*	92.0 ± 5.55	21.0 ± 1.22
	Second stage	168.2 ± 5.82*	111.2 ± 1.43*	111.0 ± 6.50*	22.4 ± 1.33
	Third stage	140.2 ± 1.26*	108.8 ± 0.92	99.0 ± 4.28	21.2 ± 1.12
	2 h. after delivery	138.2 ± 4.98*	92.6 ± 1.12*	80.0 ± 4.66*	20.1 ± 1.25
2 group	Onset of labor	138.2 ± 3.15*	102.8 ± 1.08	77.0 ± 6.81	19.8 ± 1.32
	First stage	143.3 ± 4.34*	102.1 ± 1.24*	79.0 ± 4.94	21.8 ± 1.53
	Second stage	149.8 ± 5.39*	103.4 ± 2.59*	81.0 ± 4.81	25.3 ± 1.22
	Third stage	140.2 ± 1.26*	102.8 ± 2.92	80.0 ± 2.88	22.5 ± 0.68
	2 h. after delivery	138.2 ± 2.98*	90.6 ± 1.12*	74.0 ± 1.56*	20.5 ± 0.88
3 group	Onset of labor	125.2 ± 2.15	88.6 ± 1.08	80.0 ± 1.81	18.6 ± 1.30
	First stage	125.3 ± 2.34	90.6 ± 2.24	81.0 ± 3.94	19.0 ± 1.88
	Second stage	142.8 ± 2.52	94.8 ± 0.59	87.0 ± 4.41	22.0 ± 1.56
	Third stage	130.2 ± 2.26	86.8 ± 3.92	80.8 ± 1.88	21.8 ± 1.34
	2 h. after delivery	128.2 ± 2.98	85.5 ± 2.12*	76.0 ± 2.56*	20.5 ± 1.08
4 group	Onset of labor	118.2 ± 2.15	78.8 ± 1.08	87.0 ± 2.81	18.6 ± 1.06
	First stage	113.3 ± 4.34	78.1 ± 1.24	91.0 ± 3.94	18.8 ± 1.06
	Second stage	126.6 ± 2.39	82.9 ± 0.59	99.0 ± 5.81	20.8 ± 1.42
	Third stage	121.2 ± 2.26	81.2 ± 0.92	89.0 ± 5.88	18.8 ± 1.34
	2 h. after delivery	111.2 ± 3.98	76.6 ± 1.12	80.0 ± 2.56	19.8 ± 1.12

Note: * — the values of the indices are significantly different from the control data ($p < 0.05$)

childbirth was achieved. That let to avoid sharp spikes of SBP, DBP, and heart rate, which would pose a health hazard to the mother and the newborn. Patients in this group did not suffer from shortness of breath. This indicated the provision of adequate reactivity of the circulatory system in these women.

The important indicators in obstetrics are the amount of blood loss, the weight of the newborn and his/her Apgar scale scoring and can be relevant to the protocol of antihypertensive therapy that was used for hypertensive pregnant (Tab. 2).

The highest blood loss was observed in women who neglected the treatment of arterial hypertension. In patients of Group 2, the level of blood loss did not significantly exceed the same parameters of the patients belonging to Group 3, and slightly exceeded the blood loss of healthy women. The blood loss in Group 3 was close to average blood loss of healthy childbirth in our study.

Newborn babies from mothers of the Group 1 and Group 2 had lower values of Apgar score than in newborns from mothers of Group 3 which was close to the results of newborns in the control group. The lowest rates were in newborns from mothers of Group 2 but did not differ significantly from the Group 1.

The importance of hemodynamic control in women with arterial hypertension during labour could be shown comparing the incidence of prolonged labour and the number of common complications in each group (Tab. 3).

Table 2. Some parameters the childbirth outcome in women with arterial hypertension, depending on the treatment protocol, and in the control group (M ± m)

Indicator	Group 1 (58 women)	Group 2 (57 women)	Group 3 (57 women)	Group 4 (56 women)
Blood loss, mL	331.1 ±11.2*	288.6 ± 23.1*	245.4 ± 14.6	234.5 ± 10,7
Birthweight	3118.9 ± 32.9*	3002.2 ± 31.2*	3224.6 ± 3.03	3298.5 ± 32.9
Apgar scoring 1 min	7.4 ± 1.2*	7.3 ± 1.2*	7.9 ± 1.9	8.2 ± 1.8
Apgar scoring 5 min	8.9 ± 1.4	9.0 ± 0.9	9.6 ± 0.4	9.8 ± 0.2

Note: * — the values of the indices are significantly different from the control data ($p < 0.05$)

Table 3. The frequency of labour complications comparing different protocols of arterial hypertension therapy and control group

Labor special features	Group 1 (58 women)	[%]	Group 2 (57 women)	[%]	Group 3 (57 women)	[%]	Group 4 (56 women)	[%]
Women with 1st stage lasting over 8 hours (primapara)	10	17.9	10	17.5	5	8.6	2	3.6
Women with 1st stage lasting over 2 hours (multipara)	13	23.2	13	22.8	4	7.0	2	3.6
Women with blood loss over 400 mL	17	30.4	15	26.3	5	8.8	2	3.6
Women with blood loss over 1000 mL	2	3.6	1	1.8	0	0.0	0	0.0
Neonates with birthweight less then 2500	10	17.9	11	19.3	6	10.5	2	3.6
Macrosomia	6	10.7	6	10.5	5	8.8	4	7.1
Cesarian section	2	3.6	2	3.5	1	1.8	1	1.8

A reliably higher percentage of women who experienced prolonged or discoordinated labour was detected in groups with chronic arterial hypertension and we attribute that finding being a reflection of the general, systemic problem in the body of a woman suffering from hypertension. In groups 1 and 2, there was a reliably higher number of women for whom labour induction was necessary (use of prostaglandins, oxytocin, amniotomy, etc.). The number of women required such intervention was twice lower in the group using nebivolol hydrochloride. In the control group, there were only 2 cases of prolonged labour in primipara and 2 cases in multipara, which is twice less than in Group 3, and four times less than in groups 1 or 2.

The blood loss during labour in patients with chronic arterial hypertension was significantly higher. Thus, in 17 patients of Group 1 and 15 patients in Group 2, the blood loss in childbirth was more than 400 mL. The patients in Group 1 and 2 who underwent a cesarean section, had hemorrhagic complications with a blood loss over 1000 mL. In women of Group 3, the incidence of bleeding over 400 mL was 5 women (8.8 %). In the control group, 2 women (3.6 %) had blood loss over 400 mL, 1 of which had a cesarean section.

The number of newborns weighing less than 2500 g was 10 (17.9%), in Group 1; 11 (19.3%) in Group 2; and 6 newborns (10.5%) in Group 3. While in the control group only 2 newborns weighed less than 2500 g, (2450 g and 2490 g, in mothers with asthenic body structure and small height (both women were 158 cm in height).

Macrosomia occurred uniformly in all groups from 7.1 to 10.7%, and it was most likely genetically determined and did not reliably affect the general characteristics of the studied parameters.

DISCUSSION

Nowadays, big trials provided enough evidence that hypertension is associated with increased maternal (such as stroke, myocardial infarction, heart or renal failure) and fetal risks, increased perinatal morbidity and mortality and placental abruption rate, and that treatment of chronic hypertension may prevent progression to severe hypertension [11–14]. In addition, the encephalopathy syndrome, defined as the presence of neurological symptoms coupled with the radiologic findings of vasogenic cerebral oedema, seems to occur at lower peak SBP in pregnant compared to non-pregnant patients with hypertensive encephalopathy [14–19].

There are also data showing that the presence of hypertension itself results in lower birth weights, regardless of the use of medication, because arterial hypertension impairs placentation even at the early stages of gestation compromising normal blood supply on later terms [20–22] .

The levels of blood pressure when therapy should be provided is still controversial. An important task for medical provider is to help the pregnant woman and her fetus to hold out until and during the childbirth, to ensure an adequate reserve of compensatory mechanisms and to prevent maternal cardiovascular or other complications.

The choice of antihypertensive medications has been limited to those that have proven to be relatively safe and have acceptable side-effect profiles. Methyldopa and hydralazine, respectively, are recommended as initial oral or intravenous therapy [23–25]. Methyldopa has a record of safety in pregnancy, the disadvantage is slow and low efficacy of the antihypertensive effect. For the second-line drugs are calcium antagonists and β-blockers [26, 27]. Calcium antagonists can cause a sudden or excessive decrease of blood pressure impairing uteroplacental-fetal perfusion, and therefore, fetal distress, or side effects for mother (headache, skin flushing, swelling of legs, tachycardia, dizziness). The main side effects of β-blockers for mother are bradycardia, bronchospasm, dyspeptic symptoms, skin-allergic reactions, violations of contractile activity of the uterus and intrauterine growth retardation of the fetus, or bradycardia, hypotension, hypoglycemia, respiratory depression in the newborn [27, 28].

Therefore, cardioselective β-blockers with vasodilating properties may be preferable and prevent the negative ef-

fects of non-selective β-blockers [27, 29]. In particular, nebivolol lowers the heart rate less than other cardioselective β-blockers is recognized as an advantage, in combination with peripheral vasodilatation, it has a better effect on central arterial pressure. The main mechanism of nebivolol action is associated with the stimulation of the NO synthesis and bradykinin, which provide peripheral arteriolar vasodilation [30] and restoration of vascular endothelial function. Nebivolol also did not show central sympathomimetic action, that is why it does not affect central aortal pressure, normalization of which is extremely important for the adequate provision of uteroplacental-fetal circulation [27, 29, 30].

The results obtained on nebivolol hydrochloride proved to reduce the incidence of typical obstetric complications by almost twice compared with patients who generally denied treatment or were treated with β-blockers without vasodilating properties, but the frequency of both hemodynamic and obstetric problems still remained 1.5–2 times higher than in healthy pregnant women with normal blood pressure. These results allow to achieve the better obstetric and perinatal outcomes, but are not an absolute solution of the problem, since the problem of arterial hypertension and its manifestations during pregnancy affect the extremely complex mechanisms of hemodynamics, hormonal balance, immunity, genetics and even the psychological aspects of the health of the pregnant woman.

CONCLUSIONS

Hypertension and insufficient hemodynamic control are the risk factors for prolonged or discoordinated labour and excessive blood loss during and after childbirth, and a higher incidence of low birth weight infants.

The pregnants who neglected treatment or have insufficient compliance, have the highest risk of somatic complications, their hemodynamic indices (SBP and DBP, heart rate) during childbirth exceeded significantly than required for compensatory mechanisms of the body for childbirth. They also had the highest rates of blood loss during childbirth as well as their newborns had lower average birth weight and lower Apgar score at the 1 minute compared with healthy mothers and those who received treatment with nebivolol hydrochloride.

The pregnants who were given methyldopa and classic beta blockers had reliable control of hemodynamics during childbirth, but mechanisms of responses showed decompensation and were manifested in dyspnea, as well as their newborns had lower average birth weight and lower Apgar score at the 1 minute compared with healthy mothers and those who received treatment with nebivolol hydrochloride.

Pregnants who used nebivolol hydrochloride confirmed adequate control of the central hemodynamics: SBP, DBP, heart, and respiratory rate did not exceed the referent values. The duration of labour and blood loss did not significantly exceed comparing to healthy women, and the assessment of newborns by the Apgar scale was close to the assessment of infants born from healthy mothers.

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