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Stroke in Pregnant Patient: Obstetric and Neurosurgical Outcomes

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Abstract

The aim of the study is to improve the obstetric and neurological outcomes in pregnant patients with stroke.

Objective of the study

1. To perform correct neurological diagnosis and estimate the possibilities of the pregnant patient with stroke to prolong pregnancy, endure corresponding adequate Anaesthesia during vaginal natural or operative delivery or cesarean section.
2. To minimize obstetric and extra genital complications in pregnant women with stroke during the course of pregnancy, to stabilize neurologic status with spasmolytic, hormonal, neurologic, anticoagulation preparations and vitamins.
3. To make delivery maximally natural without aggravation of the neurologic status with gradient of preference: natural vaginal delivery – the best, vaginal operative delivery, cesarean section – emergency way.
4. To avoid in the puerperium neurologic, obstetric and neonatal complications in patients with stroke by careful inspection and rational treatment.

Material and Methods: The results of pregnancy and delivery of 140 women with stroke were presented; 98 before and 42 during the current pregnancy. The etiology of the cerebral catastrophe included 82 ischemic strokes and 58 hemorrhagic strokes. All patients were consulted by neurologist, neurosurgeons, radiologists, cardiologist, and obstetricians. Routine laboratory analyses clinical biochemistry, thrombophilia screening, coagulation tests and instrumental methods such as ultrasound investigation of the pregnant uterus, magnetic resonance tomography, ultrasound duplex investigation of extra- and intracranial vessels, ophthalmoscopy, cardiotocography have been fulfilled. If indications had place angiography and spiral computer tomography echo-encephalography were accomplished.

Results: There were most term deliveries in pregnant women with stroke: 67 patients (47, 9%) had cesarean section and 73 patients (52.1%) had vaginal delivery including 24 patients (more than 1/3) with operative vaginal delivery (vacuum extraction, forceps). 142 live babies were born and 135 (95.1%) of them have been discharged home in satisfactory state and 7 babies (4.9%) were transferred to the department of the pathology of newborns predominantly due to prematurity and infection. There were no maternal and perinatal mortality.

Conclusion

1. Pregnant women with stroke should be observed with team of neurologist and obstetrician and if needed radiologist, oculist, neurosurgeon, anesthesiologist who have experience in treating such patients.
2. All needed diagnostic investigation including expensive and dangerous should be carried out promptly and neurologic operation should be performed if needed.
3. Treatment with needed medication is indicated in such small group of high risk pregnancies despite the fact of pregnancy to improve obstetric and neurologic results in women with stroke.
4. The natural vaginal delivery is preferred with possibility of vaginal operative delivery and both planned and emergency cesarean section.
5. In puerperal period strong rational recommendations about anticoagulation and neurological rehabilitation of women should be done.

Keywords: *Pregnancy; Hemorrhagic Stroke; Ischemic Stroke; Delivery of pregnant women with stroke*

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Introduction

One of the main problems of the Russian public health is t is mother's and child's care, presenting of prophylactic methods and treatment of the complications of pregnancy and labour. Nowadays 60% of pregnant patient have extra genital pathology (EGP), so the index of health of the present pregnant women is low. EGP complicates the course of pregnancy considerably. EGP in 2011-2012 has been the second reason of the maternal mortality but now it is of the first rank [1,2].

Stroke in pregnant women is the most complicated medico-social problem of the modern world. Specific anxiety causes increasing strokes in young women. In patients aged 20-24 years the frequency of stroke is 2, among patients aged 29 – 5, among patients aged 34-10, over 35 years – increased up to 30 cases per 100 000 of population [3]. Stroke during pregnancy is a rare phenomenon and according to the literature it frequency changes from 9 up to 34 cases per 100000 deliveries. The risk of stroke during pregnancy increases 3-13 times and maternal mortality up to 1, 4 cases per 100 000 deliveries [4-7]. What are the difficulties of treatment of such patients?

1. Conservative and especially neurosurgical treatment of stroke in pregnant patients may present certain risk for the gestational period.
2. Some conditions and physiological changes during pregnancy may increase the risk of decompensation of the intracranial system.
3. Generally, there is hardly ever sufficient experience in treating such patients.
4. At present the randomized controlled assays and clinical recommendations about treating such patients are missing.

The mentioned above statements lead to the main aim of the research, which is the analysis of complex clinical cases which have taken place in our institution in 2012-2017.

Material and Methods of Investigation

We have accomplished retro- and prospective analyses of the course of pregnancy, delivery and perinatal outcomes of 140 pregnant women with stroke. The pregnant women who already had stroke before pregnancy and were entirely examined and treated in neurological and neurosurgical clinics were included as well as patients who had the debut of stroke during the present pregnancy. The criteria of exclusion were traumatic subarachnoid hemorrhages and ruptures of aneurisms of the traumatic origin.

According to the type of stroke the patients have been divided in groups: 82 pregnant women with ischemic stroke (IS), 31 patients had IS during the present and 51 patients had IS formerly, 4 patients had cerebral venous thrombosis (CVT) during pregnancy. 11 patients had hemorrhagic stroke (HS) during gestation. The reasons of HS were rupture of arterial cerebral aneurism (AA), 1 patient had rupture of cavernous malformation (CM), 3 patients had CVT with hemorrhagic transformation, 1 patient had rupture of arteriovenous malformation (AVM) and 3 patients had no definite diagnosis of the cerebral hemorrhage. 47 patients had HS in formerly: 17 patients were with rupture of arterial aneurism, in 14 cases there were ruptures of AVA, 9 patients had rupture of CM and I 7 patients there were no definite reasons of HS. All patients had given informed consent about application of examination date in research. The consent of Ethic Committee has also been received.

Multidisciplinary team of obstetricians, neurologists, neurosurgeons, anesthesiologists, oculists, neonatologists, specialists in ultrasound and radiology carried out diagnostic measures, pregnancy survey, delivery and puerperal surveillance. Methods of stroke diagnosing included: transcranial dopplerography of cerebral vessels and echo-encephalography during pregnancy, delivery and postpartum; in order to determine the optimal method of analgesia, magnetic-resonance tomography, cerebral angiography, electro-encephalography, ophthalmoscopy, ultrasound examination with duplex scanning of cerebral vessels, daily monitoring of arterial pressure, ultrasound antenatal examination of the fetus and cardiotocography, common laboratory investigations. Methods of neurovizualization have been accomplished in the scientific center of the neurosurgery by academician N.N. Burdenko.

Statistic results were obtained with the help of the program «Med Calc». The data with normal distribution were presented with M+- SD (standard deviation), data with anomaly distribution were described with mediana and levels of percentiles, data of distinctive character (quality) were presented in percent's or absolute meaning. For significant difference of qualitative signs (parts in groups) strict criterion of Fisher was used. Significant level of difference was appreciated as less than 0.05.

Obtained Results

Most women included in the investigation were aged 23-42 years (middle 30 years). The patients with IS were older. In this group 69 % were multiparas having 1-3 deliveries, in the group with HS 49% were multiparas (Table 1). Previously every fourth delivery of women with IS has been terminated operatively. Half of patients with HS had caesarean delivery in anamnesis. The main indication for abdominal delivery of women with HS and IS was conclusion of neurologist and neurosurgeon due to the presence of the diagnosis of stroke.

In the 1st trimester of pregnancy IS complicated the gestational process in 15.4%, in the 2nd trimester – in 23.1%, in the 3rd trimester in 61.5% of causes, according to trimesters HS took place in 28.6%, 42.8% and 28.6 % of cases (Table 1). From our perspective high frequency of vascular spasm of ischemic origin in the 3rd trimester is caused by high rate of preeclampsia which is caused by endotheliosis. The most frequent vascular anomaly in the form of HS in the 2nd trimester may be explained by hemodynamic changes which are maximal in that trimester on the basis of preexistent anatomic anomaly.

	IS (n = 82)		HS (n = 58)	
	абс	%	абс	%
Age				
17-22	23	28,0	14	24,1
23-30	29	35,4	25	43,1
31-36	18	22,0	11	19,0
> 36	12	14,6	8	13,8
Number of pregnancies				
First pregnancy	29	35,5	18	31,0

Second pregnancy	26	31,7	23	39,7
Third pregnancy	18	22,0	11	19,0
Fourth and more	8	9,8	6	10,3
Time of stroke (in pregnancy)				
First trimester	4	4,8	3	5,1
Second trimester	8	9,7	5	8,6
Third trimester	19	23,1	3	5,1

IS - ischemic stroke, HS - Hemorrhage stroke

The data from the table 1 show that the debut of the stroke is usually in the second and the third trimesters during the first and the second pregnancies.

Table 1: *Debut of Stroke during Pregnancy.*

The investigation data of cerebral region locations of ischemic site and hemorrhagic points (Table 2) show the regions of middle cerebral artery (45.1%), rear cerebral artery (35.4%) and vertebrobasilar district (12.9%). Extra genital pathology as risk factor is present in Table 3. The ranks are as follows - arterial hypertension, cardiovascular diseases – valvular pathology, thrombophilia. Many modern authors consider arterial hypertension a crucial risk factor of stroke in pregnant women [4,9]. Our data show that arterial hypertension occurred in 53.8% and 42.9% of cases comparatively higher than in patients who had IS and HS formerly before 21.8% and 31.2%. The majority of pregnant patients had several diseases and this fact complicated both gestational process and delivery.

Region	Number
Ischemic stroke (n = 31)	
Brain-stem-cerebellum infarct	2
Middle cerebral artery	14
Posterior cerebral artery	11
Vertebro-basilar system	4
CVT	4
Hemorrhagic stroke (n = 11)	
Right hemisphere hemorrhage	2
Left hemisphere hemorrhage	9
Arteriovenous malformation	1
Arterial aneurisms	3
Cavernous malformations	1
CVT with hemorrhagic transformation	3

CVT - cerebral venous thrombosis

Table 2: *The regions of illness in patients with stroke.*

The data of Table 2 show that middle cerebral artery and posterior cerebral artery are the main of vessels in IS in pregnant patients and is HS the main sites are left hemisphere hemorrhage, arterial aneurisms and CVT with hemorrhagic transformation.

	IS (n = 82)	HS (n = 58)
Etiology		
Preeclampsia	24	3
Thrombophilia	39	17
Cardiac diseases	22	12
Hypertension	24	28
AA	-	20
AVM	-	14
CA	-	10
Unknown	8	9
CVT with hemorrhagic transformation	-	4
Risk factors		
Gestational DM	11	6
Gestational hypertension	24	28
Preeclampsia/eclampsia	21	3
Prior stroke	51	31
Cardiac diseases	5	3
Cigarette smoking	15	9
Hospitalization stay		
72 hours	27	-
5-15 days	5	-
> 20 days	2	7

A - Arterial Aneurism,

AVM - Arterio- Venous Malformation, CA – Cavernous Angioma

Table 3: *Etiology, risk factors, hospitalization stay in pregnant patients with stroke.*

The most frequent gestational complications were threatened abortion, and early toxicosis. Clinical signs of complications such as weakness, dizziness, vomiting and nausea are identical to signs of stroke. Often these clinical signs are underestimated and promote the underestimation of the pathology of CNS. That is why after pathogenetic therapy of vomiting of pregnancy in the absence of positive effect. It is needed to exclude the CNS pathology. Supplementary investigation is needed to specify the absence of the pathology of the CNS. Preeclampsia complicated the course of pregnancy of 29 patients with IS (35.4%) and of 12 patients with HS (20. 7%).

All patients with CVT were examined and thrombophilia was verified in 90%, the frequency of thrombophilia in patients with HS is 75%. Comparison of different forms of genetic polymorphisms in two examined group showed a statistically significant difference of occurrence of F V Leiden mutation which was 20% and 17% in the group of patients with CVT with hemorrhagic transformation and spontaneous HS, correspondingly these numbers exceeded the frequency of mutation of this gene in patients with IS which has been found in 4.4% of cases.

Indications for anticoagulant therapy with unfractionated heparin (UH) and low molecular weight heparins (LMWH) were defined by presence of thrombophilia and clinical course of the disease. 105 patients had prophylactic anticoagulant therapy - 67 patients with IS (81.7%) and 38 patients with HS (65.5%). It is sufficient to notice that acute stage of HS was a contraindication for heparin therapy. The appreciation of treatment effectiveness was according to notational thromboelastometry data. Difference of clotting time

parameter in Intem and Heptem tests, the level of anti FXa activity and some parameters of the test of thrombodynamics. The results of investigation of these tests in 94 patients showed insufficient effect of the standard doses of heparins in 16 cases with IS and in 12 cases with HS. Correction of the treatment with dose enlargement has been accomplished. The standard UH dose is 5000 Units twice a day subcutaneously. It was applied in 78.9% of cases of patients with diagnosed thrombophilia.

All patients with IS (in anamnesis and during the current pregnancy) had antithrombotic treatment and symptomatic therapy: anticonvulsant, dehydration, vascular and other preparation according to protocol of treatment. After discharge from neurologic clinic 10 patients were exposed to rehabilitation measures. According to our data there was vascular cerebral anomaly as the reason of HS: rupture of AA in 31.8%, rupture of AVM in 25.0%, and also cavernous angioma in 18.2% of cases. In our observations the rupture of cerebral vessels manifested in subarachnoid hemorrhage and patients had nonspecific complaints: heavy headache, nausea and vomiting, disturbances of consciousness sometimes with arterial hypertension up to 160/100 mm Hg. In all cases the verification of the diagnosis was accomplished after computer tomography.

Neurosurgical intervention was accomplished because of HS in 43 patients; 39 were not pregnant. There were such interventions as clipping of AA/AVM in 17 patients, endovascular embolization and clipping of afferent vessels of AA/AVM in 13 patients, radio surgical treatment in 1 patient, cutting off/ removement of vascular anomaly of cerebral vessels in 9 patients. 4 patients were operated during the current pregnancy at 19, 21-22, 33 and 35 weeks of gestation. Transcranial clipping of the neck of aneurism because of its rupture, and cutting off of AVM in 1 patient has been performed. All pregnancies have been prolonged up to term after surgical interventions, 1 patient was delivered by cesarean section, 2 patients had vacuum-extraction, and 1 multipara with rupture of AA after surgical treatment in the third trimester had spontaneous vaginal delivery.

Most of investigated patients had remaining neurologic symptoms after stroke. The data received after something through investigation and consultations of specialists are presented in Table 4. It seems that despite adequate treatment of IS and HS in patients 46.2% and 70.7% of them had residual neurologic symptoms. 53.8% of pregnant patients had regress of neurologic clinic. So, stroke both of ischemic and hemorrhagic origins even before gestation is a serious problem for obstetrician and neurologist at the beginning of pregnancy with extra examinations sometimes dangerous but necessary for prevention of recidive of disease and application of needed supplementary medications.

Symptoms	**IS (n = 82)**		**HS (n = 58)**	
Encephalopathy	N	%	N	%
	8	9,8	4	6,8
Headache	11	13,4	11	18,9
Hemiparesis	8	9,7	6	10,3
Monoparesis	6	7,3	2	3,4
Hemiplegia	-	-	1	1,7
Hyposteses	6	7,3	2	3,4
Hemianopsia	5	6,1	2	3,4
Atrophy of the optic nerve	4	4,8	5	8,6
Retinal angiopathy	15	18,2	4	6,8
Cyst of the brain	3	3,6	3	5,1
Symptomatic epilepsia	-	-	12	20,6
Total	66	80,4	52	89,6

Table 4: *Residual neurological symptoms after acute cerebrovascular accidents in pregnant patients with stroke.*

The data of the table 4 show encephalopathy, headache, retinal angiopathy and hemiparesis are the most frequent residual neurologic symptoms after acute cerebrovascular accidents in pregnant patients.

In the clinics of the Moscow's Regional Scientific Research Institute of Obstetrics and gynecology all 140 patients with stroke have been delivered: 67 patients (47.9%) had cesarian section, 73 patients (52.1%) had vaginal labor, among them 49 (67%) had spontaneous vaginal delivery, 21 patients (29%) had vacuum-extraction operation and 3 patients (4%) had been delivered by forceps (Table 5). Indications for vaginal operative deliveries were conclusions of neurologist and neurosurgeon about necessity of limitation or exclusion of bearning down efforts. There were no complications during operations and early puerperium. The most frequent indication for abdominal delivery has uterine scar after previous cesarian section in both groups – 47.1% for IS and 49% for HS accordingly.

Method	IS (n = 82)		HS (n = 58)	
	N	%	N	%
Vaginal delivery	35	42,7	14	24,1
Vacuum extraction	9	11	12	20,7
Forceps	1	1,2	2	3,5
Cesarian section	37	45,1	30	51,7

IS - ischemic stroke, HS - Hemorrhage stroke

Table 5: *Method of delivery of patients with stroke.*

Our results show that spontaneous vaginal delivery is possible in patients with stroke and the part of operative vaginal deliveries is rather high among such patients.

In the group with IS the second indication for Cesarian section was severe pre-eclampsia, but in patients with HS the most frequent indication has been stroke itself according to the recommendations of neurosurgeons. Other indications had obstetric origin. Most of patients (85%) did not have complications in labour even with heavy extra genital pathology. In 3.5% cases there was uterine inertia, which is corrected with oxytocic agents. Acute fetal hypoxia was noticed in 5% cases and labour was terminated by vaginal operative delivery. Antenatal hospitalization at 37-38 weeks of gestation and well-timed diagnosis of obstetric complications and treatment resulted in satisfactory obstetric outcome.

Appearance or progressing during labour common cerebral or local neurologic signs is indication for prompt abdominal operative delivery. In cases when cesarian section could not be done (low position of the fetal head in the pelvis) obstetric forceps under intravenous anesthesia are indicated. In such cases urgent consultations of neurosurgeon and neurologist are indicated and examinations with computer tomography or magnetic resonance tomography are indicated to exclude repeat bleeding or other pathology. In our series such complications never occurred, but obstetrician who delivers such patients must be alert and ready to such urgent situations.

Anesthetic help is another problem during parturition of patients with stroke. The aim of anesthesiology is support of homeostatic parameters, protection of patient's brain from ischemic, protection of fetus from hypoxia. At present regional anesthesia (RA) is widely applied in obstetric anesthesiology in forms of spinal and epidural anesthesia. According to the latest information general analgesia during cesarean sections is performed in 15-20% cases [27]. But the presence of intracranial pathology in the patient's organism may considerably change the anesthesiologist help. Why regional anesthesia may be dangerous in pregnant patients with stroke?

1. Liqvoric hypotension in case of spinal anesthesia or epidural anesthesia at random function of Dura mater in patients with AA may cause repeat puncture by increasing gradient on the wall of aneurysm from inside. Liqvoric hypotension the lumba level may provoke dislocation and inclination of the brain - the situation which is dangerous for the patients live.

2. Lowering of the systemic arterial pressure which is common in patients during RA may cause cerebral ischemia which is undesirable in patients with stroke. Bearing in account clinical situation and medico-legal consequences of possible complications even having 1% risk general anesthesia in pregnant patients during neurosurgical operations. In vaginal deliveries of patients with JS and HS epidural anesthesia is preferred.
3. The teratogenety of the used anesthetics is one more important problem. The anesthetics and other pharmacologic preparations used during anesthesia may have effect on further development of the child. To note that mainly used by anesthesiologist preparations are tested as medications with mild teratogenety category B (no proves of risk to human) for propofol or C (risk could not be fully excluded) for phentanyl according to the FDA classification of medications used during pregnancy. Benzodiazepines are an exclusion, they represent category D (there are potential proves of risk). The most risky periods of the fetal development must also be retained in mind. Classic teratogenic period is relatively short - from 14th up to 71 st days of gestation. In this period there is the risk of development of inborn defects of the central nervous system, heart, palate, gastroenterologic organs and eyes. Neurosurgical interventions are logically applied in this period. Summarizing the data on the issue - teratogenety of anesthetics stand out the opinion that "most" of anesthetics are used during such a short time that is why the potential toxicity is minimal. There are no definite data of research in humans that any often used anesthetics are especially dangerous for the fetus. Arterial hypotension and material hypoxemia expose the fetus to much more risk than any of anesthesiology preparations" [28].
4. The analysis of liquor dynamic condition and haemodynamic of cerebral circulation (HCC) in patients during spontaneous delivery to appreciate the effect of analgesia and to the check change in the system of cerebral circulation. The data of systolic peak velocity and resulting diastolic velocity in the 1 st stage of labour in the middle cerebral artery increased during uterine contraction and gradually decreased in the 2 stage during bearing down efforts in patients of both group, with restoration to initial numbers in the early puerperal period (Table 6). The width of the third cerebral ventricle (D3) had a constant tendency to increase with growing of emotional and physical strains during uterine contraction and during labors. Nevertheless, none of the patients had stroke during vaginal delivery. As our data show, epidural analgesia during natural labour gives more beneficial effect on cerebral haemodynamic but has a little postponed and longer effect. Medicamentous analgesia has more prompt but weaker effect on cerebral haemodynamic (Table7).

Method	Measure	I stage of labor		II stage of labor		Early puerperium 45 min after labor
TCD (MCA)		without uterine contraction	during uterine contraction	without labors	during labors	
	Vps sm/sec	102,2 ± 15,2	160,6 ± 23,2	165,7 ± 20	100,2 ± 7	130,4 ± 24
	Ved sm/sec	71,1 ± 16,1	102,4 ± 18,6	109,8 ± 20	51,2 ± 8,1	68,5 ± 6,3
EE	D3,mm	3,3 ± 1,1	4,4 ± 1,0	5,4 ± 1,2	6,0 ± 2,1	4,6 ± 1,1
	Q,%	14 ± 7	8 ± 2	60 ± 20	69 ± 23,3	34,5 ± 14,2

V ps - peak systolic blood flow velocity, Ved - terminal diastolic blood flow velocity

Table 6: *Echo-encephalography (EE) and transcranial dopplerography in the middle cerebral artery (TCD mca) in patients with stroke during spontaneous vaginal labor and in early puerperium*

In 137 cases (97.9%) the pregnancy has been prolonged to term, in 3 cases there were preruture deliveries 142 babies has been born (2 twins). Good condition at birth of newborns from patients with IS was in 71 (85.5%) babies, in mild asphyxia 6 babies have been born, in average asphyxia 1 baby has been born. 3 babies after cesarean delivery (2 babies from twin and 1 baby after preterm operative delivery at 34 weeks gestation were transferred to the department of the pathology of newborns, and 1 baby else was sent to specialized clinic. The condition of newborns of women with HS: 44 babies (79.7%) were born in good condition estimated 8/9 by Apgar scale, in average asphyxia with 6/8 Apgar score only 1 baby was born. 3 babies after cesarean delivery (2 from twin pregnancy, 1 baby after

preterm operative delivery and 1 baby after spontaneous vaginal delivery) were transferred to the department of the pathology of newborns. 135 babies of both groups (95.1%) were discharged home with mothers. It is important to notice that operative vaginal delivery does not worsen the babies' condition in the absence of signs of intrauterine hypoxia.

		Analgesia	
Method	**Measure**	**Epidural analgesia**	**Medicamentous**
TCD(MCA)	Vps sm/sec	132,4 ± 16	138,4 ± 14
	Ved sm/sec	65,2 ± 9,6	70,5 ± 8,3
EE	D3, mm	3,0 ± 0,7	2,9 ± 0,51
	Q,%	17 ± 4	10 ± 4

V ps - peak systolic blood flow velocity, Ved - terminal diastolic blood flow velocity

Table 7: *Echo-encephalography (EE) and transcranial dopplerography in the middle cerebral artery (TCD mca) in patients with stroke during labor according to the method of analgesia.*

The data of the Table 6 show that speed of the blood in the middle cerebral artery significantly enlarges during uterine contraction in the first stage of labour and significantly diminishes during bearing down effort in the second stage of labour. There is a tendency (statistically insignificant) to enlarge of D3 parameter during labour with decrease in puerperium.

According to the method of analgesia (data of Table №7) the speed of the blood in the middle cerebral artery does not differ statistically.

There were no complications of puerperium in females with IS and HS in 95.6% of patients, but others had complications: uterine sub involution – 3 cases, haematometra – 3cases, 1 case of abdominal wall hematoma. Six parturient had hysteroscopy for evacuation of the contents of the uterine cavity with following uncomplicated course. A subaponeurotic hematoma of the abdominal wall was evacuated and followed by conservative measures. There was no endometritis in any case.

Catamnestic inspection has been carried out for 5 years in 102 patients (79.3%) who were delivered in obstetric clinics of the Institute of Obstetrics and gynecology. There was one case of relapse of IS in patient with IS after non-sanctioned withdrawal of therapy. It should be noted that grading of thrombotic risk and prophylactic anticoagulant therapy had to be under control of qualified specialists. In the group of patients with HS 1 patient had endoscopic embolization of AVM with radiotherapy afterwards. At present this patient is in good condition. In all other cases there were no bleeding relapse, thrombosis of brain vessels and other complications. Now three patient are receiving treatment in the rehabilitation center to cure residual neurologic symptomatic after stroke.

Discussion

Currently all over the world including Russian Federation there is no universal register about frequency of stroke among pregnant women. According to our data the frequency of stroke in pregnant patients of the Moscow region was 32.7 per 100 000 deliveries [8]. The researchers are troubled by a tendency of increasing of patients with stroke consulted in the outpatient clinic of the Moscow`s Regional Scientific Research Institution of Obstetrics and Gynecology during last years: 0.96% of all deliveries in 2012 up to 1.52% in 2016. Represented data show the frequency of IS during pregnancy is 3.6 per 100 000 deliveries, of HS is 1, 8 per 100 000 deliveries.

The first report about correlation of cerebral hemorrhages (CH) and preeclampsia was published in 1941 [10], the author reported that CH has been the most frequent cause of maternal mortality in preeclampsia. Never the less it causes doubts became retrospective analysis of cases with heavy preeclampsia and eclampsia in the Moscow's region there were only 2 cases of extensive intracerebral hemorrhage and maternal mortality during 1995-2010 years. But, according to some authors the heavy preeclampsia and eclampsia are causes of maternal mortality and cerebral hemorrhage (four of the five cases) [11,12].

The frequency of intracranial hemorrhages caused by AA and AVM among pregnant patients equals 1:10000 and these hemorrhages are the third cause of maternal mortality of non-obstetric origin. Women younger then 40 years add have rupture of aneurism during pregnancy in 50% of observations [13,14]. 92% hemorrhages take place during pregnancy and delivery and only 8% during puerperium. Neurosurgical treatment is urgent and similar to non-pregnant patients with rupture of vessels. [15] From our point of view, the transcranial operation is utmost indicated for pregnant patients, because it guarantees practically 100% withdraw of aneurism from blood stream [16].

AVM are rare comparing to AA [17] and clinical picture includes hemorrhage and episyndrome. Seizures are successfully treated with antiepileptic drugs (AED) and their application is not contraindicated during pregnancy. In our series 50% of pregnant patients with AVM and cavernous angioma (CA) were treated with AEDs (Depakin chrono, Valproic acid). The rupture of AVM is the cause of maternal mortality in 5-12% of cases. It is well-known the bleeding from AVM is less heavy by clinical signs than from aneurism, but intracranial hematomata are more frequent. The volume and secondary effects of these hematomas form the treatment strategy [18].

Direct surgical intervention is indicated with considerable volume (more than 50 ml) of hematoma and signs of volumic pressure on surrounding cerebral tissue: hematoma's removal is indicated and if possible cutting AVM off. For preoperative investigation of AVM's architectonic magnetic resonance tomography and angiography with abdominal protection can be applied [19]. CA during pregnancy is rather rare. CA is considered one of the most widespread vascular cerebral anomalies with frequency 0, 6: 100000 population and the % of CA among all vascular anomalies of CNS is 10-15% [20]. CA as AVM may be manifested by bleeding or episyndrome [21]. As a cause of stroke CVT was noticed in 4 women (4.8%) with IS and 4 patients with HS. CVT presents a heavy but rare vascular pathology: the frequency among pregnant patients is 1 per 10000 deliveries [22].

It may be clinically alike heavy vascular cerebral catastrophe. There are hemostatic disturbances like thrombophilia among causes of CVT. Serious hormonal changes characteristic for the state of pregnancy may be triggers of thrombophilia clinical signs and this fact gives right to consider pregnant patients as a risk group for CVT [23]. There are no neurosurgical interventions now for this uneasy category of patients. We observed some cases with endovascular neurosurgeons accomplishing catheter thrombolysis in the region of thrombus with alteplasa with good clinical effect [24], but these pregnant patients were missed and were not included in our investigation.

Conservative treatment of HS was indicated when subarachnoid hemorrhage (SAH) had volume less than 30 ml and when the localization of malformation was in deep structures of the brain (in peduncle and stem of brain) and there were high risks of intra- and postoperative complications and no prominent neurologic deficit in pregnant patient occurred. Episyndrome was treated with AEDs. We assume the presence of stroke during gestation is not absolute indication for its termination. In case of heavy condition of the patient with large hemispheric hematomata, status epilepticus during early stages of gestation (I trimester), and the will of the patient or her near relatives the pregnancy should be terminated and the main disease should be cured.

Two moments about strategy of pregnancy searching and delivery are extremely important: the condition of the mother and her fetus and gestational age. More often the patient's condition dominates which include heavy aneurismatic SAH (Hunt-Hess IV-V grades, Fisher 3 and more points), prominent intracranial hypertension induced by enlarged intracranial volume, ischemic edema or hydrocephaly. In this situation the most of specialists consider that woman have to receive whole complex of intensive care and neurosurgical intervention if needed similar to the person without gestation [16,19,21,22].

Age of gestation may radically change all treatment regimens. A term pregnancy allows to provoke delivery and make the situation less dangerous. Sometimes with heavy and neglected intracerebral disease simultant operations would be accomplished including delivery and neurosurgical operation [14]. Commonly neurosurgery can be made only after cesarean section. The problem of delivery is solved by team obstetrician - gynecologist, neurosurgeon, neurologist and anesthesiologist.

It is important to notice that cesarean section rate in pregnant patients with HS was 28.6% and in patients with having HS before pregnancy a formerly has been 58.8%. HS is not absolute indication for cesarean delivery. Other authors also consider vaginal delivery in patients with HS, presenting cesarean section for patients with the risk of recidive of cerebral haemorrage [16,25], but there is opinion of obligatory cesarean section as a method of delivery for pregnant women with HS [26].

Vaginal delivery of such patients follows common rules and is fulfilled by team of obstetricians, anesthesiologist and neonatologist. Programmed labour in daytime is preferred. The time of delivery depend upon female and fetal conditions. Monitoring of arterial pressure and cardiotocography during parturition is carried out. Hypotensive treatment takes place during labour. Constant doses of AEDs are also used. Prophylaxis of postpartum bleeding is realized at the end of the second stage of labour with 10 IU of oxytocin intravenously in bolus or with carbetocin (Pabal -semisynthetic oxytocin with prolonged action) 100 mg (1 ml) intramuscularly or intravenously in bolus in cases of uterine inertia. During labour the oxytotic drugs are not contraindicated.

We propose seven steps for successful delivery of pregnant patients with pathology of the CNS.

- After appearance of clinical symptoms there should be promptest consultations of neurologist and obstetrician who have experience in treating such patients with pathology of CNS.
- Accomplishing of full clinic-instrumental investigation: computer tomography, magnito-resonance tomography, spiral computer tomography, angiography, ultrasound investigation, transcranial dopplerometry, decree the diagnosis and help to perform adequate neuro surgical intervention in the acute phase of the disease.
- Prophylactic anticoagulation treatment with proper laboratory control and fulfillment of rehabilitation neurologic treatment during pregnancy and puerperium.
- Evaluation by neurologist and neuroanesthesiolog patient's condition in the third trimester for choice of the strategy of delivery and anesthesia in labour.
- Evaluation of the fetal condition, concomitant extra genital and obstetric pathology, preparing to delivery, decision about the mode of delivery (vaginal or abdominal) and analgesia by anesthetist.
- Delivery of the patient with pathology of CNS in clinic where such patients are usually delivered. If possible the vaginal delivery is preferred but level of physical strains in labour must be identical to usual life conditions efforts in patients without physical deficit.
- Strict recommendations about anticoagulation and neurological investigation (magnito-resonance tomography, computer tomography, spiral computer tomography, angiography) with rehabilitating neurologic treatment are obligatory.

Conclusion

1. In the Moscow's Region of the Russian Federation pregnant patients with IS dominate over HS.
2. The multidisciplinary team of neurologist, neurosurgeon, radiologist, ophthalmologist
3. us specialist obstetrician us specialist, obstetrician, neonatology, hematology, clinical laboratory specialist, anesthetist has to ascertain the diagnosis, accomplish the surgical treatment if needed, draw up individualized principles of neurologic rehabilitation, anticoagulation and obstetric course and treatment during pregnancy delivery and puerperium.
4. Thrombophilia is often closely related to stroke in pregnancy, the investigation for thrombophilia is obligatory.
5. The spontaneous vaginal delivery is preferable and possible in patients with stroke with preserved normal physical activity.
6. The fetal outcome depends on time of termination of pregnancy and maternal and fetal conditions during delivery.
7. All possible diagnostic procedures and medications should be used in patients with stroke to save the lives of mother and baby and to improve their conditions.

P.S. Pregnant patients with stroke represent very responsible contingent for obstetricians. Good luck! - They are scanty. The most unpleasant is debut of cranial vascular catastrophe taking place during pregnancy. And especially when clinical symptoms progress

promptly or when the situation is life-threatening. When physicians act fast in most cases the life of mother and babies can be saved. The first difficult barrier for obstetrician and neurosurgeon is to overcome the fear - "syndrome of unusual patient".

Conflict of interests

Authors state that there is no conflict of interests in publishing this article.

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