Stroke in pregnancy and puerperium

Anita Arsovska
University Clinic of Neurology
University “Ss Cyril and Methodius” - Faculty of Medicine
Skopje, N. Macedonia
Disclosures and specific domain

1. Nothing to disclose

2. Specific domain: to address diagnosis and treatment of stroke during pregnancy and puerperium
Introduction

- pregnancy and puerperium- female-specific stroke risk factor
- pregnancy-associated stroke: 18% of strokes in women <35 years
- stroke incidence - 25–34 cases / 100,000 deliveries

- 9x increased stroke rate at time of delivery
- 3x increased stroke rate in early postpartum period


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Significant increase in hormonal activity, significant cardiovascular, hemodynamic and coagulation changes

A. PHYSIOLOGICAL CHANGES IN CARDIOVASCULAR SYSTEM AND COAGULATION

Decrease in
- peripheral vascular resistance (35-40%)
- blood pressure (5-10mmHg)
- anticoagulants (protein S)
- fibrinolytic system (increase in PAI-1/PAI-2, decrease in tPA activity)

Increase in
- renal plasma flow and glomerular filtration rate (~50%)
- left ventricular wall thickness
- cardiac output (~45%)
- heart rate (20-25%)
- blood volume (~40%)
- red blood cell mass (~25%)
- vasomotor sympathetic activity
- baroreceptor sensitivity
- major coagulation factors (fibrinogen, factors VII, VIII, X and XII, vWF)

B. PREGNANCY COMPLICATIONS

- Hypertensive disorders of pregnancy: chronic hypertension, gestational hypertension, preeclampsia, eclampsia
- Gestational diabetes
- HELLP syndrome
- Hyperemesis gravidum
- Cesarean section
- Postpartum infection
- Postpartum hemorrhage
- Blood transfusion
- DVT, pulmonary embolism

C. CHARACTERISTICS OF THE PREGNANT WOMAN

- Age, race
- Substance abuse: smoking, alcohol, illicit drugs
- Vascular and cardiac malformations: arteriovenous malformations, aneurysms, moyamoya, patent foramen ovale
- Genetic disorders: sickle cell trait, Cadasil
- Hematological disorders: anemia, thrombocytopenia, thrombophilia
- Heart disease: valvular heart disease, cardiomyopathy, heart failure, atrial fibrillation
- Rheumatoid diseases: SLE, antiphospholipid syndrome
- Other comorbidities: dyslipidemia, diabetes, migraine
Physiological changes in pregnancy

- hypercoagulable state - characteristic of pregnancy

- marked increase in fibrinogen and factor VIII

- fibrinolytic activity is depressed during pregnancy and labour

- DVT - common complication (1-2% for vaginal delivery; 2-10% for C-section delivery)

- pulmonary embolism - potential complication
Risk factors for pregnancy related stroke

- Hematological disorders
- Age >35 years
- Pre/eclampsia
- Race
- Gestational diabetes
- Post-partum period
Risk increases

- Risk of stroke generally increases with age.
- Risk increased dramatically among women aged 35-39 years (58.1 per 100,000 deliveries).
- Highest risk among women > 40 years (90.5 per 100,000 deliveries).


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Hematological disorders

- anemia may result from blood loss that results in cerebral hypoperfusion
- thrombocytopenia
- Sickle cell disease
Preeclampsia/eclampsia

✓ new onset of hypertension and proteinuria/ new onset of hypertension and significant end-organ dysfunction with or without proteinuria after 20 weeks of gestation or postpartum in a previously normotensive patient

- increased risk associated with 1st pregnancy, adv. maternal age, black heritage and past diabetes and hypertension

- occurs in 5 - 7 % of all pregnancies

- 1 out of 200 women who have preeclampsia, blood pressure becomes high enough to have seizures (eclampsia)


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Preeclampsia and eclampsia

- strongest risk factors for stroke (24% - 48%)
- risk potentiated by genitourinary tract infection, hypertension, prothrombotic states and coagulopathies

Preeclampsia and Pregnancy: Recommendations

- women with chronic hypertension/history of pregnancy-related hypertension should take low-dose aspirin from 12th week of gestation until delivery (Class I Level A)

- control hypertension: methyldopa, labetalol, nifedipine (Class I Level A)

– Atenolol, ACEI, ARBS are contraindicated!

- consider screening women with preeclampsia 6 months to 1 year post-partum
- evaluate and treat other stroke risk factors (hypertension, obesity, smoking, dyslipidemia) (Class IIa, Level C)
- document preeclampsia as a stroke risk factor

Gestational Diabetes

• inability to process carbohydrates during pregnancy

• all pregnant women should be screened for gestational diabetes

• in many cases blood glucose levels return back to the pre-pregnancy state after delivery

• diabetes is a risk factor for stroke
- **lifestyle behavior change**

- **Insulin** is the **preferred medication** for treating hyperglycemia in gestational diabetes mellitus

- **Metformin** and **glyburide** should not be used as first-line agents, as both cross the placenta to the fetus!

- **other oral and noninsulin injectable glucose-lowering medications** lack long-term safety data
Post-partum period

- risk of developing thromboembolic disease increased 6-8 weeks after delivery
- complications result from injuries during delivery
- greater risk after a cesarean section than after vaginal delivery

- extremely high relative risk due to decrease in blood volume/ rapid changes in hormonal status/ hemodynamic, coagulative or vessel-wall changes
Stroke risk in puerperium

- women with preterm birth and small for gestational age infants have higher rates of cerebrovascular events

- increased risk for women with prior stroke

- absolute risk depends on presence of vascular risk factors


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Diagnosis of stroke in pregnancy and puerperium

imaging done promptly

MRI - preferred first-line imaging modality in pregnancy

potential hazards: theoretical biological damage, tissue heating; and potential damage to the fetal ear

no harmful short- or long-term effects on fetus at <T1.5

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CT- most appropriate tool for rapid diagnosis

- Fetal radiation dose in non-contrast CT is 5% of naturally occurring background radiation dose during a full-term pregnancy (0.5–1.0 mGy)

- Fetal radiation dose < 0.1 Gy not associated with increased risk of adverse effects

- Fetal exposure - below regulatory limits with use of standard shielding of 0.5 mm lead equivalent
CT angiogram/CT perfusion

❖ no mutagenic or teratogenic effects in human pregnancies after administration of iodinated contrast
❖ theoretical risk of fetal thyroid suppression
❖ American College of Radiology recommends that iodinated contrast be used in pregnant women only when no alternative test is available


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Contrast MRI with gadolinium chelate

- it traverses the placenta and may accumulate in the amniotic cavity, with contrast medium cycling through the fetal GIT and GUT

- 0.01% of the gadolinium dose remains present in the fetus after 4 hours

- American College of Radiology- gadolinium based agents be used with extreme caution and informed consent


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European Stroke Organisation guidelines on stroke in women: Management of menopause, pregnancy and postpartum

Christine Kremer, Zuzana Gdovinova, Yannick Bejot, Mirjam R Heldner, Susanna Zuurbier, Silke Walter, Avtar Lal, Corina Epple, Svetlana Lorenzano, Marie-Luise Mono, Theodore Karapanayiotides, Kailash Krishnan, Dejana Jovanovic, Jesse Dawson and Valeria Caso

Abstract
Pregnancy, postpartum and menopause are regarded as periods women are more vulnerable to ischaemic events. There are conflicting results regarding stroke risk and hormone replacement therapy (HRT) during menopause. Stroke in pregnancy is generally increasing with serious consequences for mother and child; therefore, recommendations for acute treatment with intravenous thrombolysis (IVT) and/or mechanical thrombectomy (MT) are needed. The aim of this guideline is to support and guide clinicians in treatment decisions in stroke in women. Following the “Grading of Recommendations and Assessment, Development and Evaluation (GRADE)” approach, the guidelines were developed according to the European Stroke Organisation (ESO) Standard Operating Procedure. Systematic reviews and metanalyses were performed. Based on available evidence, recommendations were provided. Where there was a lack of evidence, an expert consensus statement was given. Low quality of evidence was found to suggest against the use of HRT to reduce the risk of stroke (ischaemic and haemorrhagic) in postmenopausal women. No data was available on the outcome of women with stroke when treated with HRT. No sufficient evidence was found to provide recommendations for treatment with IVT or MT during pregnancy, postpartum and menstruation. The majority of members suggested that pregnant women can be treated with IVT after assessing the benefit/risk profile on an individual basis. All members suggested treatment with IVT during postpartum and menstruation. All members suggested treatment with MT during pregnancy. The guidelines highlight the need to identify evidence for stroke prevention and acute treatment in women in more vulnerable periods of their lifetime to generate reliable data for future guidelines.
In pregnant women with AIS, does IVT improve outcome as compared to no IVT?

• Evidence-based recommendation
  no specific recommendation

• Expert consensus statement
  - pregnant women with disabling AIS, who otherwise meet eligibility criteria, can be treated with IVT after assessing individual benefit/risk profile

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In women with AIS during pregnancy, does MT or IAT improve outcome compared to MT and/or IVT or IAT?

• Evidence-based recommendation
  - no specific recommendation

• Expert consensus statement
  - pregnant women with disabling AIS, who otherwise meet eligibility criteria, can be treated with MT after assessing individual benefit/risk profile
  - MT alone should be preferred over IVT or bridging therapy (IVT+MT)


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In women with AIS during the postpartum period, does IVT improve outcome compared to no IVT?

- **Evidence-based Recommendation**
  - no specific recommendation

- **Expert Consensus Statement**
  - postpartum women with disabling IS, occurring at least 10 days after delivery, who otherwise meet eligibility criteria, can be treated with IVT with alteplase after individual assessment of benefit/ risk profile


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In women with AIS during the postpartum period, does MT or IAT improve outcome compared to no MT and/or IVT or IAT?

Evidence-based Recommendation
- no specific recommendation

Expert Consensus Statement
-postpartum women with AIS, who otherwise meet eligibility criteria, might benefit from MT after individual benefit/risk profile assessment
- prefer MT alone over IVT or bridging therapy (IVT + MT) on individual basis
Conclusion

- Team approach is essential
- Planning is important
- Management of these cases should be individualized
- Future studies focusing on identification of mechanisms, prevention and management strategies for stroke during pregnancy and puerperium are needed
THANK YOU FOR YOUR KIND ATTENTION