Stroke in pregnancy

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SUMMARY

Stroke is uncommon among young adults. However, the incidence of stroke among young women increases with pregnancy during peripartum and postpartum periods. The relative risk of suffering from haemorrhagic stroke was three times higher than ischemic stroke during these periods when compared with antenatal period. Neuroimaging should be prioritized in order to establish diagnosis and to facilitate treatment in a patient with suspected acute stroke. Prophylaxic anticoagulants should be used in high risk patients. Treatments of acute stroke in pregnant women include anti-platelet and thrombolytic agents. Further studies should be carried as there is lack of high level of evidences to formulate clear guideline for the management of stroke during pregnancy.

KEY WORDS:
Stroke, Pregnancy, Ischemic stroke, Haemorrhagic stroke, Management

INTRODUCTION

Stroke is a cerebrovascular disease which may cause acute brain dysfunction with long-term neurological disability.[1] Stroke is uncommon among young women. However, the risk increases with pregnancy.[2,3] The incidence of pregnancy related stroke is higher during peripartum and postpartum period than during pregnancy itself.[2,3] The relative risk of ischemic stroke and intracerebral haemorrhage (ICH) during postpartum periods was 8.7 (95% Confidence Interval (95%CI: 4.6-16.7) and 28.3 (95%CI: 13.0-61.4) respectively when compared with during antenatal periods.[2]

A retrospective study looking into women in child bearing age (between 15 to 49 years old) found that the rate of first stroke in these women was 24.7 per 100,000 person-years (95%CI: 23.7, 25.7). The absolute rates of both ischemic and haemorrhagic strokes were higher in the peripartum (two days before delivery to one day after delivery) and postpartum periods (two days up to 12 weeks after delivery) with 161.1 (95%CI: 80.6, 322.1) and 14.2 (95%CI: 6.8, 29.7) respectively. In other words, the incidental rate ratio (IRR) were 9.4 times higher (95%CI: 4.7, 18.8) during peripartum periods and 2.7 time higher (95%CI: 1.8, 4.1) during early postpartum periods when compared with those with first stroke during nonpregnant time. However, this study demonstrated that the antepartum period was protective against stroke with absolute risk of 10.7 (95%CI: 7.6, 15.1).[3] These findings were similar to an earlier study.[2] Causes of strokes during pregnancy include pre-eclampsia, eclampsia, amniotic fluid embolus, postpartum angiopathy and postpartum cardiomyopathy.[1]

Risk factors for pregnancy-related stroke

There are many factors that increases the risk of stroke during pregnancy, mainly related to changes in cardiovascular haemodynamic and coagulation mechanisms.[4] These factors include obesity at younger ages,[1] hypertension, diabetes, valvular heart disease, anaemia, hypercoagulable disorders, sickle cell disease, lupus, smoking, substance abuse, hyperemesis gravidarum and migraines.[5] Hypertension may be due to pre-existing disease or due to gestational, or associated with preeclampsia or eclampsia.[5] Patients with pre-existing history of previous stroke may have higher risk of subsequent stroke with or without pregnancy. Hence, those with a history of previous stroke is not a contraindication for subsequent pregnancy.[6]

Complications encountered during the duration of pregnancy, labour or delivery also increases the risk of stroke occurring.[5] These factors include postpartum haemorrhage or infection, haemorrhage leading to the need of blood transfusion, fluid and electrolyte or acid- base disorders and thrombocytopenia.[5]

Delivery method in those with previous history of stroke

Caesarean section, as a mode of delivery is advocated during the antepartum period for patients with untreated ruptured arteriovenous malformations (AVMs) or unclipped ruptured aneurysms.[7] However, studies have shown in patients with intracerebral haemorrhage, the clinical outcomes are not associated with the method of deliveries.[8] Furthermore, caesarean section itself is a risk factor for postpartum cerebral venous thromboses (CVT) due to the transient hypercoagulability associated with the surgery.[5]

Neuroimaging in Pregnancy

For patients with signs and symptoms suggestive of an acute stroke, neuroimaging should be prioritized in order to establish diagnosis to facilitate treatment. Guideline from the American College of Radiology states that pregnant patients can undergo magnetic resonance imaging (MRI) if warranted by the risk-benefit ratio.[9] However, the use of gadolinium contrast should probably be avoided in most cases prior to delivery. This is because the medium crosses the placenta, and its effects on the foetus have not been studied.[9]

In the event where MRI is not readily available or cannot be done in a timely fashion, computed tomography (CT) scan should be used for the establishment of definitive diagnosis.

This article was accepted: 4 April 2019
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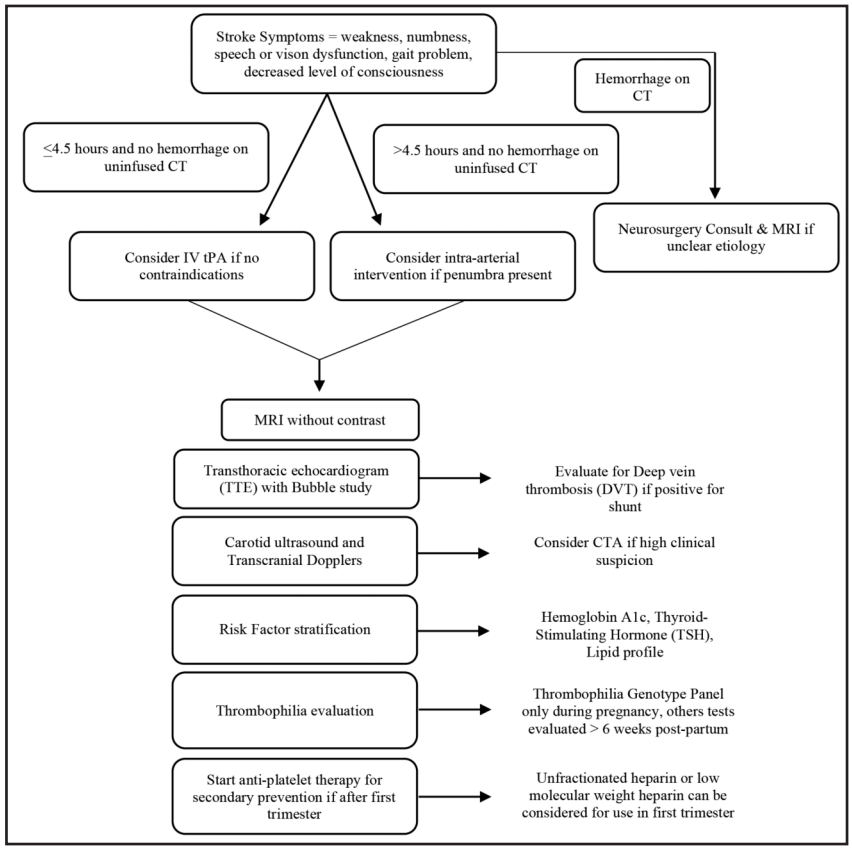

Fig. 1: Adopted from Grear KE *et al.* Algorithm for clinical evaluation and management of stroke in pregnant women: Recommendations for anti-platelet usage are from the American Heart Association/American Stroke Association guidelines.[4]

Studies have shown that the foetal dose exposure to ionising radiation is low when shielding is used. CT scan is often more accessible and readily available in most acute settings.[10]

Stroke prevention during pregnancy

High risk patients or those with pre-existing history of stroke should be started on prophylactic anticoagulants. According to the American Heart Association and American Stroke Association stroke secondary prevention guidelines, pregnant women with ischemic stroke and high-risk thromboembolic conditions such as hypercoagulable state or mechanical heart valves may be treated with one of the following methods:[11]

a. Low-molecular-weight heparin (LMWH) twice daily throughout pregnancy, with dose adjusted to achieve the LMWH manufacturer's recommended peak anti-Xa level 4 hours after injection, or
b. Adjusted-dose unfractionated heparin (UFH) throughout pregnancy, administered subcutaneously every 12 hours in doses adjusted to keep the midinterval activated partial thromboplastin time (aPTT) at least twice control or to maintain an anti-Xa heparin level of 0.35 to 0.70U/mL, or
c. UFH or LMWH (as above) until the 13th week, followed by substitution of a vitamin K antagonist (VKA) until close to delivery, when UFH or LMWH is resumed

For such patients, it is reasonable to discontinue LMWH >24 hours before induction of labour or caesarean section.[11] All of these patients should be on antithrombotic therapy during postpartum periods.[11] In those patients with pre-existing cerebral venous thrombosis, the same guidelines recommend the use of anticoagulation for at least three months followed by antiplatelet therapy.[11] Those pregnant women with at least one high risk factor for pre-eclampsia or at least two moderate risk factors for pre-eclampsia (as shown in the Table I) should be started on 75mg of aspirin daily from 12 weeks until the birth of the baby.[12]

Table I: High and moderate risks of pre-eclampsia[12]

High Risks
• hypertensive disease during a previous pregnancy • chronic kidney disease • autoimmune disease such as systemic lupus erythematosis or antiphospholipid syndrome • type 1 or type 2 diabetes • chronic hypertension.
Moderate Risks
• first pregnancy • age 40 years or older • pregnancy interval of more than 10 years • body mass index (BMI) of 35 kg/m2 or more at first visit • family history of pre-eclampsia • multiple pregnancy.

Treatment of acute pregnancy-related stroke

There is lack of high level of evidences in the current guideline used for the acute management of pregnancy-related stroke.[1] Algorithm from the American Heart Association/American Stroke Association guidelines on the recommendations for anti-platelet usage for pregnant women suffering from acute stroke is shown in Figure 1.[4] In the treatment of acute ischemic stroke especially when treating moderate or severe stroke during pregnancy, intravenous (IV) alteplase may be considered. This is because the anticipated benefits outweigh the anticipated increased risks of uterine bleeding.[13]

In the treatment of acute haemorrhagic stroke during pregnancy, medical therapy should be targeted towards management of hypertension.[10] The National Institute for Health and Care Excellence (NICE) guideline recommends labetalol as first-line agent to treat hypertension in pregnancy.[12] However, there are no clear guidelines for the medical management of subarachnoid or intracerebral haemorrhage in pregnancy.[1] Hence, drugs such as mannitol (for raised intracranial pressure), nimodipine (for cerebral protection from vasospasm) and antiepileptic (for prevention of seizure) should be used with caution in pregnant women.[1]

CONCLUSION

All pregnant women with pre-existing history of stroke or those with high risk for stroke during pregnancy should be identified early. This group of patients may benefit from management towards secondary preventions. Those who developed stroke during antepartum, peripartum and post-partum should be managed by multidisciplinary teams to prevent adverse effects to both the mother and the foetus. Further studies should be carried as there is lack of high level of evidences to formulate clear guideline for the management of stroke during pregnancy.

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Questions (True / False):

1. The risk of stroke in pregnancy is,
   A. Higher during antepartum period than during post-partum period.
   B. Higher risk during pregnancy in haemorrhagic stroke but not ischemic stroke.
   C. The risk of stroke during pregnancy is highest during peripartum period.
   D. The antepartum period is protective against stroke compared to non-pregnant women during child bearing age.
   E. Not related to pre-existing history of obesity.

2. Factors associated with risk of stroke in pregnancy
   A. Hyperemesis gravidarum
   B. Migraine.
   C. Diabetes mellitus.
   D. Sickle cell disease.
   E. Low body mass index.

3. Delivery method in pregnant women with acute stroke
   A. Caesarean section improves the clinical outcome of intracranial haemorrhage patients
   B. Vaginal delivery is contraindicated during acute stroke.
   C. Caesarean section increases the risk of post-partum cerebral venous thrombosis.
   D. Caesarean section is recommended for women with ICH, particularly recent subarachnoid haemorrhage, untreated ruptured arteriovenous malformation (AVM) or unclipped ruptured aneurysm.
   E. Vaginal delivery is not recommended for patients with unsecured intracranial aneurysm.

4. Neuroimaging in pregnant women with acute stroke
   A. Computed tomography is contraindicated due to the severe adverse effect to the foetus.
   B. Gadolinium is safe to be given as the safety profile to the foetus has been proven.
   C. Magnetic resonance imaging should be the first choice of neuroimaging to establish diagnosis in most cases if readily available.
   D. Shielding is not needed as it does not reduce the foetus dose exposure.
   E. Gadolinium does not cross the blood placenta barrier and hence it is safe to be used during pregnancy.

5. Management of acute stroke during pregnancy.
   A. For treatment of severe ischemic stroke, the initiation of anticoagulants such as alteplase is anticipated to have increased risk of uterine bleeding, outweighing its anticipated benefits.
   B. In the treatment of acute ischemic stroke during pregnancy, medical therapy should be targeted towards control of hypertension.
   C. NICE guidelines recommends IV labetolol as the first line treatment for management of hypertension during pregnancy, especially during acute haemorrhagic stroke
   D. Phenytoin can be initiated safely during the first trimester.
   E. Multidisciplinary approach is advocated for management of stroke in pregnancy