Yes, Intravenous Thrombolysis Should Be Administered in Pregnancy When Other Clinical and Imaging Factors Are Favorable
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Controversies in Stroke

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The Case:
A 37-year-old woman, gravida 2, para 0, 22 weeks pregnant, presents within 90 minutes of abrupt onset of global aphasia and right-sided hemiparesis (NIHSS score 12). MRA shows left M2 occlusion. MRI shows ipsilateral DWI/PWI mismatch.

The Questions:
1. Should she be considered for treatment with intravenous t-PA?
2. If no, should the patient receive endovascular therapy: IA t-PA, mechanical thrombectomy, or both?

The Controversy:
SHOULD THROMBOLYSIS BE CONSIDERED IN PREGNANT WOMEN WITH ACUTE STROKE?

Yes, Intravenous Thrombolysis Should Be Administered in Pregnancy When Other Clinical and Imaging Factors Are Favorable

Andrew M. Demchuk, MD, FRCPC

A cute stroke treatment decision-making is a complex process that must be performed quickly. In each case, we must balance the potential benefits with the relevant risks of each therapy to our patients. In this case, the major challenge is determining whether systemic tPA (tissue plasminogen activator) or endovascular treatment is more appropriate in pregnancy.

Pregnancy has historically been regarded as a contraindication to IV tPA treatment. Yet tPA is not known to be teratogenic and tPA is also too large a molecule to cross the placenta. To date, 8 cases have been published of IV tPA treatment in pregnancy with only 1 mother suffering a significant uterine bleeding complication and most achieving a good neurological recovery.1,2 Maternal hemorrhagic complications have been reported in 8% with systemic thrombolysis across the spectrum of clinical thromboembolic indications.3 Overall, the IV tPA risk seems reasonably low in pregnancy and not considered an absolute contraindication. This low risk during pregnancy must be balanced against the potential of a disabled outcome without treatment. Although pregnancy is a key determinant of this decision-making process, other clinical and radiological factors should also play a significant role in the art of acute stroke treatment decision-making.

These clinical and radiological factors relevant in this particular case include age, stroke severity, MR-mismatch, and occlusion site. The risk of IV tPA-related symptomatic intracerebral hemorrhage is quite low in young individuals. In fact, in over 2700 subjects treated with IV tPA with <60 years, the symptomatic intracerebral hemorrhage rate was only 2.8%, roughly half the overall symptomatic intracerebral hemorrhage risk across all ages.4 Stroke severity of baseline National Institute of Health Stroke Scale of 12 is consistent with a moderate stroke, which is sufficiently disabling to warrant consideration of systemic tPA treatment. The imaging factor of a diffusion-weighted imaging (DWI)/perfusion-weighted imaging mismatch may also be favorable for systemic thrombolysis. Mismatch suggests some salvageable tissue at risk that would benefit from successful recanalization. DWI/perfusion-weighted imaging mismatch requires more description because its meaning depends on the specific perfusion parameters used to define perfusion-weighted imaging (ie, Tmax delay of 6 seconds versus other)5 and ischemic core (ie, DWI lesion versus apparent diffusion coefficient values <550×10−9

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mm/s²). The most crucial information from the magnetic resonance imaging may be the baseline volume of the ischemic core measured by the DWI lesion. In the Echoplanar Imaging Thrombolytic Evaluation trial, baseline DWI lesions <18 mL had a remarkably low number needed to treat of only 1.8 for IV tPA (3–6 hours from onset) compared with placebo (77% versus 18% placebo; odds ratio, 15.0; P<0.001). A very small baseline DWI lesion would certainly support a role for systemic thrombolysis in this patient.

One underappreciated factor that must be considered when deciding between IV tPA and endovascular treatment is the location of the intracranial occlusion. An M2 middle cerebral artery occlusion is associated with at least moderate rates of early recanalization with systemic tPA. The main difficulty with endovascular treatment is the complete absence of any randomized clinical trial data supporting superiority of such treatment in such M2 middle cerebral artery occlusions compared with IV tPA. It remains very unclear whether endovascular treatment provides much of any advantage over IV tPA in such distal occlusions, especially given the delays typical of such an intervention after symptom onset and the additional risk required to navigate to and engage the thrombus in such locations with these large diameter devices. A reasonable assumption is that further distal the occlusion the less likely endovascular treatment will outperform standard IV tPA treatment. It is also possible that vascular wall changes common in pregnancy could increase risks of vascular wall injury with such devices. Theoretically, endovascular treatment with mechanical thrombectomy devices should limit any systemic bleeding risk if only a mechanical device is used and intraarterial tPA avoided. However, there remains no reported experience on use of these devices during pregnancy.

So should we administer IV thrombolyis in pregnancy and more specifically, in this pregnant patient? I say yes because the risk is low and the likelihood of benefit from IV tPA significant, given the presence of a distal occlusion (M2 middle cerebral artery) and MR-mismatch. If the patient is treated at a primary stroke center, I would initiate systemic therapy, but I would also transport that patient quickly to a tertiary care center/comprehensive stroke center as a drip and ship. This would offer 2 advantages. First, in case of maternal or fetal complication, the patient/fetus would have the most advanced technology and expertise available for fetal and maternal care within the neonatal intensive care unit advanced obstetric unit. Second, the neuroendovascular suite with the numerous options of mechanical thrombectomy would at least provide rescue or bridging options if no neurological improvement or worsening is seen during transport. A similar strategy could be applied if the patient is first transported directly to the comprehensive stroke center. With obstetric back-up, IV tPA should be administered followed by bridging endovascular therapy in situations where no clinical improvement seen.

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References