Stoke Thrombolysis With Tenecteplase to Reduce Emergency Department Spread of Coronavirus Disease 2019 and Shortages of Alteplase

Measures to reduce emergency department staff exposure to the severe acute respiratory syndrome coronavirus 2 have focused on screening and use of personal protective equipment. Reducing the time and intensity of interactions with individuals with known or suspected cases of coronavirus disease 2019 (COVID-19) is also desirable, insofar as such reductions do not compromise the quality or outcomes of care. The situation of an acute stroke emergency is a particularly vulnerable situation for exposure and transmission, since a substantial proportion of patients are unable to provide a history to screen them out for COVID-19.

Tenecteplase was developed as a plasminogen activator with greater fibrin specificity and reduced clearance compared with alteplase, allowing single-bolus administration. In 2000, the US Food and Drug Administration approved tenecteplase to reduce mortality in acute myocardial infarction. Since then, randomized clinical trials and meta-analyses on ischemic stroke have demonstrated that tenecteplase has noninferior safety and efficacy relative to the standard intravenous stroke thrombolytic agent alteplase and may be superior for early recanalization.

Prior to the COVID-19 pandemic, some stroke centers, including ours at the University of Texas–Austin Dell Medical School and Ascension Texas, had switched to tenecteplase as the stroke thrombolytic agent because of its workflow advantages and potential time savings relative to alteplase, especially in the time to initiate an interfacility transfer for thrombectomy or a higher level of care. Tenecteplase is given as a single, 5-second intravenous bolus that requires approximately 2 minutes to mix, prepare, and administer, whereas alteplase requires preparation of both a bolus syringe containing 10% of the weight-based dose and an intravenous pump set up for infusion of the remaining 90% of the dose over 60 minutes.

The simpler tenecteplase workflow may be additionally advantageous during the COVID-19 pandemic. Eliminating the alteplase 1-hour infusion and the dedicated second intravenous catheter that it requires reduces staff time in close proximity to the patient and removes the intravenous infusion pump that accompanies the patient through other hospital departments and wards, presenting its own set of surfaces for a virus to settle on and staff to touch.

In addition, after published case observations suggested that thrombolysis with alteplase may be beneficial as a treatment for the acute respiratory distress syndrome associated with COVID-19, some centers worldwide have been using alteplase for this potential additional indication and more rapidly consuming their supplies of alteplase. With COVID-19–associated supply chain disruptions also occurring, some centers and regions in the world temporarily do not have access to alteplase for its ischemic stroke indication.

Accordingly, since the start of the COVID-19 pandemic, interest in using tenecteplase for stroke has increased. There is an appropriate degree of caution in making the switch, since tenecteplase is not Food and Drug Administration–approved for use in stroke and does not currently have the highest level of recommendation for acute stroke thrombolysis in the most recent American Heart Association/American Stroke Association Guidelines, although it is recommended as an alternative to alteplase.

We offer the following suggestions in approaching the transition from alteplase to tenecteplase. First, hospitals should achieve consensus within and across key clinical and administrative stakeholder and oversight groups. This includes engaging neurology, emergency medicine, and pharmacy departments early, because they are most directly involved in stroke thrombolysis and will have the greatest influence with other groups. Hospitals should also critically review the clinical trial evidence with these groups and add tenecteplase to the hospital formulary, if it is not currently available. While dosages ranging between 0.1 and 0.4 mg/kg have some evidence of benefit for stroke, 0.25 mg/kg to a maximum of 25 mg has the most favorable profile based on the evidence from stroke clinical trials.

Hospitals should acknowledge that the prospective confirmation of noninferior clinical outcomes with tenecteplase in a pivotal phase 3 trial is required to satisfy the highest standard of evidence, and they should address questions about off-label use by pointing out that the standard use of alteplase for stroke between 3 and 4.5 hours is also off-label, but the stroke field has accepted this off-label use of alteplase as the clinical standard based on expert consensus of the published evidence. To assure liability concerns, the appropriate clinical oversight bodies should document the approval and adoption of tenecteplase as the local standard of care for stroke thrombolysis.

Minimizing the risk of error in selection and preparation of thrombolytic drug and dosage during the hurried activities of a stroke emergency is important. We recommend implementation of 1 drug (tenecteplase) at 1 dosage (0.25 mg/kg) as the default option in the emergency department electronic medication-dispensing systems and the order set in the electronic health record. Multihospital practice groups should make the switch at all hospitals at the same time for the same reason, if neu-
Implementing nursing and physician education about the change, emphasizing that only the drug and dosage are different, is important. There are no changes to thrombolytic eligibility criteria or posttreatment monitoring. The dosage for stroke differs from that for acute myocardial infarction. Therefore, education should stress that clinicians should use dosage as ordered and not the prescribing information in the tenecteplase kit, which describes the acute myocardial infarction dosage.

Hospitals should modify the electronic health record ordering and monitoring tools, replacing alteplase with tenecteplase. This step may take the longest to accomplish unless it is prioritized. Commitment to keeping a clinical registry of tenecteplase stroke cases and regularly reporting to the stakeholder groups the data compared with prior alteplase experience, as well as potentially participating in national COVID-19 stroke registries, are also tasks worthy of attention.

The COVID-19 pandemic has forced the medical system to adapt and accept changes aimed at reducing risk. Before the pandemic hit, tenecteplase had been recognized to be as safe and effective as alteplase in treating stroke while offering appealing workflow efficiencies at lower cost. Tenecteplase thrombolysis may also be a reasonable means of reducing risk exposure to and transmission of the COVID-19 virus during a stroke emergency in the emergency department, as well as addressing temporary shortages of alteplase that may arise from increased use in treating COVID-19–associated thrombosis.

**Box. Workflow Advantages of Tenecteplase Relative to Alteplase That Reduce Staff Exposure to Contagion**

- Shorter time to prepare
- Shorter time to administer (5 s versus 1 h)
- Does not require that a second, dedicated intravenous catheter be inserted and maintained
- Does not require an intravenous infusion pump
- Shorter time to initiate interfacility transfer after intravenous lytic administration

**REFERENCES**