Thrombolysis for Acute Ischemic Stroke

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Karolinska Stroke Update is an annual meeting of European stroke experts. The agenda includes a few important topics in which major progress has occurred or in which there is a need for a European consensus in prevention, acute care, organizing stroke services, and any other field of stroke management. The program committee selects the topics. The meeting is well attended. Thrombolysis in ischemic stroke within 3 hours from the onset of symptoms is evidence-based medicine. So far, only the German Health Authorities have approved it; the approval by the Health Authorities of the European Commission is still pending. While waiting for their decision, the program committee came to the conclusion that there is a need for a consensus statement to make thrombolysis in acute ischemic stroke more widely and safely available in Europe. Accordingly, they selected thrombolysis in stroke as the key topic of the Karolinska Stroke Update 2000.

The writing group nominated by the program committee drafted a preliminary consensus statement before the meeting. The draft was rewritten during the meeting on the basis of feedback provided by the participants. This revised draft was presented to the participants at a general session on the second day of the meeting. The consensus statement was revised at this session point by point until all participants representing experimental and clinical stroke scientists, clinicians treating stroke patients, lay people, and industry could approve the final wording. The participants of the meeting hope that the consensus statement will standardize the use of thrombolysis in acute ischemic stroke in Europe, will make it more widely and safely available for European stroke patients, and will encourage further research on it in Europe and elsewhere.

Thrombolysis for Acute Ischemic Stroke
Intravenous rtPA within 3 hours after the onset of symptoms in patients with acute ischemic stroke is a highly effective evidence-based treatment (grade A evidence). The use of rtPA is supported by results from randomized controlled trials and meta-analyses. The risk of early fatal and symptomatic intracranial hemorrhage is increased, but these hazards are offset by reduction in the proportion of patients who are dead or dependent. According to meta-analyses, for patients given rtPA within 3 hours of ischemic stroke, approximately 1 in 10 more will be independent, 1 in 14 will suffer symptomatic hemorrhage, and 1 in 100 fewer may die as a result of the treatment (grade A evidence). Overall, the net benefit of rtPA given within 3 hours of onset will result in 1 more independent survivor for every 10 patients treated.

Intravenous rtPA given within 6 hours after the onset of an ischemic stroke seems to be beneficial, but the benefit is smaller while the risks are higher. The use of rtPA up to 6 hours after onset is supported by the results of meta-analyses (grade B evidence).

The therapeutic use of intravenous rtPA is recommended within 3 hours in selected patients in acute ischemic stroke (grade A evidence) but may also be beneficial when given up to 6 hours (grade B evidence) and possibly even longer in certain subgroups of stroke patients, such as those with basilar artery occlusion (grade C evidence).

Outside randomized controlled trials, the therapeutic use of intravenous rtPA must be subject to continuous quality control. It is recommended that the use of intravenous rtPA follow the recommendations of published guidelines, with local modifications as appropriate. In most open studies the safety and efficacy of intravenous rtPA in routine clinical practice is comparable to that in randomized studies. However, there is an obvious need for continuous education and for trained local stroke specialists to be responsible for a safe stroke thrombolysis service.

The evidence strongly supports the recommendation that rtPA be made available for routine clinical use to treat stroke
patients in adequately qualified centers. The development of hospital services designed to deliver early thrombolysis 24 hours a day for acute ischemic stroke is encouraged. Continuous auditing of the routine use of thrombolytic therapy in stroke is advisable. For example, the International Stroke Thrombolyis Register (SITS), an online monitoring system designed for auditing safety and efficacy of routine therapeutic use of rtPA in acute ischemic stroke, could be used for such a purpose.

The heterogeneity for good outcome in meta-analyses implies that more data are needed on how to identify the patients most likely to benefit and least likely to be harmed by thrombolysis. The role of patient characteristics, including age, sex, stroke severity, stroke subtype, concomitant disease, drug treatments, strategies for blood pressure control, prior antiplatelet therapy, and antiplatelet and anticoagulation therapy after thrombolysis, should be further evaluated in future trials, meta-analyses, phase IV studies, and SITS.

It is recommended that future trials on the safety and efficacy of thrombolysis should assess modern imaging techniques as a part of the protocol to help in patient selection and in monitoring the effects of therapy. For example, MR diffusion- and perfusion-weighted imaging may reveal in individual patients brain tissue at risk but salvageable with thrombolysis within a 3-hour time window and possibly even longer (grade C evidence). Other imaging modalities, including perfusion CT, MR angiography, single-photon emission CT, and transcranial Doppler, may also help in selecting patients, in verifying recanalization of the occluded artery, and in detecting change of infarct size (grade C evidence).

It is strongly recommended that one of the main targets in future randomized trials should be trying to extend the time window beyond 3 hours after stroke onset, as this would increase the proportion of patients who may benefit from therapy. This would have an important public health impact in Europe. It is also recommended that new thrombolytic agents, and thrombolysis together with neuroprotective agents, should be evaluated in future randomized trials to try to increase the effectiveness and to decrease the risks involved in thrombolysis.

Future studies should include collection of data to allow the assessment of the impact on health economics and on quality of life of rtPA in acute ischemic stroke. The public should be educated about the value of early expert assessment and treatment.

Key Words: stroke management ■ stroke, acute ■ stroke, ischemic ■ thrombolysis
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