LETTER TO THE EDITOR

Thrombolytic therapy for acute ischaemic stroke: is the hype justified?

To the Editor—Implementation of thrombolytic therapy for acute ischaemic stroke[1] has to be viewed in an appropriate context.

The main justification for such therapy relies on findings from a relatively small, randomised controlled trial known by the acronym NINDS (National Institute of Neurological Disorders and Stroke rt-PA trial),[2] about which there are serious reservations.[3] Overall treatment benefits (if any) were trivial, whilst there were very high risks of adverse events such as intracranial haemorrhage, and immense logistical and financial implications. This was in marked contrast to the very favourable benefits of thrombolysis for acute myocardial infarction.

Moreover, in two particularly important respects, the NINDS trial can be regarded as flawed.[4] First, part 2 of the trial (the main impetus for this treatment) relied on a global test statistic as the primary outcome, and not on incontrovertible hard endpoints. The latter arbitrary statistic was itself a composite of four neurological scores (Table). Clinically and statistically significant differences depending on any such composite of inter-related overlapping soft endpoints must be inherently suspected. Second, patients in both the control and active treatment groups received no aspirin in the first 24 hours, so that those treated with recombinant tissue plasminogen activator (t-PA) were compared with controls who received suboptimal standard therapy. To overcome the risk of serious intracranial bleeding from combined t-PA plus aspirin therapy, dummy aspirin should have been administered to the active treatment group and genuine aspirin to the controls.

TABLE. Unadjusted relative risk and number needed to treat values derived from published National Institute of Neurological Disorders and Stroke rt-PA trial data[2]

Outcome at 3 months		RR (95% CI)*	NNT† (95% CI)
Composite Global Statistic Components‡	Favourable BI	1.3 (0.8 to 2.0)	15 (-34 to 6)
	Favourable MRS	1.5 (0.9 to 2.4)	13 (-84 to 6)
	Favourable GCS	1.4 (0.8 to 2.1)	15 (-42 to 6)
	Favourable NIHSS	1.5 (0.9 to 2.7)	16 (-66 to 6)
Symptomatic or fatal intracranial haemorrhage within 36 hours of treatment		5.9 (1.3 to 27.1)	NNH§ 17 (10 to 62)

* RR denotes relative risk, and CI confidence interval
† NNT = number needed to treat to attain a favourable outcome (for a once-off intervention)
‡ For the Global Statistic, a favourable odds ratio and 95% CI were reported (1.7 [1.2 to 2.6]) but how they were derived was not detailed; whilst individually, only when adjusted did its component scores attain statistical significance. BI denotes Barthel Index, MRS modified Rankin Score, GCS Glasgow Coma Scale, and NIHSS National Institute of Health Stroke Score
§ NNH = number needed to harm is inferred when the number needed to treat is negative

Under these circumstances, is the hype surrounding this form of treatment for acute ischaemic stroke appropriate and justified?

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