Clinical controversies

The case against thrombolysis

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Make it Idiot-Proof and They'll Go and Invent a Better Idiot

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For years stroke treatments evaded physicians. The thought was that strokes were to be watched carefully but little intervention was possible. The neurologists were quick to note the success of thrombolytics in heart attacks, and decided that since the diseases are similar, this therapy should work for them too. With that came the NINDs trial and "time is brain" campaign followed by the AHA position statement to give this treatment.

Not so simple. NINDs was performed under optimum conditions - conditions that still have not been reproduced in most hospitals and even with that the results were not that impressive. Let us take a closer look.

NINDs had a 17% mortality in the TPA group and a 21 percent mortality in the placebo group - not statistically significant. Where you see the bad stuff is looking at the rate of intracerebral bleeds - 6.4 % in TPA versus .6% in placebo. True 11% had an excellent outcome but let's look at that even closer.

NINDs used the biggest experts in stroke management including neuroradiologists and neurointensivists - I don't have one of these and I doubt you do either. Secondly, the same issue in the New England Journal in which NINDs appeared, had a study from Boston that showed that LMWH helped in stroke to the tune of – guess what? – about 10%. Yet we have since seen that this has been disproved by larger subsequent trials. This has not been done in NINDs and probably won't be. Let me also remind you that there were already four negative trials for thrombolytics in stroke before NINDs and now we have reached 10. True some of these were with streptokinase, but we only realized that TPA was superior to streptokinase in heart disease because heparin was added - something that cannot be done in stroke since it makes things worse. In heart disease where did TPA do worse than strepto? Of course, it caused more intracerebral bleeds.

We do not know how many people were rejected by NINDs so we do not know how many were enrolled. In most of our experience we enroll maybe about 4% -which is one out of 200 patients. Of these, the 10% who benefit greatly and do not bleed - well, we are talking very small numbers. The giant CAST trial showed that aspirin in acute stroke works for 1 out 100 with out the high risk of bleeds. How many get this treatment routinely?

Another point about NINDS: most of the benefit occurred in the group treated before 90 minutes which, come to think of it, is the same as for MI. So the benefit for patients is far less than 10% - since most patients will not make this time window. Furthermore, we do not read scans that well even if we are a radiologist, and we miss many stroke mimics. You do not want to give this stuff to someone who has had a seizure and is post tictal or who has a complex migraine.

The famous study in Cleveland that was published in the JAMA evoked more dismal results - less than 2% received the TPA and less than 1% should have. The results showed one out of six that had TPA had an intracerebral bleed and half of these died.

Perhaps you'll say, well, what choice do I have? Articles in the nineties have already showed the advantage of stroke units which have dedicated physiotherapists, specially trained nurses, and doctors who all day work only with stroke. Let me also point out that the Cochrane Coalition supports "clinicians who choose not to use the treatment at all" and that all three EM associations in the USA and the one in Canada do not endorse this therapy.

I couch my remarks with the following. TPA may help people - we just do not know who. Arterial thrombolysis probably helps more but this is hard to find. It may be true that time is brain, but you got to use your brain to know how to use your time.

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