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Stroke thrombolysis: Barriers to implementation

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Abstract
Stroke is a frequent emergency faced by Emergency Department (ED) staff. Evidence produced from significant trials has led to the introduction of stroke thrombolysis across the world. Campaigns to increase public awareness that 'stroke is a medical emergency,' have led to emergency departments facing necessary adjustment, re-allocation of resources and education of staff. From a review of the associated literature, barriers to implementation of the service include; non-recognition of stroke, inappropriate triage of these patients by both ED staff and ambulance personnel, delays in obtaining neuro-imaging, and inefficient processes of in-hospital emergency stroke care. Further study is required to review the educational needs and resource management, as well as the efficacy of the public education in stroke.

Introduction

In the United Kingdom (UK) alone, more than 110,000 people suffer a stroke every year, making stroke and its assessment one of the frequent emergencies that is dealt with within the Emergency Department (ED) worldwide (Department of Health, 2009). Stroke is one of the leading causes of disability, with eighty per cent of strokes in the UK being thrombotic (Stroke Association, 2008). In comparison with other acute presentations, the assessment of stroke has received less attention. The role of emergency medicine in stroke management has been re-defined in the past decade and this is primarily due to the introduction of thrombolysis (Lindsberg et al., 2006; Llinas, 2006). Following the first successful thrombolytic trials, medicine has begun to look at stroke care in a different way. In the past, the focus had been to make the diagnosis, look for other problems, and refer on to a medical consultant, with the emphasis lying on physiotherapy and rehabilitation (Rasler, 2007). Now the ED has become the focus for stroke care and research.

With stroke thrombolysis becoming a consideration for Acute Ischaemic Stroke (AIS) patients, practice and procedures within ED's are changing. Early assessment and treatment has become essential. A national campaign to emphasise that stroke is 'a medical emergency' and the adoption of the 'Face Arm Speech Test' approach (see Table 1) by ambulance and paramedic teams, are aimed at improving the early process of care (Thompson, 2006; Mohd Nor et al., 2004).

This rapid assessment helps to alert emergency staff to the consideration of the criteria for thrombolysis and early intervention. Time is critical in improving the outcome for AIS patients, and although thrombolysis is used in a minority of

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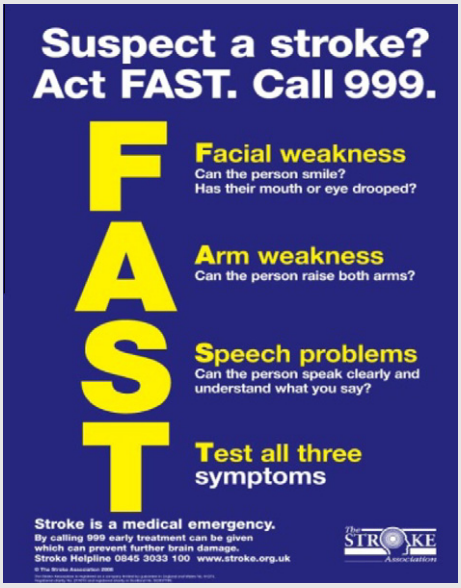
Table 1 The FAST campaign. Reproduced with kind permission of The Stroke Association 2008.



cases, its success has led to the formation of rapid treatment protocols and teams (Lindsberg et al., 2006; Thompson, 2006).

This article will examine the barriers to implementation and introduction of the thrombolysis service along with the necessary structural changes required to ensure patient safety and smooth throughput.

The literature search was performed using electronic databases (CINAHL, BNI and Medline) along with British internet gateway sites such as Institute, searching from 1995 onwards.

Keywords used were: stroke thrombolysis; stroke; ischaemic stroke; FAST. Boolean logic was applied, to increase positive results, for example stroke AND thrombolysis.

The critiquing involved making notes of key points, the research methodology with validity of methods and relevance of results.

Background of stroke thrombolysis

There has been much controversy surrounding the use of thrombolysis for AIS, and the United Kingdom has been cautious with its implementation (Harraf et al., 2002). The two thrombolytic agents that have to date been the most studied in stroke, are recombinant tissue plasminogen activator (rt-PA) and streptokinase. The trials involving streptokinase were disappointing, reporting an early increased risk of cerebral haemorrhage and death, with little long-term benefit. However, a number of large multicentre randomised placebo controlled trials have shown an overall benefit for early treatment with rt-PA, despite an increased risk of early haemorrhage (Albers, 2001; Power, 2004; Szoeke et al., 2003). The largest, most influential and statistically significant study was by the National Institute of Neurological Disorders and Stroke (NINDS) which was the first study to show benefit with rt-PA. In 1995, the 'NINDS rt-PA for Acute Ischaemic Stroke' trial was published in the New England Journal of Medicine. The trial was a randomised controlled study which was conducted in expert settings with dedicated stroke teams, laboratory and rapid radiology resources.

The study found that despite an increased incidence of symptomatic cerebral haemorrhage, treatment with rt-PA within 3 h of onset of ischaemic stroke showed significantly improved clinical outcome at 3 months (NINDS, 1995). The NINDS rt-PA trial was different to the other thrombolytic trials as it had a very strict list of criteria for use. These rules allowed for selection of patients who were most likely to benefit (Llinas, 2006). This list of criteria (see Table 2) has been included in the National Guidelines for Stroke (Royal College of Physicians, 2004) for stroke thrombolysis.

Methodological flaws in the NINDS trial have been raised, questioning its suitability for generalisation. First, the trial group with the greatest outcomes were the patients treated within ninety minutes, rather than the group treated between ninety and one hundred and eighty minutes. Patients presenting within this initial time bracket are very rarely encountered in practice, making the results difficult to generalise. Secondly, the stroke severity in the placebo group was greater than the rt-PA group, potentially biasing results (American Academy of Emergency Medicine, 2002).

Other trials failed to produce such positive findings, partly because of differences with the design and choice of time frames (some up to 6 h), along with higher doses of thrombolytic agent (Wardlaw et al., 2005). In the UK, there has been a slow uptake in the introduction of stroke thrombolysis, primarily due to the evidence which demonstrates this increase in negative and potentially catastrophic side effects for patients for a questionably small chance of benefit in outcome for AIS patients. This may also explain why emergency physicians are reluctant to initiate and take responsibility for thrombolysis in stroke and why in the UK it is being left to medical consultants to instigate.

However Wardlaw et al. (2005) included randomized controlled trials of thrombolysis in a Cochrane review. The trials selected compared any thrombolytic agent with control in patients with definite acute ischaemic stroke, which measured functional outcome (death or dependency; modified Rankin 3–6) at more than 1 month after stroke. Data was extracted and verified with principal investigators of all major trials. Published and unpublished data was used. They concluded that rt-PA thrombolysis, administered up to 6 h after ischaemic stroke, significantly reduced mortality and disability at the end of the follow-up period at 3–6 months. In the subgroup of patients who were treated within 3 h of stroke onset, thrombolysis appeared to be more effective in reducing disability, with no statistically significant adverse effect on death, and no appreciable heterogeneity in effect (Wijngaarden et al., 2006). International consensus now exists among stroke researchers and clinicians that thrombolysis using rt-PA, administered within 3 h after onset of the symptoms, is safe and effective; which is in agreement with the NINDS (1995) findings.

Table 2 Criteria for use of tissue plasminogen activator (rt-PA) in treating acute stroke (NINDS, 1995).

Clinical inclusion criteria

- Patient or family member able to give consent or approval before study procedures
- Age <18 years
- Onset of symptoms of ischaemic stroke within 0—3 h
- Clinical diagnosis of ischaemic stroke causing measurable neurological deficits (defined as impairment of language, motor function, cognition, and/or gaze, vision, or neglect)
- Score for stroke severity >4 on the National Institutes of Health Stroke Scale (NIHSS)
- Patient able to undergo computed tomography (CT) before tPA administration

Clinical exclusion criteria

- Severe symptoms suggesting total anterior circulation syndrome (coma or severe obtundation with fixed eye deviation and complete hemiplegia or NIHSS score >22)
- Minor stroke symptoms (NIHSS score <4) or those that are rapidly improving by the time of randomisation
- History of stroke within previous 6 weeks
- Any pre-existing neurological illness resulting in a modified Rankin scale score >3
- Seizure before administration of study drug
- Previously known intracranial haemorrhage, subarachnoid haemorrhage, arteriovenous malformation, aneurysm, or previously known intracranial neoplasm that, in the opinion of the investigator, is terminal or would increase the risk of intracranial bleeding after administration of thrombolytic therapy or may confound neurological assessment
- Clinical presentation suggestive of subarachnoid haemorrhage, even if initial CT is normal
- Uncontrolled baseline hypertension: systolic blood pressure [BP] > 185 mmHg or diastolic
- BP > 110 mmHg despite acute treatment
- Presumed septic embolus
- Suspected recent (within 30 days) myocardial infarction
- Recent (within 30 days) biopsy of a parenchymal organ or surgery that, in the opinion of the investigator, would increase the risk of unmanageable (e.g., uncontrolled by local pressure) bleeding after administration of thrombolytic therapy
- Recent (within 30 days) trauma, with internal injuries or ulcerative wounds
- Any active or recent haemorrhage that, in the opinion of the investigator, would increase the risk of unmanageable (e.g., uncontrolled by local pressure) bleeding after administration of thrombolytic therapy
- Known hereditary or acquired haemorrhagic diathesis (e.g., activated partial thromboplastin time [APTT] or prothrombin time [PT] greater than normal, or oral anticoagulant therapy with international normalised ratio (INR) > 1.5)
- Pregnancy, lactation, or parturition within the previous 30 days
- Hypoglycaemia, hyperglycaemia (baseline serum glucose level <2.8 or >22.0 mmol/L), or thrombocytopenia (platelet count $<100 \times 109$/L)
- Other serious, advanced or terminal illness, or any other condition the investigator feels would impose a significant hazard to the patient if intravenous tPA were initiated
- Current participation in another research drug treatment protocol

Computed tomography exclusion criteria

- Evidence of acute or chronic intracranial bleeding on CT
- Likely aetiology other than acute brain ischaemia
- Early signs indicate infarct of more than a third of the territory of the middle cerebral artery

Barriers to delivery

The evidence highlights the main barriers to efficient treatment of AIS:

- Non-recognition of symptoms of stroke by the patients or their family (Hodgson et al., 2007; SAEM, 2003; Lindsberg et al., 2006).
- Failure to seek urgent help (Harraf et al., 2002; SAEM, 2003).
- Triage of stroke patients as non-urgent by ambulance personnel or ED staff (Szoeke et al., 2003; Wijngaarden et al., 2006; Kwan et al., 2004; Mohd Nor et al., 2004; Lindsberg et al., 2006).
- Delays in obtaining CT scans (Lindsberg et al., 2006; Kwan et al., 2004; Rasler, 2007; SAEM, 2003).
- Inefficient processes of in-hospital emergency stroke care (Szoeke et al., 2003; Rasler, 2007; Kwan et al., 2004; Wijngaarden et al., 2006).

Recognition of stroke

Delays in accessing medical care is one of the largest barriers to improving stroke care, therefore research and policy directed at the education and behaviour change of the general public regarding stroke signs, symptoms and need for urgent medical attention is imperative (Society for Academic Emergency Medicine (SAEM), 2003).

Hodgson et al. (2007) performed an observational study looking at the impact of television advertising and education in the recognition of stroke symptoms. They found that the advertising contributed in reducing the age and education-related differences in knowledge of warning signs of stroke. The results also showed that for all segments of society the absence of advertising is associated with significant declines in knowledge. Because this was an observational rather than an experimental study it is not possible to prove causation, as the campaign period could have been contaminated by other

sources of stroke information. To pursue this research further, alternative methods may be required, such as using a control group or interviewing stroke patients and their families about the source of their knowledge or memory of television advertising (although validating the accuracy of such data would be difficult). Despite these problems, this study provides an insight into the value of public campaigns. The ability of television advertising to drive people to seek medical attention is important. The ''time is brain'' mantra is not trendy jargon. What happens in the pre-hospital phase and in the ED an essential for all stroke patients (Hodgson et al., 2007).

Wijngaarden et al. (2006) summarised issues that prevent efficient stroke care and found that ambulance personnel and ambulance control rooms often failed to identify the urgency of transport to hospital — particularly one with a specialised stroke unit. Kwan et al. (2004) found in their systematic literature review that seven research studies identified that stroke was often not regarded as an emergency by ambulance staff.

However, in analysing the ability of UK paramedics to identify stroke symptoms with the use of the FAST approach, Mohd Nor et al. (2004) showed that the detection of specific neurological signs was comparable to stroke physicians in accuracy and ability. Ambulance personnel are crucial for efficient assessment and treatment and, much like ED staff, are familiar with time based interventions (Power, 2004). With education and tools, the recognition of stroke can be vastly improved. Mosley et al. (2007) showed that recognition by ambulance staff is enhanced by including ambulance practice in comprehensive care pathways that span the whole process of stroke care.

Management of stroke thrombolysis in hospital

ED guidelines need to incorporate speed and efficiency in their design, which requires cooperation between stroke teams and multiple hospital departments. Extensive preparation is required for a procedure which may be rarely required, but where minutes saved at each step will reduce the extent of the final ischaemic injury (Rasler, 2007). However, many hospitals have failed to implement effective systems to facilitate the delivery of this treatment to acute stroke patients. Kwan et al. (2004) found that the most common and consistent sources of delay were in medical assessment, neuro-imaging and transferring to the ward.

Lindsberg et al. (2006) performed a retrospective study in Finland, describing the organisational steps that significantly reduced the management delays of thrombolysis. Similar evidence was produced by Tveiten et al. (2009) who compared the delays before and after organisational changes made in 2006 using a prospective treatment database in Norway. The ED's was reorganised by relocating the CT scanner next to the department, and streamlining the triage process which included enhancing the pre-hospital notification of a possible AIS by the ambulance service. Both studies reported significant 'door to needle' time reductions, which for an AIS patient improves the prognostic value of recovery.

These studies show that ED's looking to develop services can rapidly implement the necessary logistics to deliver thrombolysis to a large proportion of patients with AIS with short hospital delays.

The position statement from the Society for Academic Emergency Medicine (SAEM, 2003) recommends improvement of initial diagnostic and therapeutic strategies for care. Importantly, availability of the ED, radiology and neurology resources cannot be assumed. Overcrowding, lack of timely access to expert interpretation of imaging studies, and other problems are frequent. An organised, fast-track stroke thrombolysis service can be imperative to the success of the treatment and the optimisation of care. The narrow therapeutic window and strict protocol demands make this intervention far different from other therapeutic interventions. Also, although evidence demonstrates the therapeutic benefit for an important minority of patients, substantial increased risk of intracranial haemorrhage exists, and therefore it is crucial that the treatment and decisions are made by a stroke specialist/consultant (Szoeke et al., 2003; Rasler, 2007; NINDS, 1995).

Szoeke et al. (2003) conducted a large retrospective study reporting the experience of the initial delivery of a stroke thrombolysis service with rt-PA under similar guidelines as the NINDS trial in 1995. They found similar positive outcomes for patients but were able to identify that these outcomes were associated with the setting being a specialist stroke centre, with 24 h cover of a dedicated team of stroke nurses, registrars, fellows and neurologists. They recognised that in the absence of this specialist cover, the positive outcomes and results may not be duplicated and could result in greater hazards for patients receiving this specialist treatment.

Intravenous rt-PA for acute stroke should only be administered if the medical care providers have expertise, or access to expertise, in making a diagnosis of stroke, evaluating neuro-imaging and diagnosing and managing possible intracranial and systemic bleeding complications of thrombolytic therapy (NINDS, 1995). Facilities and staff must be available to aggressively monitor a patient's neurological and haemodynamic parameters in a specialist area following administration of the treatment, as outlined in the NINDS trial (NINDS, 1995).

Alberts et al. (2000) performed a literature review of randomized clinical trials and observational studies, and found several elements improved patient care and outcomes. Key elements of primary stroke centres include specialised teams and units, written care protocols, and an integrated emergency response system. Strong leadership with continuing education are also important elements for these specialist centres (Alberts et al., 2000). Adoption of these recommendations may increase the use of appropriate diagnostic and therapeutic modalities and reduce peri-stroke complications. The establishment of primary stroke centres has the potential to improve the care of patients with stroke. A successful example of this is demonstrated in London, where 'Heart Attack and Stroke' centres are emerging, with the ambulance service able to identify 'FAST' positive patients and re-direct them appropriately. Pre-notification by ambulance control alerts the necessary team which meets the patient on arrival and assesses the suitability for thrombolysis.

Educational requirements for ED nurses involve early recognition triggers and awareness of the new care pathways,

along with an understanding of thrombolytic agents and the necessary critical care of the patient. Relatives should also be considered, and ED nurses are valuable sources of reassurance along with explanation of treatment and the risks of, and after-care.

Conclusion

Thrombolysis is an exciting and promising answer to the debilitating and life threatening condition of AIS. With the current evidence and new protocols emerging within hospitals it is important to assess the barriers that prevent patients having access to this treatment. As the literature demonstrates, it is an international issue. Without education of the public, ambulance and emergency staff, the potential success cannot be realised.

ED nurses are frequently pressured according to targets set to time for many different emergencies, for example 'door to needle' time for myocardial infarction, analgesia administration for fractured neck of femurs and recently 'early goal directed therapy' for sepsis. With this experience, ED nurses are in a good position to initiate and adhere to such an ambitious target of 3 h for AIS patients. However without the protocols and teams in place to facilitate fast-tracking of patients for neuro-imaging and stroke specialist/consultant assessment, patients will continue to be excluded from the option of stroke thrombolysis and put at risk without being treated by these expert teams.

References

Albers, G., 2001. Advances in intravenous thrombolytic therapy for treatment of acute stroke. Neurology 57 (S2), S77—S81.

Alberts, M., Hademenos, G., Latchaw, R., Jagoda, A., Marler, J., Mayberg, M., Starke, R., Todd, R., Viste, K., Girgus, M., Shephard, T., Emr, M., Shwayder, P., Walker, M., 2000. Recommendations for the establishment of primary stroke centers. Journal of the American Medical Association (JAMA) 283, 3102—3109.

American Academy of Emergency Medicine (AAEM), 2002. Position Statement: The Use of Intravenous Thrombolytic Therapy in the Treatment of Stroke. <http://www.aaem.org/positionstatements/thrombolytictherapy.php> (accessed 22.04.08).

Harraf, F., Sharma, A., Brown, M., Lees, K., Vass, R., Kalra, L., 2002. A multicentre observational study of presentation and early assessment of acute stroke. British Medical Journal 325 (17), 5.

Hodgson, C., Lindsay, P., Rubini, F., 2007. Can mass media influence emergency department visits for stroke? Stroke 38, 2115—2122.

Kwan, J., Hand, P., Sandercock, P., 2004. A systematic review of barriers to delivery of thrombolysis for acute stroke. Age and Ageing 33, 116—121.

Lindsberg, P., Happola, O., Kallela, M., Valanne, L., Kuisma, M., Kaste, M., 2006. Door to thrombolysis: ER reorganisation and reduced delays to acute stroke treatment. Neurology 67, 334—336.

Llinas, R., 2006. Acute ischaemic stroke treatment. US Neurological Disease 35, 37.

Mohd Nor, A., McAllister, C., Louw, S., Dyker, A., Davis, M., Jenkinson, D., Ford, G., 2004. Agreement between ambulance paramedic- and physician-recorded neurological signs with face arm speech test (FAST) in acute stroke patients. Stroke 35, 1355—1359.

Mosley, I., Nicol, M., Donnan, G., Patrick, I., Kerr, F., Dewey, H., 2007. The impact of ambulance practice on acute stroke care. Stroke 38, 2765—2770.

National Institute of Neurological Disorders (NINDS) and Stroke rt-PA Stroke Study Group, 1995. Tissue plasminogen activator for acute ischaemic stroke. The New England Journal of Medicine 333 (24), 1581—1587.

Power, M., 2004. An update on thrombolysis for acute ischaemic stroke. Advances in Clinical Neuroscience and Rehabilitation 4 (3), 36—37.

Rasler, F., 2007. The new era of acute stroke management. Emergency Medicine 39 (12), 13—18.

Royal College of Physicians, 2004. National Clinical Guidelines for Stroke, second ed. RCP, London. <http://www.rcplondon.ac.uk/pubs/books/stroke/strokeguidelines2ed.pdf> (accessed 22.04.08).

Society for Academic Emergency Medicine (SAEM), 2003. Position Statement: Optimizing Care of the Stroke Patient. SAEM, Washington. <http://www.saem.org/saemdnn/AboutSAEM/Governance/PositionStatements/OptimizingCareoftheStrokePatient/tabid/173/Default.aspx> (accessed 22.04.08).

Stroke Association, 2008. Stroke is a Medical Emergency. Stroke Association, London. <http://www.stroke.org.uk> (accessed 22.04.08).

Szoeke, C., Parsons, M., Butcher, K., Baird, T., Mitchell, P., Fox, S., Davis, S., 2003. Acute stroke thrombolysis with intravenous tissue plasminogen activator in an Australian tertiary hospital. Medical Journal of Australia 178, 324—328.

Thompson, P., 2006. The challenge to increase thrombolysis of stroke within the Emergency Department. Emergency Medicine and Critical Care Review (ref sec 1—3).

Tveiten, A., Mygland, A., Ljøstad, U., Thomassen, L., 2009. Intravenous thrombolysis for ischaemic stroke: short delays and high community-based treatment rates after organisational changes in a previously inexperienced centre. Emergency Medicine Journal 26, 324—326.

Wardlaw, J., Del Zoppo, G., Yamaguchi, T., Berge, E., 2005. Thrombolysis for acute ischaemic stroke. Cochrane Database Systematic Review 1, CD00213.

Wijngaarden, J., Dirks, M., Dippel, M., Minkman, M., Niessen, L., 2006. Towards effective and efficient care pathways: thrombolysis in acute ischaemic stroke. Quarterly Journal of Medicine 99, 267—272.