Treating stroke

Alastair Buchan and Thomas Feasby champion thrombolysis for patients experiencing acute ischemic stroke.[1] In their enthusiasm, they advocate prehospital triage of patients by emergency medical service (EMS) personnel to designated urban stroke centres. For this to work, triage guidelines must allow accurate identification of candidates for thrombolysis. Unfortunately, such guidelines do not exist. The sensitivity of the most widely published prehospital guideline for identifying stroke, when used by paramedics, is only 59%.[2] This means that for every 10 patients triaged as having had a stroke, 7 patients with stroke would not be recognized as requiring triage to a stroke centre.

Since the prevalence of stroke in prehospital patients is as low as 0.4%,[3] any triage rule is bound to have an extremely low positive predictive value. This would remain true even if the prevalence of stroke in these patients were as high as 10%. Therefore, triage rules may result in preferential transport of large numbers of patients without stroke to stroke centres.[4] Many of these patients will have other serious medical conditions[3] requiring admission by a non-neurology service. Lastly, no triage rule can address the needs of patients who arrive by private transport, or have a stroke as an inpatient, at a hospital that is not a stroke centre.

A more appropriate urban EMS system design is to use stroke guidelines as a means of rapid stroke identification, not triage. Identified patients would receive high-priority transport, with advanced notification of the nearest hospital that must be "stroke ready" in any event. Once treatment was given, the EMS system could rapidly respond to initiate patient transport to a designated stroke centre for ongoing care.

Buchan and Feasby suggest that even rural centres be prepared to deliver thrombolytic therapy to acute stroke patients. There is no reason why all urban centres should not be prepared as well.

Richard Verbeek
Division of Prehospital Care
University of Toronto
Toronto, Ont.

References

1. Buchan AM, Feasby TE. Stroke thrombolysis: Is tissue plasminogen activator a defibrillator for the brain? *CMAJ* 2000;162(1):47-8.
2. Kothari RU, Pancioli A, Liu T, Brott T, Broderick J. Cincinnati prehospital stroke scale: reproducibility and validity. *Ann Emerg Med* 1999;33:373-8.
3. Smith WS, Isaacs M, Corry MD. Accuracy of paramedic identification of stroke and transient ischemic attack in the field. *Prehospital Emerg Care* 1998;2:170-5.
4. Verbeek PR, Schwartz B. Prehospital triage to stroke centres: Is it a solution to the problem? *CJEM* 2000;2(2):106-80.

[The authors respond:]

Richard Verbeek expresses the all-too-common concern that triaging acute stroke patients to stroke centres will overwhelm hospital and emergency department resources. We agree that it would be ideal if every hospital with a CT scanner could offer thrombolytic therapy for stroke. While this is not the case now, with improved telemedicine this might become feasible in the very near future. In our opinion thrombolytic therapy for stroke has many parallels with thrombolysis for acute myocardial infarction, although the therapeutic window is tighter (under 3 hours) and the neurology is more complex. The Cochrane analysis suggests that when tissue plasminogen activator is used for acute stroke 140 disabilities are prevented per 1000 treated patients. For acute myocardial infarction, 35 deaths are prevented per 1000 patients treated with tissue plasminogen activator.

We believe that stroke expertise in highly organized centres is now required and this expertise should extend beyond urban centres through use of modern communications. The triage of patients with acute ischemic stroke is a new but rapidly developing art. It is not surprising that early attempts failed to show high sensitivity and specificity. A new scale, the Los Angeles prehospital stroke screen, has been prospectively validated and shows a positive predictive value of 97% and a negative predictive value of 98%.[1] As this scale becomes more widely used it should alleviate the concern that Verbeek articulates.

It is wrong to think that triage should occur in the emergency department of community hospitals so that specific patients can then be sent on to tertiary stroke centres. Simply stated, there is not enough time when time is brain. Analysis of the National Institute of Neurological Disorders and Stroke (NINDS) stroke trial shows a reduction in benefit for every minute of increased time from onset to treatment.[2] Every month in Calgary we are disappointed when a patient arrives late because transport was delayed to allow assessment at an outlying centre.

Acute stroke care is now evolving as acute cardiac care evolved over the last 25 years. Verbeek has indeed observed this and radically proposes to put defibrillators into lay hands.[3] We suggested that thrombolysis is like a defibrillator of the brain[4] and we predict that our colleagues in the emergency department, with increased knowledge of stroke and assistance by telemedicine to evaluate CT scans, will allow local community hospitals to directly implement effective stroke care to those presenting within the therapeutic window.[5]

Alastair M. Buchan
Thomas E. Feasby
Department of Clinical Neurosciences
University of Calgary
Calgary, Alta.

References

1. Kidwell CS, Starkman S, Eckstein M, Weems K, Saver JL. Identifying stroke in the field: prospective validation of the Los Angeles prehospital stroke screen (LAPSS). *Stroke* 2000;31:71-6.
2. Marler J, Tilley BC, Lu M, Brott T, Lyden P, Broderick JP, et al. Earlier treatment associated with better outcome in the NINDS t-PA Stroke Study [abstract]. *Stroke* 1999;30:244.
3. Schwartz B, Verbeek PR. Automated external defibrillation: Is survival only a shock away? *CMAJ* 2000;162(4):533-4.
4. Buchan AM, Feasby TE. Stroke thrombolysis: Is

tissue plasminogen activator a defibrillator for the brain? *CMAJ* 2000;162 (1): 47-8.
5. Buchan AM, Barber PA, Newcommon N, Karbalai HG, Demchuk AM, Hoyte KM, et al. Effectiveness of t-PA in acute ischemic stroke: Outcome relates to appropriateness. *Neurology* 2000;54:679-84.

Vitamin B_{12} injections for the elderly

In their article on the use of vitamin B_{12} injections for elderly patients by primary care practitioners in Ontario, Carl van Walraven and David Naylor acknowledge that a major problem with their study is that overutilization is identified but underutilization is not.[1] Patients with cobalamin deficiency, but with normal serum vitamin B_{12} levels according to current definitions, may present with neuropsychiatric symptoms ranging from innocuous paresthesias and fatigue to dementia and psychosis.[2,3] Practitioners cognizant of the serious morbidity possible with cobalamin deficiency might opt to risk overutilizing this safe, inexpensive therapy: serum vitamin B_{12} determinations cost the system approximately $20 and vitamin B_{12} therapy is relatively inexpensive. Although functional biochemical testing of methylmalonic acid and homocysteine levels prior to commencing therapy would reduce overutilization (and underutilization), these tests, which cost $160 in total, are currently not covered by the Ontario Health Insurance Plan. This is an unacceptable financial burden for the elderly population.

Metabolic evidence from the Framingham study showed that cobalamin deficiency is present in 1 in 8 or 1 in 5 elderly people.[4] Yao and colleagues suggested that serum cobalamin screening be done for every person aged 65 and older and that the normal range be increased to 250–300 pg/mL.[5] Screening for cobalamin deficiency at our southwestern Ontario community health clinic yielded a 20% prevalence in the elderly.

Dementia and impaired cognitive functioning may result from vitamin B_{12} deficiency, although most of the evidence is from observational studies.[4-6] The costs of misdiagnosing a potentially reversible dementia resulting from cobalamin deficiency may justify erring on the side of overutilization until more studies are done on the utility of vitamin B_{12} treatment. Fewer interventions in primary care are as simple, safe and satisfying to both practitioner and patient as the detection and appropriate treatment of symptomatic cobalamin deficiency.

Francesco Anello
Family physician
Woolwich Community Health Centre
St. Jacobs, Ont.

References

1. van Walraven CG, Naylor CD. Use of vitamin B_{12} injections among elderly patients by primary care practitioners in Ontario. *CMAJ* 1999;161(2):146-9.
2. Pennypacker L, Allen R, Kelly J, Matthews LM, Grigsby J, Kaye K, et al. High prevalence of cobalamin deficiency in elderly outpatients. *J Am Geriatr Soc* 1992;40:1197-204.
3. Healton EB, Savage DG, Brust CM, Garrett TJ, Lindenbaum J. Neurologic aspects of cobalamin deficiency. *Medicine (Baltimore)* 1991;70:229-45.
4. Lindenbaum J, Rosenberg I, Wilson P, Stabler S, Allen R. Prevalence of cobalamin deficiency in the Framingham elderly population. *Am J Clin Nutr* 1994;60:2-11.
5. Yao Y, Yao SL, Yao SS, Yao G, Lou W. Prevalence of vitamin B_{12} deficiency among geriatric outpatients. *J Fam Pract* 1992;35:524-8.
6. Bell IR, Edman JS, Marby DW, Satlin A, Dreier T, Liptzin B, et al. Vitamin B_{12} and folate status in acute geropsychiatric patients: affective and cognitive characteristics of a vitamin nondeficient population. *Biol Psychiatry* 1990;27:125-37.

[The authors respond:]

We agree that treatment of true cobalamin (vitamin B_{12}) deficiency is very important and should continue. We also agree that one might reasonably err on the side of overtreatment.

However, 2 issues regarding vitamin B_{12} deficiency must be considered when framing the problem of variations in utilization. First, as indicated by Francesco Anello, many of the symptoms of vitamin B_{12} deficiency are extremely nonspecific. Second, measurements of serum vitamin B_{12} levels do not discriminate between those patients with true vitamin B_{12} deficiency and those with low serum levels.[1] We believe that the combination of nonspecific symptoms with a nonspecific laboratory test helps explain the large variations in parenteral vitamin B_{12} utilization between practices that we reported in our article.[2]

Anello raises several interesting points on which we would like to comment. First, the prevalence of biochemical evidence of vitamin B_{12} deficiency in the Framingham cohort was low.[3] Review of Fig. 2 in the report by Lindenbaum and colleagues[3] shows that 14 elderly patients with low serum levels of vitamin B_{12} had elevated serum methylmalonic acid levels. Since the cohort involved 548 elderly people, 2.5% showed biochemical evidence of vitamin B_{12} deficiency.

Second, the data reported by Yao and colleagues[4] do not justify screening for vitamin B_{12} deficiency.[5,6] Since 8% of the study participants had symptoms or signs of vitamin B_{12} deficiency prior to testing and would therefore have been tested on a case-finding basis, it does not appear that this was a general inception cohort. More generally, evidence for screening is lacking and is not recommended by others.[7]

Finally, the cost of vitamin B_{12} injections could be considerable at the population level. We used the database of the Ontario Drug Benefit program to identify all 34 264 elderly people who were prescribed parenteral vitamin B_{12} in 1996. Using claims in the Ontario Health Insurance Plan database, we calculated the direct cost of all physician visits associated with vitamin B_{12} injections in the year following the prescription date to be $4.2 million. This would pay for approximately 250 uncomplicated coronary artery bypass graft surgeries in elderly patients.[8]

Where should we go from here? First, we need further research using appropriate methodologies[9,10] to find methods of determining true vitamin B_{12} deficiency. Second, the role of high-dose oral vitamin B_{12} supplementation needs elucidation.[11–13] Finally, since low serum levels do not necessarily equate with vitamin B_{12} deficiency, we need natural history studies and rigorous intervention trials to determine the most effective and efficient way to manage patients with nonspecific symptoms and