REVIEW PAPER

Management of Acute Stroke: A Debate Paper on Clinical Priorities. A Literature Review

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Abstract:

Stroke is a leading cause of death and disability globally. Also, it is expected that the burden of stroke will increase due to the rise of the elderly population within societal age structures. The aim of this literature review is to present in detail the important issues regarding contemporary management of stroke. For this reason, a thorough search was undertaken via Medline, CINHAL and ELIN from 2004 to 2014. Analysis of the search results led to the corresponding domains as presented below, namely: nursing implications for stroke, interventions in the acute phase, investigations/other treatment options and cost implications. In this context, a number of goals for more efficient care of stroke patients are now set, using advanced, integrated care plans and critical pathways. From the above, it can be concluded that stroke has a major impact on society and hospital resources and its high incidence and frequency of prolonged survival requires a heavy investment in human and financial recourses for provision of care. On the other hand, the rising hospital costs coupled with a growing elderly population are limiting the financial resources of the health care system, and therefore, an improved development of the long-term care continuum is required.

Key words: stroke, management, interventions and cost

Background

Stroke is the third leading cause of death and an important cause of hospital admission and long-term disability in all industrialised populations (Paul et al. 2007; Brown et al. 2007). The global incidence of stroke is 300/100,000 in the general population (Brainin et al, 2000). According to the World Health Organisation, despite recent advances in medical treatment for stroke, more than 30% of all stroke patients die within the first year of onset (WHO, 2004).

Stroke mortality rates declined for several populations during the twentieth century. In the first two decades of the last century, this was 0.5% per year in the U.S., and rose to approximately 1.5% per year from 1950 to 1970 (Feigin et al., 2009). All age groups were affected, suggesting that this was a period effect rather than a cohort effect. Yet, this decrease began long before effective therapies for stroke prevention treatment were available, and thus cannot be ascribed to medical care. This trend has not continued in the latter part of the century.

In the U.K the link between incidence, outcome and socioeconomic status has been documented whereby unskilled manual workers had a 60% higher risk of stroke compared to blue collar workers. In addition, there was a 50% higher age-adjusted mortality rate. While age-specific death rates for stroke have declined during the 20th century, currently they remain greater for women than men. In the U.S, the projected increase is from approximately 700,000 in 2002 to 1,136,000 in 2025 (Broderick and Wiliam, 2004).

It has been over 20 years since the logarithmic relationship between stroke mortality and age was first described. Consequently, it is expected that the burden of stroke will increase due to the rise in median age and the alteration of the population age structure,

despite stable or falling age-adjusted incidence rates (Brice et al., 2002).

It is well documented that the risk factors for stroke overlap significantly with those for ischaemic heart disease. Following age, the most important risk factor is blood pressure. The risk of stroke increases across both elevated systolic and diastolic blood pressure. The relative risk of stroke increases by a factor of 2.3 for each 10 mm Hg increase in systolic blood pressure or 5 mm Hg increase in diastolic pressure (Weiner et al., 2007). Yet, significant reductions of risk for first and subsequent stroke can result from effective anti-hypertensive treatments (Chapman et al., 2004).

Diabetes and smoking each increase the relative risk by a factor of 2.35 while hyper-homocysteinaemia is another significant risk factor with a relative risk of 5 to 7 between the highest and lowest quartiles of serum homocysteine concentration (Myint et al., 2010). Heart arrhythmias such as atrial fibrillation also hold a relative risk of 5 for stroke (Engström et al., 2010). Serum cholesterol is somewhat more complex for stroke than for coronary artery disease as some observational studies show that elevated cholesterol levels do not necessarily increase risk. It is notable that low cholesterol may result in an increased risk of hemorrhagic stroke. Yet a major therapeutic trial of lipid lowering therapy has demonstrated reduced ischaemic stroke incidence without any increase in hemorrhagic stroke, but in a sub-group within this trial, patients with prior ischaemic stroke placed on statin therapy showed no reduced incidence of stroke (Goldstein, 2011).

Literature review

The aim of this review is to cover the important management issues related to stroke both from a medical and a nursing aspect. For this reason, a thorough literature search was undertaken via Medline, CINHAL and ELIN from 2004 to 2014 using the following key words: stroke, management, interventions and cost. Analysis of the search results led to the corresponding domains as presented below, namely: nursing implications for stroke, interventions in the acute phase, investigations/other treatment options and cost implications.

Nursing implications for stroke

Acute stroke poses a challenge for nursing as it is a demanding condition within the spectrum of neurological disorders. Staff nurses need to correct not only for obvious neurological deficits such as reduced mobility and other degrees of limb paresis bit also for systematic implications such as respiratory problems to give one major example (Theofanidis, 2003).

According to Ali et al., (2007) hypoxia is a serious clinical problem after stroke, and may lead to serious complications and slower recovery. At present, supplemental oxygen is commonly administered in the acute stroke phase as some current guidelines and standard nursing practice suggest that oxygen saturation after acute stroke should be maintained at 95% or higher and at a dose of 2 to 4 L/minute via nasal cannulae.

Yet, not all abnormal findings should be treated spontaneously as in some cases evidence is conflicting and some recommendations are not based on controlled clinical studies (Ali et al., 2005). Patients with milder strokes may experience worse outcomes with oxygen treatment. Although hypoxia has been well associated with aggravation of damage to the ischaemic parts of the brain after stroke, early in vitro evidence in experimental animals suggest that administration of pure O_2 may aggravate the situation even more by enhancement of free radical formation and lipid peroxidation. Singhal, (2006) in a small randomised controlled trial found mean NIHSS scores at 24 hours to be significantly lower in patients receiving high flow oxygen therapy for eight hours via face mask, in comparison to receiving room air. Moreover, Sjöberg and Singer, (2013) caution that hyperoxia on normal vasculature may have a vasoconstrictor effect and, consequently, significant reduce blood flow to the tissue at-risk.

Overall, there is a lack of clear consensus among stroke physicians whether O_2 should be administered after acute stroke, and if so how much, and which route should be selected (Poli and Veltkamp, 2009). However, Singhal

(2007) suggests that an alternative benefit of early administration of O_2 in acute stroke is the 'buy time' effect, whereby the window for administration of thrombolytic or neuro-protective drugs can be expanded. Yet, Summers et al., (2009) emphasised that supplemental oxygen should be administered to patients with O_2 saturation <90% and decreased level of consciousness.

Despite controversies over benefits and risks of oxygen therapy, strong emphasis has been placed on routine, accurate monitoring of O_2 saturation, coupled with correct positioning of the patient in order to achieve higher O_2 saturation levels; patents should be placed up-right where appropriate, preferably in a chair with care to avoid slumping (Jones et al., 2007).

Thrombolytic therapy in current practice

Thrombolytic therapy for acute stroke has received widespread, though not universal, support as it is a complex intervention which requires intensive use of resources and personnel in order to meet its narrow therapeutic window, which is 3-hour from symptom onset (Lee et al., 2004). Current clinical protocols advocated by the Brain Attack Coalition (BAC) in the U.S. and the Heart and Stroke Foundation of Canada (HSFC) indicate multilevel system change to increase the number of patients eligible for increased therapeutic time window, increased age limits, and increased administration of thrombolytic therapy including improved in-hospital infrastructure ranging from acute stroke wards to a minimum of specialised units (Barber et al., 2004).

Some western countries have undergone major system changes in stroke care (Donnan et al., 2008). This process is unique among large jurisdictions and forms an important framework for initiating and evaluating such strategies. Over a decade ago, the Heart and Stroke Foundation of Ontario, Canada, introduced a coordinated system of stroke care locally (Schneider et al., 2003). Over the next years, the Ministry of Health funded a coordinated province-wide stroke strategy and a total of nine regional stroke centres were designated as the development of integrated acute stroke care was seen as a key role of these centres (Goldstein and Amarenco, 2004).

The core rational behind this process was that effective delivery of acute stroke therapy involves a pre-hospital phase and a Casualty phase. The latter requires a rapid and intense application of clinical, radiological (Computed Tomography / Magnetic Resonance Investigation), and biochemical analyses of the patient who is eligible for thrombolysis. These evaluations serve to interpret compliance with eligibility criteria, thereby maximising the probability of positive outcomes (Marks et al., 2008).

Yet, the main determinant of eligibility remains the time since onset and earlier treatment is associated with improved outcomes (Lansberg et al., 2009: Hacke et al., 2004). Thus, attention should be focused on the pre-hospital phase. In order to reduce delay times in the pre-hospital phase, public awareness of the urgency for treatment is essential. This requires good recognition of symptoms, action to contact emergency services and rapid transportation to a facility capable of delivering specialised stroke care (Goldstein and Simel, 2005).

A successful public awareness campaign was launched in the UK in 2009, i.e. Act F.A.S.T. (Face, Arm, Speech, Time), aiming at improving public knowledge on the signs of stroke and the need for rapid admission to hospital which improves chances of patient outcomes. Despite criticisms, this simple test is helping people to recognise the signs of stroke and understand the importance of emergency treatment (Mellon et al., 2013; Dombrowski et al., 2013; Bietzk et al., 2012).

Although many educational strategies have been shown to increase the public's awareness of stroke urgency, the problem in many countries is poor infrastructure and limitations in the hospital settings where thrombolysis for stroke and other treatments are severely limited as specialised stroke care is not readily available (Rudolf et al., 2011).

Patient Selection for Thrombolysis

Thrombolytics restore cerebral blood flow in some patients with acute ischaemic stroke and may lead to improvement or resolution of

neurologic deficits. Thrombolytic therapy is of proven and substantial benefit for these selected patients. The current treatment protocols rely on the entry criteria used for the National Institute of Neurological Disorders and Stroke (NINDS) Trial and are as follows: a prompt diagnosis of acute ischaemic stroke of less than 3 hours from onset, absence of haemorrhage on CT scan, good blood pressure control, a National Institute of Health Stroke Scale Score of greater than 4 along with exclusion of those at high risk for bleeding with therapy (Hacke et al., 2008; Adams et al., 2007).

Reanalysis of the results from the original trial suggest a better outcome if treated within 0 to 90 minutes compared to 91 to 180 minutes (Saver and Levine, 2010). Yet, the 3-hour window has been challenged by some authors claiming that clinical benefits can be seen up to 4.5- hours from onset (Del Zoppo et al., 2009). The counter challenge to this is that when the time-window is extended the number of patients eligible for thrombolytic therapy increases only marginally. Therefore, prompt transfer to hospitals that are properly prepared for rt-PA therapy remains a priority (Mihout et al., 2012; Macleod et al., 2005).

Data from these trials are congruent in supporting the following conclusions:

- Intravenous fibrinolytic therapy at the cerebral circulation dose within the first 3 hours of ischaemic stroke onset offers substantial net benefits for virtually all patients with potentially disabling deficits (Huang et al., 2011).
- Intravenous fibrinolytic therapy at the cerebral circulation dose within 3-4.5 hours offers moderate net benefits when applied to all patients with potentially disabling deficits (Huang et al., 2011)
- MRI of the extent of the infarct core (already irreversibly injured tissue) and the penumbra (tissue at risk but still salvageable) can likely increase the therapeutic yield of lytic therapy, especially in the 3- to 9-hour window (Diedler et al., 2010)
- Intra-arterial fibrinolytic therapy in the 3- to 6-hour window offers moderate net benefits when applied to all patients with potentially disabling deficits and large artery cerebral thrombotic occlusions (Wahlgren et al., 2008; Graham, 2003).

Thus, rt-PA treatment should remain a priority as this has proven to be a highly effective treatment within the tight time-window and other constrains imposed.

Investigations and other treatments for stroke

Investigations like Computed Tomography (CT scanning), Magnetic Resonance Imaging (MRI), diffusion and perfusion weighted MRI which may help to differentiate between infarcted tissue and tissue at risk, are used most commonly in defining a stroke with CT being the most widely used, as access to MRI can be more limited (Fiebach et al., 2001). A CT is highly reliable in distinguishing between hemorrhagic and ischaemic stroke and early signs of ischaemia can be detected as early as 2 hours after the onset of stroke and thus is considered to be the 'gold standard' diagnostic measure (Adams et al., 2007). It also identifies haemorrhages almost immediately and detects sub-arachnoid haemorrhages in the majority of cases (Lin et al., 2008).

Other investigations which can provide a baseline for management of the stroke patient are: chest radiography, urea and electrolytes, full blood count, urinalysis, random blood sugar, electrocardiogram, and serum cholesterol and triglycerides (Andre et al., 2008). These tests are far cheaper than CT and MRI, and they are regarded as the minimum series of investigations that a new stroke patient should have. These investigations and tests assist clinicians to subcategorise patients at three specific levels: to separate strokes from non-strokes (for example, cerebral tumours), to distinguish haemorrhage from infarction and to identify specific pathophysiological subtypes of cerebral infarction which influence decisions concerning therapy and prognosis. However, it is mainly neuroimaging that can help clinical decision making and subsequent treatment options (Kane et al., 2008; Kane et al., 2007).

Globally, there are two main types of medical treatment that are prescribed for patients with stroke (Rothwell et al., 2011; Sakai et al., 2008).

a) *Basic medical treatment* which includes standard medical treatment, routine nursing care and simple dietary recommendations that is often given with little or no monitoring to virtually all patients and usually delivered in conventional medical wards and,

b) *Interventional treatments* which are complex and are more invasive, costly and technically challenging to administer and monitor, usually delivered in specialised neurology or stroke-specific dedicated wards.

The first type of treatment consists of administrating aspirin, fixed-dose subcutaneous heparin, oral calcium antagonists and corticosteroids (Georgiadis et al., 2013; Hills and Johnston 2008).

The complex ones are fibrinolytic drugs, isorolalmic haemodilution, intravenous naftidrofuryl, hyperbaric oxygen, intravenous inhibitors of excitatory amino acids and the administration of thrombolytic agents (Nutescu et al., 2004). Yet, in the recent years, highly sophisticated devices came in use, designed to stabilise an intracranial aneurysm, thus avoiding a haemorrhagic stroke. Moreover, in patients beyond the systemic thrombolysis therapeutic window, other devices have been used more often, to perform mechanical embolectomy. These are also known as clot retrievals such as the Stentriever or the Merci Retriever device. Overall, these have shown higher recanalisation rates and better outcomes for embolic stroke (Mokin et al., 2014; Murthy et al., 2014; Hassan et al., 2013; Alshekhlee A., et al., 2012).

For many years stroke was believed to be a low-urgency medical situation. Yet, today the recognition for urgency of treatment is of paramount importance as the most important aim in treating stroke is maintenance of perfusion of the ischaemic penumbra, which is the area of the brain where blood supply is restricted due to the thrombus or emboli but these nerve cells have a good chance of survival if the occlusion is removed soon (Jauch et al., 2013; Boatright, 2003). Currently, thrombolysis for stroke with the innovation of Recombinant Tissue Plasminogen Activator (rt-PA) is a major breakthrough in the treatment of acute stroke although the therapeutic window for such a treatment is narrow, that is 3 hours from onset (Butcher et al., 2003). Furthermore there are certain inclusion criteria that have to be met before a patient is offered this option but in any case stroke should be treated as a very urgent condition where every minute counts (Wardlaw et al., 2003).

Along these lines, the American Stroke Association proposed an alternative term for stroke, which is: "Brain Attack", in order to underline the message: "time is brain" and just as a myocardial infarction is conceived as an urgent medical condition by the health care personnel and the wider public, likewise, the brain's version of heart attack should be treated as a medical emergency accordingly (Dhamija and Donnan, 2007; Alberts et al., 2005).

Cost implications of stroke

The above mentioned interventions are measures for acute stroke management and should be carefully budgeted. This is especially relevant to date due to the heavy burden of austerity that most national health care systems are facing in combination with the rising numbers of elderly at risk of stroke.

Stroke currently consumes significant resources through healthcare costs and disability. The cost of stroke to the British NHS is estimated to be £2.8 billion and the financial burden extended to the wider economy is summed up to £1.8 billion (Lee et al., 2011). These costs are mainly due to the complexity of nursing stroke patients as their care requires a multi-disciplinary approach.

A recent study shows that stroke units could reduce costs by **$** 240 million in Canada (Gladstone et al., 2009). It is also worth noting that at the turn of the millennium, 28% of total stroke incidence occurs in individuals under the age of 65 and accounts for 20% of all acute, and 25% of all chronic care beds. There has also been a significant increase in the absolute figure of hospitalisations for acute

stroke over the last 20 years with a projected increase of 10% in 1996 to a projected 15% in 2016 (Matchar and Samsa, 2000).

Hospitalisation makes up 87% of the total direct cost of stroke care, which was estimated by the Heart and Stroke Foundation of Canada to be 2.8 billion dollars in 1996. However, this cost does not include costs related to either short- or long-term disability. Such costs may be considerable since, in the case of ischaemic stroke, only 25% of people make a full recovery (Goeree et al., 2005). More recent costs are available for the U.S., where the estimated direct cost for stroke in 2004 is 33 billion dollars - 41% of this is due to hospital costs reflecting the expense of acute care (Luengo-Fernandez et al., 2009). Indirect costs due to loss of productivity are estimated at 53.6 billion dollars (van Exel et al., 2003).

Given the trends observed in stroke worldwide over the last three decades and the associated steep rise in costs, stroke is, and will remain a significant problem for North American and other societies, especially in the western world although considerable savings can be made with prompt and readily available comprehensive services for stroke patients.

Acute stroke care on a neurological ward is less costly than care on a stroke unit but the latter is known to have better outcomes. The higher costs of stroke unit care are due to diagnostic procedures and personnel. However, intensive non-medical costs tend to decrease. Thus, stroke unit care seems to be more outcomes oriented but selection bias of patients could lead to underestimation of cost differences. As cost-effective medical care for stroke is important, future studies are needed to assess this plus the cost-benefit ratio of different stroke care concepts (Epifanov et al, 2007).

A study in Greece by Gioldasis et al., (2008) calculated the in-hospital cost of stroke based on real costs for the resources used, showing notable differences depending on the type of stroke. The average cost of an ischaemic stroke was €3,710 whereby patients with Primary Intracerebral Haemorrhage (PICH) were the most costly, at approximately €5,300 on average. In contrast, patients with a lacunar stroke were the least costly, at approximately €2,300 on average. Overall, the highest costs are associated with stroke patients who died in hospital as compared to survivors with similar length of stay. Independent predictors of cost included the stroke type, stroke severity on admission, type of admission ward and status on discharge.

Approximately half of all individuals who survive a stroke are disabled to some degree because of a persisting neurological impairment. The cost of treatment is expensive as it accounts for approximately 10% bed-day costs. Therefore, the rehabilitation process must either improve functional ability in patients or must reduce long-term cost. In this light, acute stroke unit care is more cost-effective than medical ward care when it reduces disability within a relatively short length of stay (Sheppard and Ko, 2009).

Conclusions

Stroke has a major impact on society and yet there is notable room for improvement even in countries with sophisticated health care systems. Its high incidence and frequency of prolonged survival requires a heavy investment in human and financial resources for provision of care. On the other hand, the rising hospital costs coupled with a growing elderly population limit the financial resources of the health care system, and therefore, a better analysis and development of the long-term care continuum is required.

Overall, stroke patients necessitate a higher acuity medical setting with specialised personnel providing complex diagnostic and treatment modalities. Although these services are expensive in the acute phase, the benefits ensuing from them lead to notable savings and improved patient outcomes during the rehabilitation phase. Therefore, stroke units and swift medical and nursing interventions not only save lives but can also improve the quality of life for stroke survivors.

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